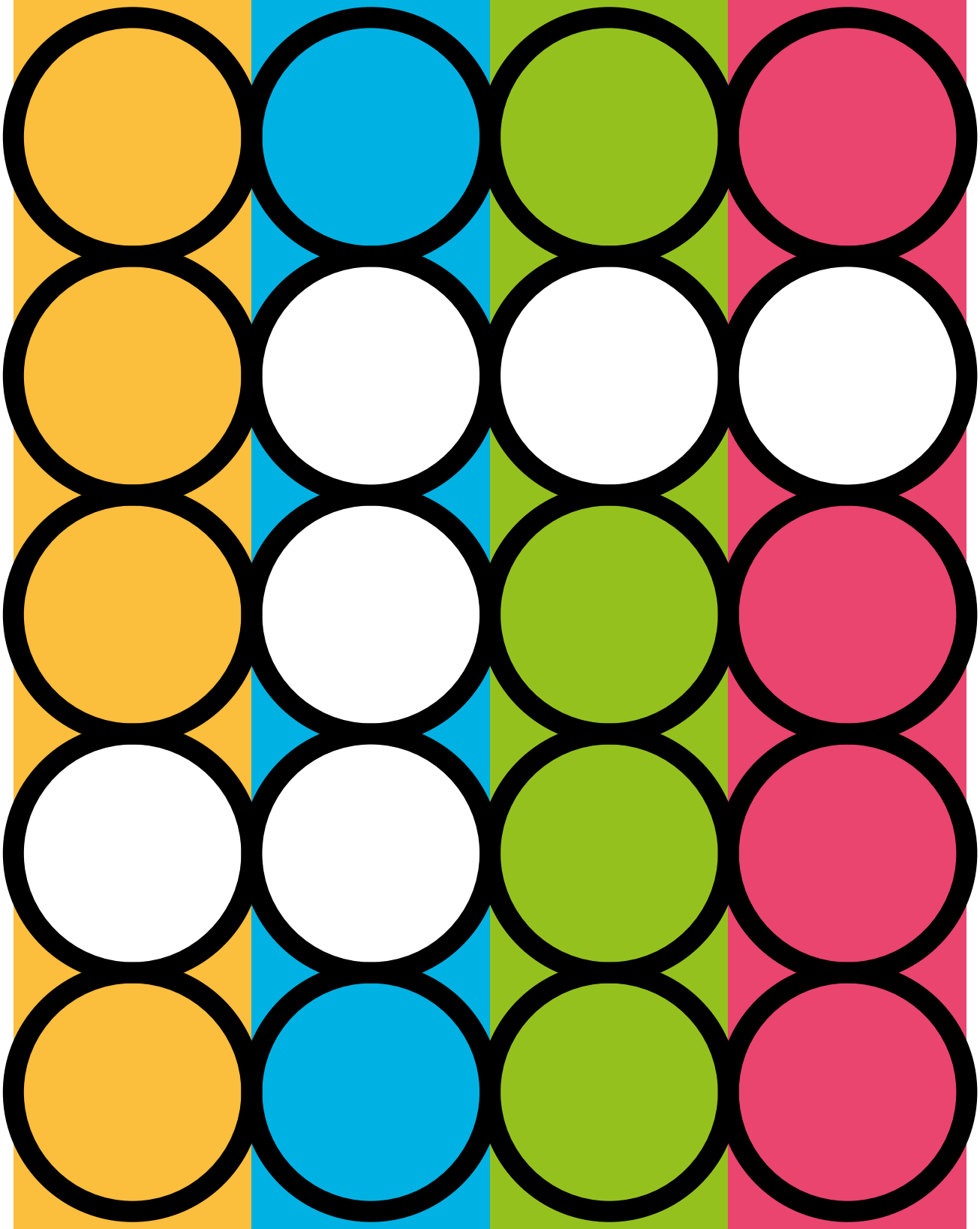
11th IMIBIC Young Investigators Meeting

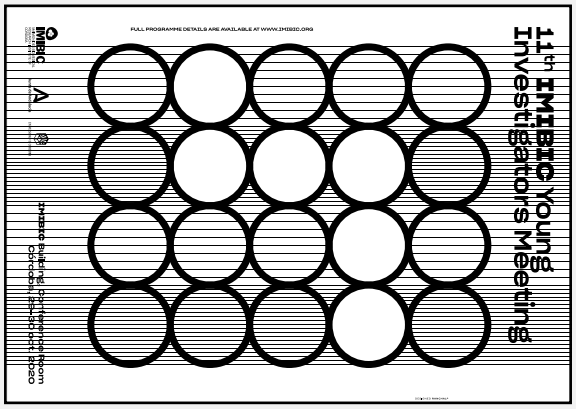


IMIBIC
MAIMONIDES BIOMEDICAL RESEARCH INSTITUTE OF CORDOBA

Junta de Andalucía

UNIVERSIDAD D CÓRDOBA

BOOK OF ABSTRACTS



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11th IMIBIC Young Investigators Meeting

IMIBIC Building,
Conference Room

Córdoba,
29-30 oct. 2020

BOOK OF ABSTRACTS

IMIBIC
MAIMONIDES BIOMEDICAL RESEARCH INSTITUTE OF CORDOBA

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UNIVERSIDAD D CÓRDOBA

INDEX

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Acknowledgements

We thank the External Reviewers and the members of the Scientific Committee for their kind collaboration. We greatly acknowledge the Colegio Oficial de Médicos de Córdoba for its support and commitment to promote research among residents.

PROGRAMME

Day 1 (29th OCT)

08:40 - 09:00
Opening ceremony

09:00 - 10:30
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→ Ia. 09:00 - 09:15
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→ Ib. 09:15 - 09:30
Dysregulation of the splicing factor SF3B1 in pancreatic ductal adenocarcinoma empowers Pladienolide-B as a therapeutic tool. ***Emilia Alors-Perez.***
→ Ic. 09:30 - 09:45
From the classical Ronnett classification to the new PSOGI classification for pseudomyxoma peritonei in a reference centre. ***Blanca Rufián Andújar.***
→ Id. 09:45 - 10:00
Clearance of circulating tumor cells in patients with hepatocellular carcinoma undergoing surgical resection or liver transplantation. ***Javier Manuel Zamora Olaya.***
→ Ie. 10:00 - 10:15
Somatostatin/somatostatin receptor system in rare neuroendocrine tumors: pheochromocytomas and paragangliomas. ***Alejandro Ibáñez-Costa.***
→ If. 10:15 - 10:30
Quantitative proteomic analysis reveals a key role of splicing machinery in hepatocellular carcinoma. ***Natalia Hermán Sánchez.***

10:30 - 11:00
Break

11:00 - 12:30
SESSION II. Nutrition and fragility
Chairs: ***Dr. Lourdes Ladehesa*** *&* ***Dr. Silvia Guil***

→ IIa. 11:00 - 11:15
3D fibrosis model: Composition, distribution, and link with adipose tissue dysfunction. ***Carmen Tercero Alcázar.***
→ IIb. 11:15 - 11:30
Influence of obesity in the miRNome: miR-4454, a key regulator of insulin response via splicing modulation in prostate. ***Vicente Herrero Aguayo.***
→ IIc 11:30 - 11:45
Novel role of hypothalamic endoplasmic reticulum stress in obesity-induced precocious puberty. ***Elvira Rodríguez Vázquez.***
→ IId 11:45 - 12:00
Clinical, cellular, and molecular evidence of the additive antitumor effects of biguanides and statins combination in prostate cancer. ***Antonio Jesús Montero Hidalgo.***

→ IIe 12:00 - 12:15
miR-223-3p as circulating biomarker and player for adipose tissue dysfunction related to type 2 diabetes onset. ***Julia Sánchez Ceinos.***
→ IIf 12:15 - 12:30
Lyophilization as pre-processing for sample storage in the determination of vitamin D3 and metabolites in serum and plasma. ***Laura de los Santos Castillo Peinado.***

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SESSION III. Cancer II
Chairs: ***Dr. Elena Mateos & Dr. Nuria Barbarroja***

→ IIIa. 12:30 - 12:45
Characterization of a new signalling pathway regulating the tumour suppressor FBXW7 in cancer. ***Alejandro Correa Sáez.***
→ IIIb. 12:45 - 13:00
Dysregulation of the splicing machinery as a target for Pancreatic Ductal Adenocarcinoma. ***Ricardo Blázquez Encinas-Rey.***
→ IIIc. 13:00 - 13:15
The splicing factor PRPF8 is overexpressed and increases aggressiveness and malignancy in hepatocellular carcinoma. ***Juan Luis López Cánovas.***
→ IIId. 13:15 - 13:30
Nitric oxide and metabolic reprogramming in colorectal cancer. ***Rafael Mena Osuna.***
→ IIIe. 13:30 - 13:45
Characterization and pathophysiological role of exosome component DIS3 in human high-grade astrocytomas. ***Jesús Miguel Pérez Gómez.***
→ IIIf. 13:45 - 14:00
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14:00 - 16:00
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16:00 - 17:30
SESSION. Oral Poster
Chairs: ***Dr. Antonio Romero & Dr. Juan Moreno***

→ SPa. 16:00 - 16:10
A diet-dependent microbiota profile associated with incident type 2 diabetes: from the CORDIOPREV study. ***Cristina Vals Delgado.***
→ SPb. 16:10 - 16:20
DYRK2 novel regulation mechanism determine its activity via cis-autophosphorylation compromising cell cycle, DNA damage response pathway and carcinogenesis. ***Rafael Manuel Jiménez Izquierdo.***
→ SPc. 16:20 - 16:30
Evaluation of the cardiovascular risk of a Spanish population in secondary prevention and its comparison with other populations. ***Marta Millán Orge.***
→ SPd. 16:30 - 16:40
Impact of distinctive autoimmune and molecular signatures of childhood- and adult-onset systemic lupus erythematosus patients in the development of lupus nephropathy and cardiovascular disease. ***Alejandra María Patiño Trives.***

→ SPe. 16:40 - 16:50
Sexual dimorphism of mitochondrial complexes, autophagy markers and nutritional sensors in skeletal muscle and liver for transgenic mice overexpressing NADH-cytochrome b5 reductase-3. ***Luz Marina Sánchez Mendoza.***
→ SPf. 16:50 - 17:00
Protist enteroparasite in wild boar (Sus scrofa ferus) and Iberian pig (Sus scrofa domesticus) in Southern Spain: A protective effect on Hepatitis E acquisition? ***Pedro López López.***
→ SPg. 17:00 - 17:10
Sexual dysfunction, self-esteem and risk of depression in the postpartum period. ***Andrea Jiménez Ruiz.***
→ SPh. 17:10 - 17:20
The effect of dietary magnesium supplementation on the endothelial dysfunction in a model of metabolic syndrome andchronic kidney disease. ***Rodrigo López Baltanás.***
SPi. 17:20 - 17:30
n-3 Polyunsaturated fatty acids enhance coenzyme Q biosynthesis. ***Sandra Rodríguez López.***

*** Note: REGULAR POSTERS will be available at Imibox during the celebration of the Meeting.**

Day 2 (30th OCT)

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SESSION IV. Cancer III
Chairs: ***Dr. Irene Gracia & Dr. Antonio Camargo***
→ IVa. 09:00 - 09:15
Circulating cell-free DNA-based liquid biopsy markers for the non-invasive prognosis and monitoring of metastatic pancreatic cancer. ***Marta Toledano Fonseca.***
→ IVb. 09:15 - 09:30
New insights in the pathological association between prostate cancer and obesity: miR-107 as a novel personalized diagnostic and therapeutic tool. ***Prudencio Sáez Martínez.***
→ IVc. 09:30 - 09:45
Molecular characterization of Pseudomyxoma Peritonei and development of biomarkers and target therapies in a mouse model with human xenograft. ***Francisca Valenzuela Molina.***
→ IVd. 09:45 - 10:00
Splicing machinery dysregulation drives glioblastoma development and aggressiveness: oncogenic role of SRSF3. ***Antonio Carlos Fuentes-Fallos.***
→ IVe. 10:00 - 10:15
Incidence and prognostic impact of cancer after liver transplantation. ***Víctor Amado Torres.***
→ IVf. 10:15 - 10:30
Using autonomous AI to reduce the workload of breast cancer screening with breast tomosynthesis: a retrospective validation. ***Esperanza Elías Cabot.***

10:30 - 11:00
Break

11:00 - 12:30
SESSION V. Inflammatory and Infectious diseases
Chairs: ***Dr. Ana Gordon & Dr. André M. Sarmento***

→ Va. 11:00 - 11:15
Interplay among inflammation and metabolic alterations in Psoriatic Arthritis. Effects of a novel PDE4 inhibitor and conventional therapy on the metabolic components and cardiovascular risk: cross-sectional and longitudinal studies. ***Ivan Arias de la Rosa.***
→ Vb. 11:15 - 11:30
Betulinic acid hydroxamate activates the HIF pathway through post-transcriptional dephosphorylation of Prolyl Hydrolase 2. Implications in neuroprotection in Huntington Disease. ***María Eugenia Prados González.***
→ Vc. 11:30 - 11:45
Association between rectal colonization by Klebsiella pneumoniae carbapenemase-producing K. pneumoniae and mortality: a prospective, observational study. ***Ángela Cano Yuste.***
→ Vd. 11:45 - 12:00
Serum inflammatory molecules and microRNAs as potential biomarkers of early and established response to TNFi therapy in rheumatoid arthritis patients. ***María Luque Tévar.***
→ Ve. 12:00 - 12:15
Excimer Laser Coronary Atherectomy for Uncrossable Coronary Lesions. A multicenter registry. ***Rafael González Manzanares.***
→ Vf. 12:15 - 12:30
Zoo animals as potential sentinels for zoonotic flaviviruses monitoring. ***Javier Caballero Gómez.***

12:30 - 13:30
Plenary Lecture: "Computational and mathematical tools to solve biomedical problems". ***Dr. Luis María Escudero.*** Instituto de Biomedicina de Sevilla (IBIS)

13:30 - 14:00
Awards and Closing ceremony

Description of the review process for selecting oral/poster presentations

Authors submitted their works through the Young Investigator abstract submission website from June 9th to July 3th. During the submission process, each author selected a specific scientific category (among the five IMIBIC Scientific Programs) and a preferred type of presentation (oral or poster).

At the deadline, a total of 113 abstracts were received. On July 21th, the Organization Committee distributed all abstracts received among 8 external reviewers during a face to face meeting without any information of authors, affiliation, etc. All reviewers were selected based on their distinguished scientific background and solid experience in evaluating research projects. The full list of the external reviewers can be found at the beginning of this book. External reviewers evaluated abstracts from July 22th to September 14th, scoring the communications between 0 and 5. **It should be noted that the Organization Committee has not evaluated or scored any of the submitted abstracts.**

On September 15th, the Organization Committee held a new face to face meeting to distribute all abstracts evaluated into oral communications, oral posters or regular posters based on the score provided by the reviewers and the preference of selection of the participants (oral vs. poster). Thus, oral communications were divided in 5 sessions (6 communications/each), while oral posters were included in 1 session (9 presentations were selected). Regular posters were decided to be available at Imibox. Considering the number of oral presentations submitted for each category, the Organization Committee decided to establish three sessions for Cancer, one session for Nutrition and fragility, and one session for Inflammatory and Infectious diseases.

Description of the review process for award selection

In order to motivate and boost high-quality presentations, IMIBIC establishes awards to the best oral communication within each of the 5 sessions, and the best oral poster among the 9 highest scored poster abstracts according to the external reviewers. These awards will be selected based on the scores of the (i) Scientific Committee, which includes 1 senior clinical researcher and coordinator and 3 researchers (1 clinical and 2 translational), (ii) all the chairs of the oral communication sessions (12 researchers), and (iii) the external reviewers (8 researchers). The full list of members of the Scientific Committee, chairs and external reviewers can be found in this book. The Scientific Committee and Chairs will score every presentation from 0 to 5, taking into consideration the following criteria: (i) scientific quality of the work, (ii) presentation skills of the presenter, and (iii) capacity to answer the questions raised by both the audience and chairs. The final score for each presentation will consist of the average of the score obtained by the Scientific Committee and chairs, and also the score provided by the external reviewers. The five highest scored oral communications will compete for the Best Presentation Award of the Meeting. The best oral communication presented by a Resident Medical Intern will be also awarded by the “Colegio Oficial de Médicos de Córdoba. Presenters who were awarded in the last editions will be excluded of the process.

ORAL COMMUNICATIONS

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Abstracts

SESSION I. Cancer

Ia. A preclinical platform based on humanized mice for the development of personalized immunotherapeutic strategies in colorectal cancer

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Authors: Ana Mantrana 1, Silvia Guil-Luna 1,2, Rafael Mena 1, Rafael González-Fernández 3, Cesar Díaz 4, F. Javier Medina 4, Carlos Villar 5, Marta Toledano-Fonseca 1,2, Juan de la Haba-Rodríguez 1,2,5,6,7, Enrique Aranda 1,2,5,6,7 and Antonio Rodríguez-Ariza 1,2,5.
Affiliations: 1.- Maimónides Biomedical Research Institute of Córdoba (IMIBIC), Córdoba, Spain. 2.- Cancer Network Biomedical Research Center (CIBERONC), Madrid, Spain. 3.- Immunology Department, IMIBIC, Reina Sofia University Hospital, University of Córdoba, Córdoba, Spain. 4.- General Surgery and Digestive System Department, Reina Sofía University Hospital, Córdoba, Spain. 5.- Pathological Anatomy Department, Reina Sofía University Hospital, Córdoba, Spain. 6.- Medical Oncology Department, Reina Sofía University Hospital, Córdoba, Spain. 7.- Department of Medicine, Faculty of Medicine, University of Córdoba, Córdoba, Spain.
Scientific Program: Cancer.
Keywords: Anti-PD1, colorectal cancer, immunotherapy, PDX, T-cells.

Abstract: An important issue for the development and efficacy of immunotherapy in colorectal cancer (CRC) is the lack of adequate preclinical models, due to the substantial complexity and heterogeneity of this disease. In this regard, highly immunocompromised mice reconstituted with a human immune system and bearing human tumors represent a promising model for developing novel and more personalized cancer immunotherapies. Here, we describe the development of a preclinical platform of humanized CRC patient derived xenografts (PDXs) models to analyze the response to immune checkpoint (PD-1) blockade immunotherapy taking into account the consensus molecular subtypes of CRC (CMS1-CMS4). In particular, we focused on CMS1 subtype, characterized by a high microsatellite instability (MSI) status, and CMS4 subtype, which has a poor prognosis. Peripheral blood mononuclear cells (PBMCs) from healthy donors were isolated and injected intravenously or intraperitoneally in NSG-β2m mice engrafted with human CRC tumors molecularly classified. Survival and proliferation of human PBMCs were observed over time in the peripheral blood of mice, which resulted in 15-20% of human CD45+ cells after one month with prevalent population of human CD3+ T cells. Tumor volume decreased in those mice infused with human PBMCs compared with control mice and an inverse correlation was observed between the percentage of circulating hCD45+ and tumor volume. Moreover, anti-PD1 treatment delayed tumor progression of CMS1, but not CMS4 tumors, and this effect was associated with higher levels of CD8+ cells in peripheral blood,. However, injected human T cells were shown to effectively infiltrate grafted CMS4 tumors, reinforcing the notion of the immunosuppressive microenviroment that characterizes this poor prognosis subtype. Altogether, our results indicate that humanized CRC PDXs can mimic human response to immunotherapy and constitute a valuable platform for the development of personalized immunotherapeutic strategies, opening novel perspectives for the treatment of CRC. Funded by PI-0150-2017 and AECC (PRDC019003MANT_001).

Ib. Dysregulation of the splicing factor SF3B1 in pancreatic ductal adenocarcinoma empowers Pladienolide-B as a therapeutic tool

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Authors: Emilia Alors Pérez 1,2,3,4; Ricardo Blázquez-Encinas 1,2,3,4; Sonia Alcalá 5; Laura Martin-Hijano 5; Sergio Pedraza-Arévalo 1,2,3,4; Juan Manuel Jimenez-Vacas 1,2,3,4; Pablo Cabezas-Sainz 6; Laura Sanchez 6; Cristina Viyuela-Garcia 1,3,7; Álvaro Arjona-Sánchez 1,3,7; Juan M. Sánchez-Hidalgo 1,3,7; Marina E. Sánchez-Frías 1,8; Aldo Scarpa 9; Manuel D. Gahete 1,2,3,4; Alejandro Ibáñez-Costa 1,2,3,4; Bruno Jr Sainz 5; Raúl M. Luque 1,2,3,4; Justo P. Castaño 1,2,3,4.

Affiliations: 1.- Maimonides Institute of Biomedical Research of Cordoba (IMIBIC), 14004 Cordoba, Spain. 2.- Department of Cell Biology, Physiology and Immunology, University of Cordoba, 14004. 3.- Reina Sofia University Hospital (HURS), 14004 Cordoba, Spain. 4.- CIBER Physiopathology of Obesity and Nutrition (CIBERobn), 14004 Cordoba, Spain. 5.- Department of Biochemistry, Autonomous University of Madrid (UAM); Department of Cancer Biology, Institute of Biomedical Research "Alberto Sols" (IIBM), CSIC-UAM; Chronic Diseases and Cancer Area 3-Ramón y Cajal Institute of Medical Research (IRYCIS), Madrid, Spain. 6.- Department of Zoology, Genetics and Physical Anthropology, University of Santiago de Compostela, Lugo, Spain. 7.- Surgery Service, Reina Sofia University Hospital (HURS), 14004 Cordoba, Spain. 8.- Anatomical Pathology Service, Reina Sofia University Hospital (HURS), 14004 Cordoba, Spain. 9.- Department of Diagnostics and Public Health, Section of Pathology, University and Hospital Trust of Verona, Verona, Italy; ARC-Net Research Center, University and Hospital Trust of Verona, Verona, Italy.

Scientific Program: Cancer.

Keywords: PDAC, Splicing, SF3B1, Pladienolide-B, CSC.

Abstract: Pancreatic ductal adenocarcinoma (PDAC) is still one of the most lethal and aggressive cancers, due to its late diagnosis and poor response to treatment. Part of PDAC complexity arises from its diverse cellular composition, where distinct cell types, like cancer stem cells (CSC), can act as key drivers of tumor initiation and progression. In this context, recent evidence indicates that a common hallmark in cancer are splicing machinery alterations, which disrupt normal gene expression and spur the appearance of aberrant, oncogenic splice variants. One of the spliceosome components most frequently altered in cancer is SF3B1. Interestingly, specific inhibitors can block SF3B1 selectively, thereby exerting antitumoral effects. We aimed to evaluate the role of SF3B1 as a potential target in tumoral/stem PDAC cells, which could contribute to understand the development and/or progression of PDAC. To achieve this goal, we analyzed SF3B1 (mRNA and protein) in a cohort of FFPE PDAC vs. adjacent non-tumoral tissues, public databases, PDAC and normal pancreatic cell lines, as well as PDX-derived CSCs cell lines. In addition, the effect of Pladienolide-B treatment on different functional endpoints in tumoral and CSCs cells was evaluated and corroborated by in vivo models as Zebrafish and xenograft mice. Results revealed a higher expression of SF3B1 in the different tumor models studied. Moreover, Pladienolide-B treatment markedly decreased key tumor-related functional parameters, including cell proliferation of PDAC cell lines in vitro and xenograft tumor growth in vivo. Furthermore, Pladienolide-B reduced CSCs stemness capacity, lending CSCs more sensitive to chemotherapy treatment, which reinforces its putative potential as a therapeutic target in PDAC. Altogether, these findings suggest that SF3B1 is profoundly altered in PDAC, and its blockade by Pladienolide-B in tumoral cells and CSCs exerts clear antitumoral effects, thus paving the way to explore its value as a novel therapeutic target for this dismal pathology.

Fundings: JdA (BIO-0139), MINECO (BFU2016-80360-R), ISCIII (PI16-00264), and CIBERobn.

Ic. From the classical Ronnett classification to the new PSOGI classification for pseudomyxoma peritonei in a reference centre

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Authors: Rufián Andújar Blanca 1,2; Valenzuela Molina Francisca 1,2; Durán Martínez Manuel 1,2; Rufián Peña Sebastián 1,2; Casado Adam Ángela 1,2; Sánchez Hidalgo Juan M 1,2; Rodríguez Ortiz Lidia 1,2; Martínez Ana 3; Ortega Salas Rosa 3; Romero-Ruiz Antonio 1,2; Arjona Sánchez Álvaro 1,2.
Affiliations: 1.- Maimonides Biomedical Research Institute of Cordoba (IMIBIC). Spain. 2.- General Surgery Unit - Reina Sofia University Hospital. Spain. 3.- Pathology Unit. Reina Sofia University Hospital. Spain.
Scientific Program: Cancer.
Keywords: Pseudomyxoma peritonei, hyperthermic intraperitoneal chemotherapy, peritonectomy.

Abstract: Background. Pseudomyxoma Peritonei (PMP) is a rare malignant disease defined by the progressive accumulation of mucinous tumor tissue in the peritoneal cavity. The most used histological classification of PMP based on the peritoneal disease has been Ronnett classification, dividing it into three categories: disseminated peritoneal adenomucinosis (DPAM), peritoneal mucinous carcinomatosis (PMCA) and an intermediate grade (PMCA-I). Recently a new classification from PSOGI consensus has been established: low-grade PMP, high-grade PMP and PMP with signet ring cells. The purpose of our study was to evaluate the prognostic factors of survival of patients with PMP and to compare the predictive power of survival of the Ronnett classification against the new one proposed by PSOGI.
Methods. We selected 117 patients with PMP treated by cytoreductive surgery and HIPEC at the Hospital University Reina Sofía. Survival curves were calculated using the Kaplan-Meier method and log-rank test to analyze the effect of clinical and pathological factors on overall survival (OS) and disease-free survival (DFS). Proportional Cox models and time-dependent curves ROC analysis were used to assess the predictive capacity for OS and DFS of both classifications adjusted by the degree of cytoreduction (CC score).
Results. Statistically significant differences on 5-year OS rate were evidenced between the different histological grades according to PSOGI (p = 0.05) and Ronnett (p = 0.01) classifications, as well as based on the CC score (p = 0.006). The predictive capacity according to the time-dependent ROC curves in time “100” for OS and DFS is optimal for both classifications adjusted by CC score, showing an AUC around 69% for OS and 62% for DFS in both cases.
Conclusions. Both PSOGI and Ronnett classifications show
significant differences in 5-year OS rate, as well as CC score achieved in surgery. Both classifications adjusted by CC score show optimal predictive capacity in 5-year OS and DFS rates.
Sources of Research Support: *National Institute of Health Carlos III (ISCIII). Reference: PI19/01603. *Nº EudraCT: 2015-001801-15 / NCT02614534. Evaluated and Accepted by Regional Ministry of Equality, Health and Social Policies (CISPS) and funded by FIBICO. Reference: PI-0424-2018.

Id. Clearance of circulating tumor cells in patients with hepatocellular carcinoma undergoing surgical resection or liver transplantation

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Authors: Javier Manuel Zamora Olaya, V. Amado, R. Alejandre, G. Ferrín, S. González Rubio, R. Fernández González, M. Sánchez Frías, R. Ciria, M. D. Ayllón, I. Gómez Luque, J. Briceño, P. Barrera Baena, A. Poyato González, M. De la Mata, M. Rodríguez-Perálvarez.
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Scientific Program: Cancer.
Keywords: Circulating tumor cells, hepatocellular carcinoma, liver transplantation.

Abstract: Background: The persistence of circulating tumor cells (CTCs) in patients with hepatocellular carcinoma (HCC) after resection or liver transplantation (LT) could be explored as a possible mechanism of tumor recurrence.
Methods: Prospective study including HCC patients undergoing surgical resection or LT (September/2017-May/2019). Enumeration of CTCs in peripheral blood samples (7 ml) was performed using Isoflux system (Fluxion biosciences) immediately before surgery, at post-operative day 5 and at post-operative day 30. An amount of >30 CTCs was considered clinically relevant.
Results: 35 patients were included (mean age 56.6±16 years, 77.8% men). Surgical resection was performed in 12 patients (34.3%) and 23 patients underwent LT (65.7%). The main aetiology of liver disease was chronic hepatitis C (63.9%), followed by alcohol (50%). In the surgical pathology, multinodular disease was observed in 34.3% (largest nodule 2.8±1.9 cm). Incomplete clearance of CTCs on the postoperative day 30 occurred in 15 patients (41.7%). CTCs persistence was more frequent in patients undergoing liver resection (58.3%) vs LT (34.8%). The elimination of CTCs was not influenced by sex, aetiology of liver disease, or tumor pathology. In patients undergoing LT with baseline alpha-fetoprotein >100 ng/mL, incomplete clearance of CTCs was observed in all cases (p=0.049), in contrast to resected patients (33.3%). The enumeration of CTCs before the procedure was associated with their incomplete elimination one month later (p=0.039).
Conclusion: The incomplete clearance of CTCs in patients with hepatocellular carcinoma undergoing resection or LT is a frequent finding. Longer follow-up is needed in order to determine its association with tumor recurrence.

Ie. Somatostatin/somatostatin receptor system in rare neuroendocrine tumors: pheochromocytomas and paragangliomas

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Authors: Alejandro Ibáñez-Costa 1,2,3,4, Antonio C. Fuentes-Fayos 1,2,3,4, Emilia Alors-Pérez 1,2,3,4, Ricardo Blázquez-Encinas 1,2,3,4, Aura D. Herrera-Martínez 1,5, Esther Rivero-Cortés 1,2,3,4, M.ª Ángeles Gálvez-Moreno 1,5, Anne Barlier 6, Mercedes Robledo 7, Raúl M. Luque1,2,3,4, Justo P. Castaño 1,2,3,4.
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Scientific Program: Cancer.
Keywords: Somatostatin; ghrelin; pheochromocytoma; paraganglioma; neuroendocrine tumors.

Abstract: Pheochromocytomas (PCC) and paragangliomas (PGL) are rare neuroendocrine tumors derived from chromaffin cells of the adrenal medulla and from neural crest progenitors of extra-adrenal paraganglia, respectively. These tumors often overproduce catecholamines causing hypertension and severe acute cardiovascular complications. Most of them are benign, however a subset may present distant metastasis. About 40% are caused by autosomal inherited syndromes. The correct diagnosis requires serologic evaluation of catecholamines and nuclear medicine techniques. Treatments of these rare neuroendocrine tumors comprise surgery, metabolic or conventional radiotherapy, embolization, and chemotherapy. Identification on novel biomarkers of diagnosis, progression or response would help to avoid unnecessary tests and may facilitate personalized medicine approaches. Somatostatin, cortistatin, and their receptors (SST1-5) regulate multiple cell functions, from hormone secretion to proliferation and are used as biomarkers, diagnostic tools or therapeutic targets in various endocrine-related tumors. In contrast, there is still no consensus on the clinical value of somatostatin analogues (SSA) or somatostatin receptor-based theranostics in PCC and PGL. Accordingly, we analyzed here the somatostatin/cortistatin/SST1-5 system in fresh tissue derived from three cohorts (Marseille, Madrid, and Córdoba) comprising 67 PCC and 28 PGL, as well as in silico in an online database of 144 PCC and 29 PGL (TCGA). We found a characteristic receptor profile, where SST2 and SST1 are predominantly expressed, being the levels of both receptors different between PCC and PGL. CORT levels are higher in PGL than PCC in all cohorts. Intriguingly, higher SST2 levels were associated to metastatic disease and aggressive behavior (extensive invasion, local regional disease, and local recurrence) in the TCGA cohort. Finally, in vitro studies on primary cell cultures from PCC and PGL, revealed that these cells are responsive to somatostatin and SST2-preferred SSA. Altogether, these results support the potential value of using SST-based therapies and tools on these rare neuroendocrine tumors.
Fundings: JdA (BIO-0139), MINECO (BFU2016-80360-R), ISCIII (PI16-00264), and CIBERobn.

If. Quantitative proteomic analysis reveals a key role of splicing machinery in hepatocellular carcinoma

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Scientific Program: Cancer.
Keywords: Hepatocellular carcinoma; proteomics; SWATH; splicing; RBM3; TCERG1.

Abstract: Hepatocellular carcinoma (HCC) is the sixth cancer type in incidence and the fourth in mortality but the molecular events underlying its development and progression are still to be fully elucidated. Since proteomic approaches represent unbiased, high throughput methods to detect tumour-specific alterations with clinical application, we performed herein the first quantitative proteomic analysis in an ample, representative and well-characterized cohort of HCC samples/patients. Thus, the nuclear and cytosolic protein composition from hepatic tissues of a cohort of HCC patients (n=43; tumor vs. non-tumor adjacent tissues) was determined by SWATH-MS and the results analysed by IPAR to perform pathways and regulators enrichment and activation analysis. Elements of the most relevant pathways were selected to validate their dysregulation in other HCC cohorts and to evaluate their diagnostic potential and their relationship with progression. In vitro proliferation assays after silencing specific targets were performed in three HCC cell-lines (HepG2, Hep3b and SNU-387). The proteomic analysis identified cytosolic (n=507) and nuclear (n=925) tumour-dysregulated proteins, which were mostly related to cellular metabolism, immune response and cancer-related cellular functions, as well as dysregulated upstream regulators such as FXR and C/EBP. Remarkably, mRNA splicing appeared strongly dysregulated and the alteration of 15 key components of the splicing machinery was confirmed in several retrospective and in silico HCC cohorts. Among them, PTBP1, RBM3 and TCERG1 showed a high diagnostic potential, individually or in combination with others, were related to aggressiveness parameters and invasive capacity, and/or their silencing (using specific siRNAs) decreased the proliferation of HCC-derived cell lines. Therefore, this study provides novel insights into the molecular alterations underlying HCC development and progression, demonstrating the alteration of key cellular processes, including splicing. Indeed, key splicing factors such as PTBP1, RBM3 and TCERG1 may represent novel diagnostic biomarkers or potential therapeutic targets in HCC.
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SESSION II. Nutrition and Fragility

IIa. 3D fibrosis model: Composition, distribution, and link with adipose tissue dysfunction

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Scientific Program: Nutrition and Fraility.
Keywords: Extracellular matrix, proteoglycans, fibrosis, adipose tissue, obesity.

Abstract: Fibrosis, commonly attributed to excessive deposition of collagen, is a newly appreciated hallmark of the pathological expansion of adipose tissue in obesity. Adipose tissue extracellular matrix remodelling plays a pivotal role in adipocyte renewal and tissue architecture and is crucial to accommodate obesity-induced cellular changes. Along with collagen I, other collagens and additional proteins have been proposed to contribute to tissue fibrosis. Herein, we aimed at characterizing the impact of the obesogenic extracellular milieu on adipocyte physiology by using three-dimensional (3D) culture systems mimicking the human obese adipose tissue. To this end, 3T3-L1 adipocytes were cultured in collagen-I matrices, in the presence of other extracellular matrix components, lumican and/or collagen VI, that are dysregulated in obese individuals with insulin-resistance. Scanning electron microscopy and physical tests were employed for ultrastructural characterization of the collagen matrices, and adipocyte differentiation was evaluated by lipid droplet staining (Nile Red) and expression analysis of adipogenesis and cell stress markers. A phosphoproteomic approach was used to characterize mechanotransduction and signalling pathways. Results show that adipocytes grown in obesogenic 3D matrices containing lumican exhibit impaired adipogenesis and reduced glucolytic activity, as measured by aldolase analysis. In contrast, adipogenesis and aldolase activity were increased in the presence of collagen-VI. . Insulin signalling in adipocytes was modified in the presence of lumican and/or collagen-VI. Finally, our phopshoproteomic analysis evidenced differences in mechanotransduction pathways affecting the nuclear envelope protein, lamin, in lumican and collagen-VI-containing matrices. Our observations suggest that obesity-associated changes in the extracellular proteins, lumican and collagen-VI, evoke differential responses in extracellular matrix remodelling that likely contribute to adipose tissue (dys)function and the development of metabolic disease in obesity.
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IIb. Influence of obesity in the miRNome: miR-4454, a key regulator of insulin response via splicing modulation in prostate

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Scientific Program: Nutrition and Fragility.
Keywords: miRNA; obesity; insulin-resistance; insulin receptor; splicing.

Abstract: Obesity is a major health problem associated with severe comorbidities, including type-2 diabetes and cancer, wherein microRNAs might be useful as diagnostic/prognostic tools or therapeutic targets. We aimed to explore the differential expression pattern of microRNAs in obesity and their putative role in obesity-related comorbidities such as insulin resistance. To that end, an Affymetrix-miRNA array was performed in plasma samples from normoweight (n=4/BMI<25) and obese subjects (n=4/BMI>30). The main changes were validated in two independent cohorts (n=221/n=18). Additionally, in silico approaches were performed and in vitro assays applied in tissue samples and prostate (RWPE-1) and liver (HepG2) cell-lines. Our results revealed that 26 microRNAs were altered (p<0.01) in plasma of obese subjects compared to controls using the Affymetrix-miRNA array. Validation in ampler cohorts revealed that miR-4454 levels were consistently higher in obesity, associated with insulin-resistance (HOMA-IR, insulin) and modulated by medical (metformin/statins) and surgical (bariatric surgery) strategies. miR-4454 was highly expressed in prostate and liver tissues and its expression was increased in prostate and liver cells by insulin. In vitro, overexpression of miR-4454 in prostate cells resulted in decreased expression levels of INSR, GLUT4, and phosphorylation of AMPK and AKT, as well as in altered expression of key spliceosome components (ESRP1/ESRP2/RBM45/RNU2) and insulin-receptor splicing variants. Altogether, our data demonstrated that obesity was associated to an alteration of the plasmatic miRNA landscape, wherein miR-4454 levels were higher, associated with insulin-resistance and modulated by obesity-controlling interventions. Insulin regulated miR-4454, which, in turn may impair the cellular response to insulin, in a cell type-dependent manner (i.e. prostate gland), by modulating the splicing process.
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IIc. Novel role of hypothalamic endoplasmic reticulum stress in obesity-induced precocious puberty

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Scientific Program: Nutrition and Fragility.
Keywords: Puberty, Endoplasmic Reticulum (ER) stress, obesity.

Abstract: Mounting evidence suggests a link between the rising prevalence of childhood obesity and precocious puberty; a phenomenon that has been associated with higher disease burden later on life. While it has been proposed that perturbations of hypothalamic signaling pathways might contribute to such a phenomenon, the targets and underlying mechanisms remain unknown.
Recent data support that hypothalamic alterations in endoplasmic reticulum (ER) homeostasis, known as ER stress, are implicated in the pathophysiology of obesity. However, its potential contribution to obesity-induced precocious puberty has not been addressed so far.
Here, we explore whether hypothalamic ER stress is involved in the timing of puberty and might contribute to obesity-induced precocious puberty. To this end, we evaluated (1) the expression of ER stress markers in the hypothalamus of early overfed female rats with precocious puberty; and (2) the impact of the pharmacological manipulation of central ER stress on pubertal development in both lean and early overfed female rats.
Early overfed rats with precocious puberty showed alterations in the hypothalamic expression of relevant ER stress markers, involving increased levels of the phosphorylated forms of protein kinase R-like endoplasmic reticulum kinase (pPERK) and the eukaryotic initiation factor 2 (peIF2β, and reduced content of activating transcription factor 6 (ATF6β. Furthermore, chronic stimulation of central ER stress with thapsigargin, a well-known ER stress inducer, resulted in precocious puberty onset in lean female rats, as evidenced by earlier vaginal opening and first ovulation, without affecting body weight or food intake. In contrast, central blockade of ER stress with tauroursodeoxycholic acid (TUDCA), a potent ER stress inhibitor, partially normalized the timing of puberty in early overfed female rats.
Overall, our data document a novel role of hypothalamic ER stress in the control of puberty onset; a phenomenon that likely contributes to obesity-induced precocious puberty.

IId. Clinical, cellular, and molecular evidence of the additive antitumor effects of biguanides and statins combination in prostate cancer

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Scientific Program: Nutrition and Fragility.

Keywords: Metformin, statins, prostate cancer, therapy, androgen receptor, mTOR, cell-cycle inhibitors.

Abstract: Prostate cancer (PCa) is one of the leading causes of cancer-related death among male population worldwide. Unfortunately, current medical treatments fail to prevent PCa progression in a high percentage of cases; therefore, new therapeutic tools to tackle PCa are urgently needed. In this sense, biguanides and statins have emerged as antitumor agents for several endocrine-related cancers. Therefore, we aimed to evaluate the direct effects of different biguanides (metformin, buformin, phenformin), statins (atorvastatin, simvastatin, lovastatin), and their combination, on key functional endpoints and associated molecular events and signaling mechanisms in normal and tumor prostate cells [normal (RWPE-1-cells/primary prostate cell-cultures); tumor (LNCaP/22Rv1/PC-3/DU145 cell-lines)]. We found that biguanides and statins exerted strong antitumor actions (i.e. inhibition of proliferation, migration, and tumorspheres-formation) on PCa cells, and that their combination further decreased, additively, these functional parameters compared with the individual treatments. These actions were mediated through modulation of key oncogenic signaling-pathways (i.e. AR/mTOR/AMPK/AKT/ERK) and molecular mediators (MKI67/cMYC/androgen-receptor/cell-cycle inhibitors). Interestingly, retrospective analysis of a cohort of patients with or without PCa, treated or not with metformin and/or statins (n=75) revealed that the combination of metformin+statins was associated to lower Gleason-score and longer biochemical recurrence-free survival. Altogether, our results reveal that biguanides and statins significantly reduced tumor aggressiveness in PCa, being this effect more potent (in vitro and in vivo) when both compounds are combined. Therefore, given the demonstrated clinical safety of biguanides and statins, our results suggest a potential therapeutic role of these compounds, especially their combination, for the treatment of PCa.

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IIe. miR-223-3p as circulating biomarker and player for adipose tissue dysfunction related to type 2 diabetes onset

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Scientific Program: Nutrition and Fragility.
Keywords: Adipose tissue, adipocyte, circulating microRNAs, inflammation, miR-223-3p, type 2 diabetes.

Abstract: Circulating microRNAs (miRNAs) have been proposed as biomarkers for type 2 diabetes (T2D). Adipose tissue (AT), whose dysfunction is widely associated with T2D development, has also been reported as a major source of circulating miRNAs. However, the role of dysfunctional AT in the altered pattern of circulating miRNAs associated with T2D onset remains unexplored. Here, we investigated the relationship between previously known T2D-associated circulating miRNAs and AT/adipocyte function. 462 non-diabetic patients at baseline from the CORDIOPREV study were included and classified according to T2D development or not during the median follow-up of 60 months (incident-T2D vs. non-T2D patients). Baseline plasma levels of miRNAs related to the development of T2D and AT insulin resistance index (ATIRI) was measured. In vitro analyses with patients' sera and the candidate miRNA, miR-223-3p, were performed in 3T3-L1 adipocytes at different stages of differentiation. Among the plasma miRNAs related to T2D incidence in the CORDIOPREV-DIAB cohort at baseline, miR-223-3p levels (diminished in Incident-T2D) were negatively and significantly correlated with ATIRI. Exposure to baseline serum from incident-T2D participants induced inflammation and IR in 3T3-L1 adipocytes, suggesting that AT dysfunction may precede T2D development. TNFβ significantly decreased miR-223-3p secretion and enhanced its intracellular accumulation in adipocytes, likely by blocking exosome sorting and release. In line with our in-silico research of miR-223-3p potential targets, overexpression studies showed that intracellular increase of miR-223-3p impairs glucose metabolism (i.e. GLUT4 content and translocation to the plasma membrane, and glucose uptake upon insulin stimulation), lipid metabolism and storage capacity in adipose cells. Our findings provide mechanistic insights into the alteration of circulating miRNAs preceding T2D, suggesting that low circulating miR-223-3p may be related to AT dysfunction preceding T2D onset through inflammation-mediated down-regulation of miR-223-3p secretion by adipocytes. Concomitant intracellular accumulation of this miRNA would contribute to adipocyte dysfunction and whole-body metabolic dysregulation.

IIf. Lyophilization as pre-processing for sample storage in the determination of vitamin D3 and metabolites in serum and plasma

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Scientific Program: Nutrition and Fragility.
Keywords: Vitamin D3; 25-hydroxyvitamin D3; 1,25-dihydroxyvitamin D3; SPE-LC-MS/MS; lyophilization; long-term storage.

Abstract: Human low vitamin D levels have been related to several biological disorders, therefore interest of vitamin D determination in biological samples has increased over the past decades. Actually, vitamin D deficiency has turned into a health problem including all ages and genders around the world. From an analytical point of view, concerning biological matrices status conservation, storage is a relevant factor to be considered for determination of vitamin D and metabolites. The aim of this research was to evaluate lyophilization as a pre-processing step for serum and plasma storage prior to quantitation of vitamin D3 and its main hydroxylated metabolites –25(OH) D3, 24,25(OH)2D3 and 1,25(OH)2D3. The proposed protocol with prior lyophilization of samples was characterized in terms of analytical features and compared to the same method (SPE-LC-MS/MS), without lyophilization. Analytical characteristics were not affected by lyophilization of serum nor plasma and results from a set of twenty-four serum samples from DEQAS (Vitamin D External Quality Assessment Scheme) were in compliance with 25(OH)D3 and 1,25(OH)2D3 reference values. Metabolites stability was periodically assessed for 9 months and results demonstrated that concentration of target metabolites in lyophilized serum and plasma, stored at room temperature, was not significantly altered through this period of time. In conclusion, this research has demonstrated that the quantitation of target metabolites is not under the influence of lyophilization. Furthermore, lyophilization prior to analysis could reduce shipment and storage costs, avoid delays of sample processing, and increase the stability of the target analytes due to an effective quenching process.

SESSION III. Cancer II

IIIa. Characterization of a new signalling pathway regulating the tumour suppressor FBXW7 in cancer

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Scientific Program: Cancer II.
Keywords: FBXW7, DYRK2, ubiquitin ligase, kinase, DDR pathway and carcinogenesis.

Abstract: All biological processes in mammals are regulated by highly complex mechanisms where proteins play an essential function, amongst which the ubiquitination proteasome system (UPS) can be highlighted. The most widely studied component of the UPS to date due to its frequent alteration in human tumours is the ubiquitin ligase FBXW7. This relevant tumour suppressor is among the most mutated genes associated with cancer development, and almost all its substrates are relevant in the control of tumorigenesis, such as c-Myc, Cyclin E, Notch and c-Jun. All these data support the role of FBXW7 as a key candidate in the search of new regulatory mechanisms enabling new anticancer therapies.
In this work, we show for the first time a new relevant mechanism that regulates the expression and activity of FBXW7 mediated by DYRK2, a kinase with a central role in maintaining cellular homeostasis. Through different experimental approaches, we demonstrate how DYRK2 regulates FBXW7 expression at post-transcriptional level in a kinase activity-dependent manner via phosphorylation. Additionally, this reduction of FBXW7 expression is proteasome-mediated and is independent of FBXW7 ubiquitin ligase activity. We reveal the residues responsible for this event as well as the responsible regions through which the interaction between both proteins takes place. We prove how these events happen in an oncogenic stress response context, involving the DNA damage response pathway (DDR). Intriguingly, an enhanced degradation and a higher colocalization of these two proteins in the nucleus after exogenous DNA damage were observed. These data were verified modifying DYRK2 expression through the use of siRNAs and the generation of different DYRK2 -/- cell lines using CRISPR/Cas9 methodology. We show that DYRK2 regulation by chemotherapeutic agents has a relevant effect on gene expression and cellular development through FBXW7. In summary, we reveal a novel regulation mechanism for FBXW7 which might help us to better understand its role in cancer biology, with important consequences on cell-cycle control and DNA damage response pathway in cancer cells.

IIIb. Dysregulation of the splicing machinery as a target for Pancreatic Ductal Adenocarcinoma

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Scientific Program: Cancer II.

Abstract: Available upon request.

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IIIc. The splicing factor PRPF8 is overexpressed and increases aggressiveness and malignancy in hepatocellular carcinoma

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Scientific Program: Cancer II.

Keywords: Hepatocellular Carcinoma, Splicing, PRPF8, preclinical model.

Abstract: Most tumor pathologies, including hepatocellular-carcinoma (HCC), are associated with the expression of aberrant splice variants involved in tumor development and/or progression. A dysregulation of the machinery responsible for the splicing process (spliceosome and splicing factors) could be responsible for this alterations. In fact, the expression of PRPF8, an essential component of the spliceosome, is dysregulated in some tumors; however, the role of PRPF8 has not been described in HCC. Thus, we aimed to analyze the expression of PRPF8 in different HCC cohorts, and to characterize its putative role in tumor development/progression. Specifically, PRPF8 expression was analyzed in a retrospective cohort of patients with HCC (n=172: HCC vs. non-tumor tissues) and validated in two different in silico cohorts (TCGA and Proteomics-Zhou). PRPF8 was silenced (using specific siRNAs) to understand the functional and mechanistic consequences in HCC cell-lines (HepG2/Hep3B/SNU-387) and in xenograft-tumors (Hep3B). Moreover, RNAseq and Clipseq data were analyzed. This study shows that PRPF8 was overexpressed in HCC samples and associated with increased tumor aggressiveness (tumor size, patient survival, etc.) and with the expression of splicing variants involved in HCC. In vitro PRPF8 silencing reduced parameters related to tumor aggressiveness (proliferation, migration, tumorospheres and colonies formation) and increased apoptosis. Accordingly, in vivo PRPF8 silencing significantly reduced tumor size in the preclinical model. Finally, RNAseq data from PRPF8-silenced HepG2 and Clipseq in HepG2 suggested a role of PRPF8 on important cancer-pathways (cell cycle, apoptosis, etc.), by modulating the expression of key genes and important splicing variants (i.e. FN1). These results were validated in vitro in the HCC cell-lines used. In conclusion, PRPF8 is overexpressed and associated with aggressiveness in HCC, and exerts important role in tumorigenic pathways, suggesting a key role in modulating the development and/or progression of HCC.

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IIId. Nitric oxide and metabolic reprogramming in colorectal cancer

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Scientific Program: Cancer II.
Keywords: Colorectal cancer, mitochondria, metabolism, nitric oxide, S-nitrosylation.

Abstract: S-nitrosylation is a reversible nitric oxide (NO)-related post-translational modification, which regulates protein function equivalently to protein phosphorylation. Recent research has characterized enzyme-mediated processes regulating protein S-nitrosylation and denitrosylation. In this regard, S-nitrosoglutathione reductase (GSNOR) is a highly evolutionarily conserved denitrosylase enzyme, which is coded by human ADH5 gene. Previous studies in our group have shown that GSNOR inhibition in HER2 breast cancer increased protein S-nitrosylation and reduced the efficacy of anti-HER2 therapy, while low ADH5 gene expression was associated with poor survival in patients with HER2 tumors. Therefore, the main goal of this study was to analyze the significance of GSNOR in colorectal cancer (CRC).
Immunohistochemical and gene expression studies showed that low GSNOR/ADH5 expression was associated with worse prognosis and poor survival in CRC. Moreover, genetic ablation experiments using CRISPR-Cas9 technology confirmed that GSNOR deficiency in CRC cells increased their tumorigenic properties. Thus, compared to parental cells, ADH5-/- cells possessed greater ability to generate tumorospheres and organoids, and were more efficient in initiating tumors in immunosuppressed mice. Importantly, this higher tumorigenic capacity was not associated to a greater proliferative capacity but to metabolic disturbances, involving increased aerobic glycolytic activity and lactate production. It is known that fragmentation of the mitochondrial network occurs during cell dedifferentiation or malignant transformation, accompanied by increased aerobic glycolysis and lactate production. Significantly, our mitochondrial network analysis in CRC cells revealed that, compared to parental cells, ADH5-/- cells were characterized by a higher number of mitochondria per cell and a smaller mitochondrial diameter, which is compatible with a higher rate of mitochondrial fission.
In conclusion, our results support that metabolic reprogramming induced by GSNOR deficiency may constitute an important mechanism connecting the aberrant production of NO, the S-nitrosylation of proteins, and the acquisition of aggressive and invasive phenotypes in CRC.
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IIIe. Characterization and pathophysiological role of exosome component DIS3 in human high-grade astrocytomas

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Scientific Program: Cancer II.
Keywords: Exosome, glioblastoma, DIS3, RNA metabolism.

Abstract: Gliomas comprise the most frequent malignant tumor of the Central Nervous System. Astrocytomas are the main gliomas type graded from I to IV by their aggressiveness (WHO-classification), being grade-III/-IV considered as high-grade tumors. Grade IV-Astrocytoma, known as glioblastoma-multiforme (GBM) is the most frequent, malignant, and invasive subtype, been nowadays virtually incurable. Currently, the standard treatment of GBM consists of surgery followed by radiotherapy and/or chemotherapy, but the survival rate is still ~14 months after the first intervention. Thus, the identification of new diagnostic/prognostic-tools and therapeutic strategies for the management of high-grade astrocytomas (HGAs) are urgently needed. In this sense, the dysregulation of cellular/molecular machineries involved in RNA-homeostasis is a common feature of several tumors. Among these cellular machineries, the RNA-exosome, a multiprotein nuclease complex, is the most versatile RNA-degradation machine and the central effector of a major RNA-surveillance pathway in eukaryotes. Here, we aimed to determine whether the components of the RNA-exosome complex were altered in HGAs, and the potential functional role of this machinery in the development/progression of HGAs. A customized microfluidic-array was designed to determine the expression levels of the RNA-exosome components in human HGA (n=75) which revealed a significantly dysregulation of most these elements compared to healthy-control brain-tissues (n=21). Our data and in silico analysis highlight DIS3 enzyme (i.e. RNA-exosome component significantly overexpressed in several cohorts of HGA-samples) as the key candidate to be further explored. Silencing of DIS3 expression (using specific siRNA) in GBM cell-models (U-87/U-118MG cell-lines) significantly reduced key functional aggressiveness parameters (proliferation/migration/tumorspheres-formation) and altered the expression pattern of key tumor-associated genes. Altogether, these results demonstrate a drastic dysregulation in RNA-exosome components expression in HGAs and identified DIS3 as a key component strongly associated with malignant features, supporting its potential utility as therapeutic tool in this devastating pathology.
Fundings: Junta de Andalucía (CTS-1406/BIO-0139), MINECO/MECD (FPU16-05059/FPU18-06009/PID2019-105564RB-I00), ISCIII (PI16-00264/PI17-02287), CIBERobn.

IIIf. The first protein profile of Pseudomyxoma Peritonei: Ready for a molecular characterization by "omics" approaches

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Scientific Program: Cancer II.
Keywords: Pseudomyxoma peritonei, Molecular Characterization, protein profile, mass spectrometry.

Abstract: Pseudomyxoma peritonei (PMP) is a rare malignant growth characterized by the progressive accumulation of mucus-secreting (mucinous) tumour cells within the abdomen and pelvis. PMP is divided into two main subtypes, low and high grade. The most common cause of PMP is appendiceal mucinous neoplasm. As mucinous tumour cells accumulation, the abdominal cavity becomes swollen, and the digestive function becomes impaired with fatal outcome. In the last few years, reference centres have published a survival benefit after a macroscopic cytoreduction via peritonectomy and multi-visceral resection with microscopic chemical cytoreduction, using intraoperative hyperthermic intraperitoneal chemotherapy (HIPEC). Despite positive results, a considerable number of patients experience recurrence and a tumour progression with a fatal end. In addition, the treatment in case of recurrence after cytoreduction is unclear; the only available option is the use of secondary surgeries or the chemotherapy protocols applied in colorectal cancer, which have not shown positive evidence in PMP. In this context, it is urgent to find specific markers for this type of tumor as well as drugs capable of preventing its progression and/or recurrence. For this reason, the molecular characterization of this rare tumor will allow us to find targets for a personalized and effective treatment. However, the main obstacle to reaching this milestone is the formation of a mucus called mucin, which is composed by tumoral cells and glycoproteins, mainly MUC-2. To our knowledge, no one study has been published about the protein profile of PMP. We have developed a new protocol, based in mucin depletion using a liquid chromatography system followed by a mass spectrometry platform. This strategy has enabled us to get a library with more than 1500 different protein species. This new protein profile might be the starting point to carry out a differential expression analysis between control, low grade and high grade of PMP.
Sources of Research Support: *National Institute of Health Carlos III (ISCIII). Reference: PI19/01603.

SESSION IV. Cancer III

IVa. Circulating cell-free DNA-based liquid biopsy markers for the non-invasive prognosis and monitoring of metastatic pancreatic cancer

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Scientific Program: Cancer III.
Keywords: Cell-free DNA; liquid biopsy; MAF; pancreatic cancer; RAS mutation.

Abstract: Liquid biopsy may help in the management of cancer patients, and this is particularly relevant for pancreatic ductal adenocarcinoma (PDAC). In this study we investigated the utility of circulating cell-free DNA (cfDNA)-based markers as prognostic tools in metastatic PDAC. Plasma was obtained from 61 metastatic PDAC patients, and cfDNA levels and fragmentation were determined. BEAMing technique was used for quantitative determination of RAS mutation allele fraction (MAF) in cfDNA. We found that prognosis was more accurately predicted by RAS mutation detection in plasma than in tissue. RAS mutation status in plasma was a strong independent prognostic factor for both OS and PFS. Moreover, RAS MAF in cfDNA was also an independent risk factor for poor OS and was significantly associated with primary tumours in the body/tail of the pancreas and liver metastases. Higher cfDNA levels and fragmentation were also associated with poorer OS and shorter PFS, body/tail tumors, and hepatic metastases, whereas cfDNA fragmentation positively correlated with RAS MAF. Remarkably, the combination of CA19-9 with MAF, cfDNA levels and fragmentation improved the prognostic stratification of patients. Furthermore, dynamics of RAS MAF better correlated with patients' outcome than standard CA19-9 marker. In conclusion, our study supports cfDNA-based liquid biopsy markers as relevant clinical tools for the non-invasive prognosis and monitoring of metastatic PDAC patients.

IVb. New insights in the pathological association between prostate cancer and obesity: miR-107 as a novel personalized diagnostic and therapeutic tool

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Scientific Program: Cancer III.
Keywords: miRNome; miR-107; Prostate cancer; Obesity; Non-invasive biomarker; Therapeutic target.

Abstract: Prostate cancer (PCa) is one of the most common causes of cancer-related deaths in men worldwide. Therefore, more specific and non-invasive diagnostic biomarkers as well as novel therapeutic targets are urgently needed. As miRNAs have been proposed as promising elements for the identification of novel diagnostic and therapeutic tools for different pathologies, including cancer, we investigated the miRNA landscape in PCa and explored their putative diagnostic/therapeutic utility. Specifically, the miRNome of plasma samples from healthy (n=18) and PCa patients (n=19) was initially determined using an Affymetrix-miRNA array. The main changes were validated in two independent cohorts (n=296/n=84). Additionally, in silico and in vitro assays in cell-lines were performed. Results from the array revealed that the expression of 104 miRNAs was significantly altered ($p<0.01$) in plasma samples from PCa patients compared with healthy controls. Of note, 6 of these miRNAs also exhibited a significant ROC curve to distinguish between healthy and PCa patients (AUC=1). The validation using indipendent cohorts demonstrated that miR-107 was the most profoundly altered miRNA in PCa ($p<0.0001$) exhibiting AUC=0.75. Interestingly, miR-107 significantly overcome the ability of PSA to distinguish between control and PCa patients, as well as between non-significant (Gleason-Score=6) and significant (Gleason-Score≥7) PCa patients, being its expression correlated with relevant clinical parameters. All these comparisons were even stronger in those patients with BMI>30. In addition, miR-107 was also dysregulated in PCa-tissues (compared to non-tumor tissues) and in PCa cells (compared to non-tumor cells). Moreover, the in vitro overexpression of miR-107 significantly reduced cell proliferation, migration and tumorsphere formation in PCa-cells. Finally, in silico analysis revealed that miR-107 could interact with key gene target for PCa-agresiveness such as AKT2/CCNE1/HSP90AA1. Altogether, we concluded that miR-107 might represent a new diagnostic/therapeutic tool in PCa, especially in obesity conditions.
Fundings: ISCIII (PI16-00264/PI17-02287), MINECO (PID2019-105564RB-I00/FPU16-06190/FPU17-00263), Junta de Andalucía (BIO-0139) and CIBERobn.

IVc. Molecular characterization of Pseudomyxoma Peritonei and development of biomarkers and target therapies in a mouse model with human xenograft

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Scientific Program: Cancer III.
Keywords: Pseudomyxoma peritonei, xenograft mouse model, molecular characterization, target therapy.

Abstract: Background. Pseudomyxoma Peritonei (PMP) is a rare disease characterized by mucinous ascites and peritoneal implants. As an indolent neoplasm with nonspecific manifestations, PMP tends to be misdiagnosed or discovered in advanced stages that can lead to highly debilitating and even fatal complications. The low number of cases (less than 2 cases/million of people/year) makes it difficult to know the molecular mechanisms of genesis, proliferation and recurrence of the tumor. In that sense, the development of animal models to reproduce human PMP is mandatory. We present here the development of the first Low-Grade-PMP animal model replicating the PMP.
Methods. Human tumor tissue was obtained from patients with PMP during the cytoreductive surgery. Locally bred female BALB/c nude mice were used. The fresh tumor was cut into 3 X 3 mm and implanted intraperitoneally (i.p.). For the implantation a small midline laparotomy was performed, and six tumor pieces were placed in the peritoneal cavity in both upper and lower abdominal quadrants as well as in both flanks.
Results. We have developed a Low-Grade PMP tumor mouse line. The gene expression levels of three human tumoral biomarkers (Ki67, CK7 and CK20), were analyzed by qPCR in the tumor collected from the patient (HT) before and after being transplanted in the mouse (MT). Ovaries from mouse (MOs) were used as a negative control. In both cases, HT and MT, the tumor biomarkers Ki67, CK7, and CK20 were positive; likewise, MOs were negative for CK7, CK20 and Ki67, indicating that the MT is a human tumor.
Conclusions. The first Low-Grade-PMP animal model replicates human low-grade PMP. This advance might be essential to find specific biomarkers of this kind of tumor, as well as the development of new pharmacology treatments with the ability to stop the progression and/or the recurrence of this malignant disease.
Sources of Research Support: *National Institute of Health Carlos III (ISCIII). Reference: PI19/01603.

IVd. Splicing machinery dysregulation drives glioblastoma development and aggressiveness: oncogenic role of SRSF3

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Scientific Program: Cancer III.

Keywords: Glioblastoma; Spliceosome components; Splicing factors; SRSF3; PDGFRB pathway; Glioblastoma mouse models; Antitumor Therapy.

Abstract: Glioblastomas remain the deadliest brain tumor, with a dismal ~12-16-month survival from diagnosis. Therefore, identification of new diagnostic, prognostic and therapeutic tools to tackle Glioblastomas is urgently needed. Emerging evidence indicates that the cellular- machinery controlling the splicing process (spliceosome) is altered in tumors, leading to oncogenic splicing events associated with tumor progression and aggressiveness. Here, we identify for the first time a profound dysregulation in the expression of relevant spliceosome components and splicing factors (at mRNA and protein levels) in well-characterized cohorts of human high-grade astrocytomas, mostly Glioblastomas, compared to healthy-brain control samples, being SRSF3, RBM22, PTBP1 and RBM3 able to perfectly discriminate between tumors and control samples, and between proneural-like or mesenchymal-like tumors vs. control samples from different mouse models with gliomas. Results were confirmed in four additional and independent human cohorts. Silencing of SRSF3, RBM22, PTBP1 and RBM3 decreased aggressiveness parameters in vitro (e.g. proliferation, migration, tumorsphere-formation, etc.) and induced apoptosis, especially, SRSF3. Remarkably, SRSF3 was correlated with patient survival and relevant tumor markers, and its silencing in vivo drastically decreased tumor development and progression, likely through a molecular/cellular mechanism involving PDGFRB and associated oncogenic signaling-pathways (PI3K-AKT/ERK) which may also involve the distinct alteration of alternative splicing events of specific transcription factors controlling PDGFRB (i.e. TP73). Altogether, our results demonstrate a drastic splicing machinery-associated molecular dysregulation in Glioblastomas, which could be potentially considered as a source of novel diagnostic and prognostic biomarkers as well as therapeutic targets for Glioblastomas. Remarkably, SRSF3 is directly associated to Glioblastoma development, progression, aggressiveness and patient survival and represents a novel potential therapeutic target to tackle this devastating pathology.

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IVe. Incidence and prognostic impact of cancer after liver transplantation

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Scientific Program: Cancer III.
Keywords: Liver transplantation, immunosuppression, cancer, screening.

Abstract: Background & Aims: Cancer screening protocols after liver transplantation (LT) are lacking. We aimed to determine the incidence of cancer after LT and its clinical risk factors.
Methods: Observational multicenter study including a consecutive cohort of patients who underwent LT (2010-1015) in 10 Spanish institutions who survived longer than 1 year and received tacrolimus-based immunosuppression. Exclusion criteria: Age<18, combined organ transplantation, retransplantation and HIV+. The incidence of cancer and related mortality were evaluated by using Cox's regression. Standardized incidence rate (SIR) was calculated with general population data obtained from Globocan 2018 (available at https://gco.iarc.fr/).
Results: A total of 1,732 patients were included: mean age 54.4±9.6, 76.3% males, 49% alcoholic cirrhosis, 37.4% with hepatitis C. The indication for LT was hepatocellular carcinoma in 703 patients (40.6%). Median follow-up after LT was 64 months (IQR 48-86). Three hundred and thirty-two patients developed cancer: cumulative incidence=17% at 5 years; incidence rate=0.038 cases/person*years; SIR=3.19 (excluding hepatocellular carcinoma). The incidence of cancer remained unchanged during the inclusion period. The onset of cancer impacted negatively on post-LT survival: 64.1% vs 91.3% at 5 years. Letality of cancer was 46.4%, with a median life expectancy of 6 months (IQR 2-15). After controlling for baseline hepatocellular carcinoma, the independent risk factors of cancer were: Age>50 years (RR=2.49; p<0.001), active smoking (RR=1.44; p=0.002) and alcoholic cirrhosis (RR=1.42; p=0.003). The number of risk factors was associated with a progressive increase of cancer rates at 5 years: 5.1% in absence of risk factors, 12.5% with 1 risk factor, 20.7% with 2 risk factors and 25.1% with 3 risk factors (figure).

Conclusion: The incidence of cancer after LT is high and carries a dismal prognosis. A consensus is needed to delineate cancer screening strategies after LT, which should be tailored according to the history of smoking and alcoholism.

IVf. Using autonomous AI to reduce the workload of breast cancer screening with breast tomosynthesis: a retrospective validation

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Scientific Program: Cancer III.
Keywords: Tomosynthesis. Artificial intelligence. Digital mammography. Breast cancer screening.

Abstract: Purpose: To determine the impact of using an artificial intelligence (AI) system to autonomously read a large fraction of breast tomosynthesis (DBT) screening exams in terms of workload reduction, recall rate and sensitivity of screening.
Materials and Methods: A consecutive cohort of DBT screening exams (12470 examinations) was retrospectively collected from a previous trial study (Cordoba Tomosynthesis Trial) comparing DBT to digital mammography (DM). Each DBT screening exam was single read with access to the synthetic mammogram.
All the DBT exams were processed by an AI system (Transpara, ScreenPoint Medical), which categorizes them on a scale 1-10 representing the likelihood of containing visible cancer.
The hypothesis was that two groups of DBT exams could be created based on AI: exams with scores 1-7 (the least suspicious) would be excluded from human reading and automatically labeled as normal. Exams with scores 8-10 (more suspicious) would be single-read.
Sensitivity, recall rate and workload were compared between the original reading and the autonomous AI-based scenario using a McNemar test.
Results: During the original reading with DBT, 362 women were recalled (recall rate 2.90%) and 67 cancers were detected (sensitivity 77.0%). Using the autonomous AI-based scenarioz, 368 women would have been recalled (recall rate 2.95%, 95% CI = 2.66-3.26%, P=0.81), 69 cancers would have been detected (sensitivity 79.3%, 95% CI = 69.3-87.3%, P=0.62), and there would have been a workload reduction of 70.7% (only 3653/12470 screening DBT exams would have been read).
Conclusion: Using AI to autonomously label a large fraction of DBT screening exams as normal without the involvement of radiologists could reduce screening workload by 70%, with minimal impact in recall rate and sensitivity.

SESSION V. Inflammatory and Infectious diseases

Va. Interplay among inflammation and metabolic alterations in Psoriatic Arthritis. Effects of a novel PDE4 inhibitor and conventional therapy on the metabolic components and cardiovascular risk: cross-sectional and longitudinal studies

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Keywords: Psoriatic Arthritis, inflammation, metabolic alterations, insulin resistance.

Abstract: Objectives: 1) To explore the impact of Psoriatic Arthritis (PsA) in the development of metabolic alterations at both, clinical and molecular levels, 2) To analyze the in vivo effects of a PDE4 inhibitor (apremilast) and conventional therapy (methotrexate, MTX) in the metabolic components and cardiovascular risk in PsA patients and 3) To evaluate the in vitro effects of apremilast and MTX in endothelial cells and adipocytes treated with serum from PsA patients.
Methods: Cross-sectional study: One hundred PsA patients and 100 age and gender-matched healthy controls (HCs) were recruited. Prospective longitudinal study: 30 PsA patients: 10 patients treated with MTX, 10 patients treated with PDE4 inhibitor and 10 treated with the combined therapy for 6 months. An extensive clinical analysis was performed. Serum, plasma and peripheral blood mononuclear cells (PBMCs) were isolated. A panel of 92 proteins involved in CVD was analyzed in plasma. The activation of 18 intracellular pathways and the expression of genes involved in inflammation and cardiovascular risk were analyzed in PBMCs. In vitro experiments: Endothelial cells and adipocytes were treated with serum from PsA patients and HCs with MTX or/and apremilast.
Results: Disease activity and inflammation was correlated with the increased insulin resistance (IR) rates. Levels of plasma proteins and phosphorylation of intracellular pathways and expression of genes in PBCMs, involved in inflammation and CVD, were altered in PsA patients. These molecular alterations were associated with clinical features and metabolic comorbidities. Apremilast significantly improved lipid profile, IR and decreased BMI and metabolic syndrome. Different plasma proteins and intracellular pathways were specifically regulated by both therapies. Inflammation was deeper reduced after combined therapy, keeping the beneficial effects of apremilast in metabolic alterations. In vitro treatment of adipocytes and endothelial cells recapitulated these results.
Conclusions: 1) Metabolic alterations in PsA are closely associated with disease activity and chronic inflammation. 2) Apremilast is a novel anti-inflammatory therapy that targets metabolic pathways in PsA, 3) Apremilast and MTX combination induces a deeper reduction in the disease activity, maintaining, in turn, the positive effects of apremilast on the cardiovascular risk.
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Vb. Betulinic acid hydroxamate activates the HIF pathway through post-transcriptional dephosphorylation of Prolyl Hydrolase 2. Implications in neuroprotection in Huntington Disease

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Scientific Program: Inflammatory and Infectious diseases.
Keywords: Huntington disease; hypoxia-inducing factor; prolyl-hydroxylases; neuroprotection.

Abstract: Huntington disease (HD) is a rare neurodegenerative disorder of the central nervous system characterized by unwanted choreatic movements, behavioral and psychiatric disturbances and dementia. The activation of the hypoxic response pathway through the pharmacological inhibition of hypoxia-inducing factor (HIF) prolyl-hydroxylases (PHDs) is a promising approach for CNS neurodegenerative diseases, including HD. Herein, we have studied the mechanism of action of the compound Betulinic acid hydroxamate (BAH), a hypoximimetic derivative of betulinic acid, and its efficacy against striatal neurodegeneration using complementary approaches. Firstly, we showed the molecular mechanisms through which BAH modifies the activity of the PHD2 prolyl hydroxylase, thus directly affecting HIF-1βstability. BAH treatment not only alters PHD2 interactome, but it also reduces PHD2 phosphorylation on Ser125 residue, responsible for the control of its hydrolase activity. Furthermore, in striatal cells bearing a mutated form of the huntingtin protein, BAH stabilized HIF-1βprotein without altering the levels of PHDs, induced Vegf and Bnip3 gene expression and protected against mitochondrial toxin-induced cytotoxicity. To determine the neuroprotective effects of the compound, HIF-1βdependent genes were analyzed in brain microvascular cells showing an increase in the expression of Angptl4, Nrdg1, Slc2a1, Epo and Vegf. BAH was also able to induce angiogenesis in vascular endothelial cells. In vivo experiments performed in a mouse model of striatal neurodegeneration induced by 3-nitropropionic acid administration showed that BAH modified the clinical symptoms by improving locomotor activity, hind limb clasping, dystonia and kyphosis. In addition, BAH also prevented neuronal loss, decreased reactive astrogliosis and microglial activation, inhibited the upregulation of proinflammatory markers and improved antioxidant defenses in the brain. Taken together, our results show BAH's ability to alter the response pathway to hypoxia through the decrease of PHD2 phosphorylation levels, which has important implications in the treatment of HD and perhaps other neurodegenerative diseases.

Vc. Association between rectal colonization by Klebsiella pneumoniae carbapenemase-producing K. pneumoniae and mortality: a prospective, observational study

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Scientific Program: Inflammatory and Infectious diseases.
Keywords: Carbapenemase-producing Klebsiella pneumoniae, colonization, mortality, severe infection.

Abstract: Background. We evaluated the association of Klebsiella pneumoniae carbapenemase-producing Klebsiella pneumoniae (KPC-Kp) rectal colonization with crude and attributable mortality.
Methods. Prospective cohort study of patients followed up 90 days after a study of rectal colonization. Cox-regression was used to study the variables associated with crude mortality and a competing risks analysis for variables associated with attributable mortality.
Results. A total of 1244 patients (1078 non-colonized and 166 colonized) were included. None of the non-colonized patients and 78 (47.0%) of the colonized patients developed KPC-Kp infection. Crude 90-day mortality was 18% (194/1078) in non-colonized patients and 41.6% (69/166) in colonized patients. Rectal colonization was not associated with crude mortality (Hazard Ratio [HR] 1.03; 95% CI 0.69-1.54; p = 0.85) when the model was adjusted for severe KPC-Kp infection (INCREMENT-CPE score [ICS] > 7). KPC-Kp infection with ICS > 7 was associated with an increased risk of all-cause mortality (HR 2.21; 95% CI 1.35-3.63; p = 0.002). In the competing risk analysis, infection with ICS > 7 (subdistribution hazard ratio [SHR] 95.95; 95% CI 43.4-212.4; p < 0.001), but not rectal colonization, was associated with attributable mortality. The high-risk period (July 2012-June 2014) was also associated with attributable mortality (SHR 2.42; 95% CI 1.10-5.32; p = 0.03).
Conclusions. KPC-Kp rectal colonization was not associated with either crude or attributable mortality. Attributable mortality increases when colonized patients develop severe KPC-Kp infection (ICS > 7). Rectal colonization was a necessary although insufficient condition to die from a KPC-Kp infection.

Vd. Serum inflammatory molecules and microRNAs as potential biomarkers of early and established response to TNFi therapy in rheumatoid arthritis patients

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Scientific Program: Inflammatory and Infectious diseases.
Keywords: Rheumatoid arthritis, therapeutic response, TNF-βnhibitors, early response, established response, inflammatory profile, microRNAs.

Abstract: Background/Purpose. To evaluate changes occurred in circulating inflammatory mediators and their regulatory microRNAs in Rheumatoid Arthritis (RA) patients after 3 and 6 months of treatment with TNFβnhibitors (TNFi), in order to identify biomarkers of clinical efficacy and potential predictors of response to TNFi therapy.
Methods. In a prospective RA cohort multicenter study, serum from 125 RA patients with moderate/high disease activity was collected prior and after 3 and 6 months of TNFi treatment. Patient's response was determined according EULAR criteria. Serum inflammatory profile and levels of selected microRNAs were analyzed by multiplex assay and RT-PCR respectively. Then, their discriminative ability and their added value were assessed by logistic prediction models.
Results. Among RA patients, 79% showed early response after 3-months of TNFi, of which 67% showed clinical response after 6-months. Inflammatory mediators related to activation and proliferation (IL-6, IL-13), adhesion and migration (MIP-1a, RANTES, FGFb), chemotaxis (MIP1b, IL8, IP-10) and angiogenesis (VEGF), showed a trend to reduction after 3-months, but were significantly downregulated only after 6-months of treatment. Furthermore, several molecules upregulated after 3-months of therapy were thereafter downregulated, consolidating the reduction in the inflammatory response. Moreover, a decline in 7 of these molecules correlated with DAS28 reduction. High DAS28/SDAI scores or levels of auto-antibodies at baseline were not predictive of response. Instead, atherogenic index, smoking habit and hyperlipidemia at baseline were predictors of a worse response. Besides, high baseline levels of both, various inflammatory mediators and several microRNAs regulating their expression, were predictive of response to TNFi treatment at 3 and 6 months.
Receiver operating characteristic analyses allowed us to identify specific signatures of circulating biomolecules that may serve as predictors of response to TNFi therapy with high sensitivity and specificity.
Conclusion. The extensive analysis of the serum inflammatory and microRNAs profiles allowed to identify specific and distinctive signatures of biomolecules that, along with clinical and serological profiles, might predict early and established response of RA patients to TNFi treatment.
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Ve. Excimer Laser Coronary Atherectomy for Uncrossable Coronary Lesions. A multicenter registry

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Scientific Program: Inflammatory and Infectious diseases.
Keywords: Coronary heart disease; Percutaneous coronary intervention; Coronary chronic total occlusion; Laser, Calcification.

Abstract: Introduction and Objectives: Uncrossable lesions constitute a challenge for percutaneous coronary intervention (PCI).We sought to assess the immediate and long-term outcomes, as well as, the factors associated with excimer laser coronary atherectomy (ELCA) failure in this setting.
Methods: This multicenter registry included 126 patients with 126 uncrossable lesions. Study endpoints were ELCA success, technical success and a composite of cardiac death, myocardial infarction (MI), and target-lesion revascularization (TLR) on follow-up. Predictors of ELCA failure were analyzed.
Results: Moderate or severe calcification was present in 79 (62.7%) of the lesions and 58 (46%) were a chronic total occlusion. ELCA success was obtained in 103 (81.8%) patients. Rotational atherectomy was attempted as bailout in 21 out of 23 ELCA failure (91.3%), being successful in 14 (66.7%) of them. Finally, technical and procedural success were achieved in 114 (90.5%) and 110 (87.3%) of the patients. Severe calcification was independently associated with ELCA failure (OR:3.73, 95% CI:1.35- 10.32; p= 0.011). Two (1.6%) patients died (one of them after a stroke and another patient because of heart failure), 4 (3.2%) presented a non-Q MI without clinical consequences and 1 (0.8%) patient had a Q-MI. Other complications were ventricular tachycardia/fibrillation (n=2; 1.6%) and flow-limiting dissection (n=1, 0.8%). At follow-up (median 424 days), 3 (2.4%) patients died (1 (0.8%) from cardiovascular cause) and 15 (11.9%) required TLR.
Conclusions: In our multicenter experience, ELCA use demonstrated to be safe and reasonably effective with a rate of events on follow-up relatively low. Severe calcification was associated with ELCA failure.

Vf. Zoo animals as potential sentinels for zoonotic flaviviruses monitoring

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Keywords: West Nile; Usutu; Tick-borne Encephalitis; emergence; wildlife; public health; sentinel.

Abstract: Flaviviruses are important emerging and re-emerging zoonotic vector-borne pathogens. During the last decade, flaviviruses have widely spread in Europe, representing an increasing threat for public and animal health. A serosurvey was carried out to assess emerging flavivirus exposure in zoo mammals in Spain and to determine the dynamics of seropositivity in species longitudinally sampled during the study period. Sera from 570 zoo animals belonging to 120 mammal species were collected in ten zoos from Spain between 2002 and 2019. Twenty-one of these animals, belonging to ten different species, were longitudinally sampled in four of the zoos during the study period. Antigenically-related flavivirus antibodies were detected in 19 (3.3%; 95%CI: 2.0-5.2) out of the 570 animals analyzed using bELISA.
Seropositivity was observed in ten (8.3%) of the 120 species tested. Five (23.8%) of the 21 animals sampled more than once presented seropositivity in all samplings whereas seroconversion was only observed in one white rhinoceros (Ceratotherium simum). Flavivirus antibodies were found in six of the ten sampled zoos and in consecutive years between 2008 and 2018. Virus neutralization tests confirmed West Nile virus (WNV), Usutu virus (USUV) and tick-borne encephalitis virus (TBEV) infection in ten (1.8%; 95%CI: 0.7-2.8), five (0.9%; 95%CI: 0.1-1.6) and one (0.2%; 95%CI: 0.0-0.5) animal, respectively. Anti-Meaban virus antibodies (0%; 95%CI: 0.0-0.7%) were not found in the tested sera. The results demonstrate WNV, USUV and TBEV exposure in zoo mammals, which may be of public health and conservation concerns. Seropositivity to WNV and USUV was detected in regions where these viruses have not been previously reported. Anti-WNV antibodies found in zoo animals sampled in 2009 point to WNV circulation at least one year before the first outbreaks were reported in horses and humans in Spain. Our results indicate that zoo mammals could be useful sentinel species for monitoring emerging flaviviruses activity in urban areas.

ORAL POSTER

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Abstracts

SESSION

PSa. A diet-dependent microbiota profile associated with incident type 2 diabetes: from the CORDIOPREV study

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Scientific Program: Nutrition, endocrine and metabolic diseases.
Keywords: Gut microbiota, diet, type 2 diabetes, risk score, prevention.

Abstract: Background. We aimed to explore the differences between the baseline gut microbiota of patients who developed T2D consuming a low-fat (LF) or the Mediterranean (Med) diet, and further to build microbiota-based diet-specific risk scores by two approaches (Random Survival Forest and Lasso models), in order to predict the individual T2D risk associated to the consumption of a LF or the Med diet.
Methods. We included in this study all the patients from the CORDIOPREV study without T2DM at baseline (n=462) to which fecal samples were available (n=319), randomized to receive a LF diet (n=148, 28 developed T2D) or the Med diet (n=171, 41 developed T2D). Gut microbiota was analyzed by 16S sequencing, and the risk of T2D after a median follow-up of 60 months assessed by COX analysis according to the microbiome-based risk scores built for each diet.
Results. Linear discriminant analysis Effect Size showed a different baseline gut microbiota from patients who developed T2D consuming a LF and the Med diet. The scores built associated higher abundance of Paraprevotella, and lower of Gammaproteobacteria and B. unformis to T2D risk (HR=3.66 RSF-LF score, 3.15 Lasso-LF score; 95% CI) whether LF diet was consumed. By contrast, a higher abundance of Saccharibacteria, Betaproteobacteria, and Prevotella was associated to T2D risk (HR=4.00 RSF-Med score, 3.45 Lasso-Med score; 95% CI) whether Med diet was consumed.
Conclusion. Our results suggest that the differential interactions of the microbiome with nutrients may at least partially determine the risk of T2D development, which may be used for selecting personalized dietary models to prevent T2D.

PSb. DYRK2 novel regulation mechanism determine its activity via cis-autophosphorylation compromising cell cycle, DNA damage response pathway and carcinogenesis

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Scientific Program: Cancer (Oncology and Oncohematology).
Keywords: DYRK2; autophosphorylation; cancer; regulation; cell signaling.

Abstract: Dual-Specificity Tyrosine-Phosphorylation-Regulated Kinase 2 (DYRK2) is known to have a key role in the regulation of cellular processes such as proliferation and cell differentiation, as well as a relevant part in tumour development and/or progression. Despite being considered by the scientific community an “essential protein” for the control of tumourigenesis, the regulatory mechanisms of its activity still remain unknown. In this work, we describe for the first time a new regulation mechanism by autophosphorylation of this kinase and its implications via the dual specificity phosphatase Cdc25A. Through in vitro kinase assays and later analysis with mass spectometry, we describe 9 autophosphorilation residues in DYRK2 via single mutants (Thr32, Thr33, Thr82, Ser483, Thr484, Thr488, Ser489) and mutiple mutants (Ser498-499-501, 5A, 9A). Single mutants for each residue show a slightly higher protein stability, also preserving kinase activity intact, as well as the ability of self-phosphorilation and substrate phosphorilation both in vitro and in vivo. Conformational analyses based on X-ray crystalography show the importance of these residues in the native conformation of the enzyme. Through different experimental approaches we demostrate the ability of autophosphorylation in cis and significant differences on the activity of several known substrates, such as CDC25A. This has important functional consequences due to the alteration of signalling pathways as relevant as the control of the cell cycle or cell differentiation. By analysing the somatic mutations described in human cancer, we show the existence of mutations with a function-structure similar to those we described in this study. These results help us explain the alterations in cell signalling pathways, as well as the biological significance in the progression of cancer associated to mutations in DYRK2. To conclude, our results demostrate for the first time the existence of a self-regulation mechanism of the activity of this kinase, with a relevant role in the control of tumorigenesis, which could be subjected to a possible pharmacological regulation with a potential clinical use.

PSc. Evaluation of the cardiovascular risk of a spanish population in secondary prevention and its comparison with other populations

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Scientific Program: Nutrition, endocrine and metabolic diseases.
Keywords: Cardiovascular risk, secondary prevention, score.

Abstract: INTRODUCTION: Patients with a previous cardiovascular event have a probability of up to 30% of suffering new recurrences in the following five years. In order to identify those patients most at risk and to be able to carry out more comprehensive treatment, different scales have been created. The Thrombolysis in Myocardial Infarction Risk Score for Secondary Prevention (TRS2P) has been used in several populations where it has demonstrated its ability to discriminate on the risk of long-term recurrence. Our aim is to test the applicability of this scale in the Cordioprev study population, comparing it with the relevant international populations previously studied (TRA2P, IMPROVE-IT, SAVOR and FOURIER). With this, we will be able to establish the baseline risk of our population, compare it with others and determine which of them can serve as a reference population.
METHODOLOGY: TRS2P was applied to a sample of 500 patients from the Cordioprev study and they were classified according to the score obtained. We then compared the distribution of patients in the different established risk categories to identify the one most similar to ours.
RESULTS: The average score obtained was 1.57 points with a median of 2 points. The most prevalent factors included in this scale were high blood pressure (70.2%) and type 2 diabetes mellitus (54.6%). When comparing the distribution of the score between our population and the other populations, the IMPROVE-IT study population was identified as the one with the greatest similarity.
CONCLUSIONS: The CordioPrev study population has a median score classified as “intermediate risk” on the cardiovascular event recurrence scale. Furthermore, the population with the most similar distribution to ours was that of the IMPROVE-IT study. These results will allow us to compare the clinical recurrence data that occurred in this population with those that will appear in the CordioPrev study.

PSd. Impact of distinctive autoimmune and molecular signatures of childhood -and adult- onset systemic lupus erythematosus patients in the development of lupus nephropathy and cardiovascular disease.

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Scientific Program: Chronic and Inflammatory diseases.
Keywords: childhood-onset SLE, adult-onset SLE, interferon signature, atherothrombotic status.

Abstract: Background/Purpose. This study aimed at identifying and characterize distinctive molecular signatures between childhood-onset (cSLE) and adult-onset Lupus (aSLE) patients, along with their involvement in immunological and clinical features, and to analyze the relevance of the sustained positivity for anti-dsDNA antibodies.
Methods.Ninety-four subjects were enrolled, comprising two main combined study groups: 1) eleven consecutive children with cSLE and 11 age/sex matched healthy-children (cHD); 2) sixty aSLE patients and 20 healthy-adults (aHD). Total RNA was extracted from purified monocytes and a nanostring autoimmune profiling array was developed.
Results. Gene expression array identified 279 altered genes in monocytes from cSLE vs cHD.
Comparatively, less than a half (130) were altered in aSLE monocytes vs aHD. Nineteen genes were simultaneously upregulated in both patients' cohorts. Interestingly, GO-enrichment analysis identified as main biological processes integrated by these genes the interferon signature (IFNs). Moreover, cSLE displayed at least a double-fold change in the levels of these genes vs cHD than aSLE vs aHD. Likewise, in both cohorts the altered expression of several genes integrating the IFNs was linked to clinical features (i.e. activity of the disease, CV-risk factors, nephropathy (LN), etc).
Interestingly, most of them were further associated with the positivity for anti-dsDNA. A deeper study demonstrated that a third of the aSLE patients' displayed sustained anti-dsDNA positivity for more than 7 years. Besides, these patients showed altered expression of several IFN-genes and presented LN, impaired microvascular endothelial function and prevalence of atheroma plaques, supporting the impact of the IFNs in the severity of the disease and the development of CVD.
Conclusion. Gene expression profile allowed the identification of distinctive molecular pathways among monocytes of cSLE and aSLE patients. 2. An IFN-signature, more strongly deranged in cSLE than in aSLE, is related to disease activity, CVD, and renal involvement. 3. The sustained positivity for anti-dsDNA in aSLE, further linked to that deranged IFNs and to the development of LN, might fosters the establishment of an atherothrombotic status in these autoimmune patients.
Supported by ISCIII (PI18/0837 and RIER RD16/0012/0015), Co-funded with FEDER.

PSe. Sexual dimorphism of mitochondrial complexes, autophagy markers and nutritional sensors in skeletal muscle and liver for transgenic mice overexpressing NADH-cytochrome b5 reductase-3

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Scientific Program: Active aging and fragility.
Keywords: CYB5R3, sexual dimorphism, skeletal muscle, liver.

Abstract: Existing data on the differential susceptibility to diseases or a different effect of drugs in men and women demonstrates the existence of sexual dimorphism, which must be taken into account when designing research strategies. Differences between males and females have been also shown for model organisms, which can affect a multitude of processes. Including both sexes in the design of the studies is thus important to gain a greater relevance of the research from a biomedical point of view. Previous studies developed in our group have been focused on NADH-cytochrome b5 reductase-3 (CYB5R3) as a new pro-longevity gene. We documented that male mice overexpressing CYB5R3 showed greater longevity and enhanced protection against aging-associated diseases. Since our previous investigation has demonstrated that the outcome of an antiaging intervention as calorie restriction is strongly influenced by sex, the main objective of our work was to study the potential existence of sexual dimorphism in several markers of biochemical pathways related with the hallmarks of aging, such as the levels of mitochondrial complexes, autophagy markers and nutritional sensors. Studies were carried out in skeletal muscle and liver samples obtained from CYB5R3 transgenic and control mice of both sexes in a C57BL/6 background at three months of age. The effects of CYB5R3 overexpression on mitochondrial complexes, autophagy markers and nutritional sensors showed sexual dimorphism that was also tissue specific. The increased autophagic flow in liver and skeletal muscle seen in CYB5R3 transgenic males, did not occur in females. On the other hand, the increase in hepatic mitochondrial complexes was more noticeable in CYB5R3 transgenic females. These observations reinforce the need for further in-depth studies, including longevity studies, focused on animals of both sexes.

PSf. Protist enteroparasite in wild boar (Sus scrofa ferus) and Iberian pig (Sus scrofa domesticus) in Southern Spain: A protective effect on Hepatitis E acquisition?

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Scientific Program: Infectious diseases, immunological and organ transplantation.
Keywords: Hepatitis E virus; enteric parasites; Cryptosporidium; Giardia; Blastocystis; Strongyloides; Transmission; Pigs, Wild boars; Co-infection; Spain.

Abstract: Background/Objective: There are several studies evaluating the prevalence of both Hepatitis E virus (HEV) and enteroparasites in swine, however, there is a lack of survey studies evaluating the prevalence and genetic diversity of all these microorganisms in pigs and wild boars, the sympatric transmission between species, as well the possible interaction between enteroparasites and HEV. Therefore, the objetive of our study was to evaluate the interaction between HEV and enteroparasite co-transmission in swine.
Methods: We prospectively collected serum and feces samples from black Iberian domestic pigs and wild boar from South Spain between 2015–2016. We evaluated for HEV in serum and faeces, and the presence of enteroparasites (Giardia duodenalis, Cryptosporidium spp., Blastocystis sp., Neobalantidium coli, and Strongyloides spp.) in the same feces samples. The prevalence of each intestinal parasite species in the was calculated.
Results: A total of 328 animals were included in the study; 56.7% black Iberian pigs and 43.3% wild boars. The overall global prevalence of HEV in serum was 16.8%. The overall global prevalence of enteroparasites was 19.5% for Giardia duodenalis, 8.2% for Cryptosporidium spp., 41.8% for Blastocystis sp., 31.4% for Neobalantidium coli, and 8.8% for Strongyloides spp. Those animals infected by HEV showed a significantly lower prevalence of Giardia duodenalis (3.2% vs. 20%; P = 0.002) and Blastocystis sp. (38.7% vs. 80%; P < 0.001) than those animals uninfected by HEV. Animals with both detectable Giardia duodenalis and Blastocystis sp. showed a significant lower rate of HEV infection than those not bearing these enteroparasites (P < 0.001).
Conclusions: Our study found a high prevalence of enteroparasites in pigs and wild boars for Southern Spain, suggesting a sympatric co-transmission of some of the species investigated. We found that extracellular Giardia duodenalis and Blastocystis sp. could have a protective effect on HEV acquisition in swine.

PSg. Sexual dysfunction, self-esteem and risk of depression in the postpartum period

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Scientific Program: Nutrition, endocrine and metabolic diseases.
Keywords: Sexual Dysfunction; Birth; Depression, Postpartum; Self-esteem.

Abstract: Introduction: Pregnancy and childbirth can lead to major changes in women's sexual function and be a source of postpartum sexual dysfunction problems (Gutzeit et al., 2020).
Objective: To assess the women's sexual function in postpartum and the relationship with the risk of depression and personal self-esteem.
Methodology: Descriptive study carried out in a province in southern Spain on women attended in Primary Care after childbirth between October 2019 and April 2020. Consecutive sampling. Women who had had low-risk labor and who agreed to participate in the study were included. At four months after birth, they were offered to fill out three questionnaires: Rosemberg, Edinburgh and sexual function scales. A descriptive analysis of sociodemographic, obstetric, and neonatal variables was performed.
Results: Of the 75 women included, 68% were primiparous, 73% ended in vaginal birth (16% instrumented) and 27% by cesarean section. Most of the women had high self-esteem (78%). 17% reported not having sex in the last 4 weeks. The remaining 83% who reported having sex, presented problems related to: sexual desire (32%), excitement (25%), problems achieving orgasm (24%), penetration (53%), degree of anxiety about sexual intercourse (62%), communication problems (13%) and some type of general sexual dissatisfaction (23%). The risk of depression appeared in 44% of the women, and was related to women who manifested problems with orgasm (OR 3.42; 95%CI 1.02-11.50; p=0.042) and general sexual dissatisfaction (OR: 4.02; 95%CI: 1.10-14.70; p=0.029). Having high self-esteem is a protective factor for this risk (OR: 0.24; 95%CI: 0.07-0.78; p=0.014).
Conclusions: Sexual dysfunction problems and disorders that can trigger depression are frequent in the postpartum period. There seems to be a certain relationship between both factors, although it is necessary to deepen the research. It is essential to influence the early detection of these disorders during the postpartum period.

PSh. The effect of dietary magnesium supplementation on the endothelial dysfunction in a model of metabolic syndrome and chronic kidney disease

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Scientific Program: Chronic and Inflammatory diseases.
Keywords: Hepatitis E virus; enteric parasites; Cryptosporidium; Giardia; Blastocystis; Strongyloides; Transmission; Pigs, Wild boars; Co-infection; Spain

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Abstract: INTRODUCTION. Cardiovascular diseases (CVD) are the main cause of death in patients with chronic kidney disease (CKD). The endothelial dysfunction appears as a common link between cardiovascular risk factors and CKD as well as with metabolic syndrome (MS), which is also an independent risk factor contributing to the development of CKD. Previous studies demonstrated an inverse relationship between serum Mg and the prevalence of MS, as well as a beneficial effect of Mg at the vascular level.
OBJETIVE. To evaluate in vivo, in an experimental model of rats, the effect of dietary Mg supplementation on the endothelial dysfunction associated to MS in the setting of CKD.
MATERIALS AND METHODS. The experimental groups, Zucker (MS) rats with 5/6 nephrectomy (Nx) were fed a high P diet (0,9%), with either a normal (0,1%) or a high Mg (0,6%) content for 28 days. Sham rats fed a normal P and Mg diet were used as controls. Biomarkers of the kidney and endothelial function were determined in blood and kidney tissue.
RESULTS. As compared to controls, MS-CKD animals fed the 0.1%-Mg diet showed a dramatic alteration in the renal (increased creatinine) and endothelial function (increased blood pressure and plasma endothelin-1 and decreased serum nitric oxide) and in oxidative stress (decreased plasma Gpx activity), which was accompanied by a decrease in Klotho expression in the kidney (see table). However, animals fed the 0.6%-Mg diet showed a less severe decrease in the renal function and nitric oxide, while the values observed for the rest of biomarkers were similar to those in controls.
CONCLUSIONS. In a model of simultaneous SM and CKD, dietary Mg supplementation reduced the renal and endothelial dysfunction and preserved the levels of renal Klotho.

	Control	Nx+Mg 0.1%	Nx+Mg0.6%
Creatinine (mg/dl)	0.52±0.11	1.59±0.22[a]	0.99±0.1[a,b]
Endotelin (%vs control)	100±12.9	176.5±24.4[a]	90.4±15.8[b]
Gpx activity (nmol/min/ml)	2878±238.9	1610±136.4[a]	2295±214.3[b]
Nitric oxide (µM)	621.3±9.483	545.7±9.469[a]	581.8±7.896[a,b]
Blood pressure (mmHg)	121.2±5.90	168.0±3.97[a]	130.2±3.65[b]
Klotho (D.0.I vs control)	100±7.44	29.6±4.83[a]	88.1±35.6[b]

a, p<0.05 vs control group; b, p< 0.05 vs Nx group +Mg 0.1%

PSi. n-3 Polyunsaturated fatty acids enhance coenzyme Q biosynthesis

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Scientific Program: Active aging and fragility.
Keywords: Coenzyme Q, dietary fats, and n-3 PUFAs.

Abstract: Coenzyme Q (CoQ) is an essential component in biological membranes that is produced naturally in all cells by a highly regulated pathway. CoQ acts mainly as electron carrier in the mitochondrial respiratory chain, but it is also a powerful antioxidant that protects biological membranes from lipid peroxidation. Due to its unique properties, CoQ has always been in the spotlight of researchers to treat mitochondrial disorders and as an anti-aging therapy, and its use in cosmetics as well as a dietary supplement has spread. Dietary fat can alter the composition of biological membranes and their susceptibility to oxidative stress. Therefore, CoQ content and the expression of genes involved in CoQ synthesis can be influenced by different types of dietary fats. However, the relation between specific fat dietary intake, particularly n-3 polyunsaturated fatty acids (PUFAs) and the enhancement of CoQ system remains unclear. We therefore studied this relationship using both in vivo and in vitro models to deepen into the regulation of the CoQ system by dietary fats. We found a dramatic increase of CoQ content in liver of mice that had been fed with a diet containing fish oil as the predominant dietary fat. Similar results were observed in Hepa 1.6 cells that were cultured in a media supplemented with a lipid emulsion based on fish oil n-3 PUFAs, which enhanced CoQ biosynthesis by upregulating several COQ proteins. Furthermore, n-3 PUFAs altered the proportion between CoQ isoforms, inducing the biosynthesis of CoQ10 over CoQ9. Of note, that both pharmacological inhibition and genetic silencing of farnesyl diphosphate synthase recapitulated the dysregulation of CoQ isoforms ratio. Our results demonstrate by the first time that n-3 PUFAs are major contributors to the regulation of endogenous CoQ biosynthesis in mammals, suggesting that dietary interventions could be valuable strategies against pathologies related with CoQ deficiency.

REGULAR POSTER

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Abstracts

Cancer (Oncology and Oncohematology)

Ia. Exposure to mixtures of persistent, bioaccumulative, and toxic chemicals and cancer risk: a systematic review

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Keywords: cancer; pollutant mixtures; PBTs; persistent pollutants; endocrine disruptors.

Abstract: Environmental risks are responsible for one in five of all deaths worldwide. Persistent, bioaccumulative, and toxic substances are chemicals that can subsist for decades in human tissues and the environment. They include heavy metals, organochlorines, polychlorinated biphenyls, organobromines, organofluorines, and polycyclic aromatic hydrocarbons among others. Although humans are often exposed to multiple pollutants simultaneously, their negative effects on health have generally been studied for each one separately. Among the most severe of these harmful effects is cancer.

Here, to compile and analyze the available evidence on the relationship between exposure to mixtures of persistent, bioaccumulative, and toxic chemicals and the risk of developing cancer in the general population, we provide a systematic review based on the main databases (Cochrane, PubMed and Embase), together with complementary sources, using the general methodology of the PRISMA Statement. The articles analyzed were selected by two researchers working independently and their quality was evaluated by reference to the Newcastle-Ottawa scale.

The initial search yielded 2379 results from the main sources of information and 22 from the complementary ones. After the article selection process, 22 were included in the final review (21 case-control studies and one cohort study). Analysis of the selected studies revealed that most of the mixtures analyzed were positively associated with risk of cancer, especially that of the breast, colon-rectum or testis, and more strongly so than each contaminant alone.

In view of the possible stronger association observed with the development of cancer for some mixtures of pollutants than when each one is present separately, exposure to mixtures should also be monitored and measured, preferably in cohort designs, to complement the traditional approach to persistent, bioaccumulative, and toxic chemicals. The results presented should be taken into account in public health policies in order to strengthen the regulatory framework for cancer prevention and control.

Ib. Relation between Helicobacter spp. isolated in bile and biliary tract malignancies

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Keywords: Cholangiocarcinoma, pancreatic cancer, Helicobacter pylori.

Abstract: The increased incidence of neoplastic lesions of the biliary tract, as well as their high mortality, require measures to detect factors associated with their development. Helicobacter spp. has been related to this type of cancer, however, there are big differences in the results, according to geographic factors and the methods used for the detection. Helicobacter isolation has been performed in bile tissue or bile from intraoperative samples. Demonstrating the association of this pathogen in bile would represent an advance in the prevention and knowledge of these malignancies.
Objectives: To compare the proportion of Helicobacter spp in bile of patients with malignant or benign biliary obstruction. To analize the association between the bacteria and bile tract cancer. To describe the baseline characteristics, laboratory values, and comorbidities of these patients, as well as characteristics related to
ERCP procedure and its complications.
Methods. Cases and controls prospective study. We included 98 patients admitted between April and November 2019, who underwent a bile drainage procedure by ERCP. Samples of bile were obtained, after biliary cannulation, with the sphincterotome. Helicobacter detection was carried out by polymerase chain reaction. Variables related to demographic data, comorbidities, hospital stay and ERCP procedure were collected. Descriptive statistical calculation of the variables of interest, differentiating between the presence of malignancy or not was performed. We analyzed the data with SPSS using Chi-square test for qualitative variables and Mann-Whitney test.
Results. We studied 55 men and 43 women, who underwent ERCP due to bile duct pathology. Average age 72.7 (28-94) years. Median time from diagnosis of biliary pathology to admission, 13 days, and from admission to ERCP 1 day. The reason for ERCP was 73.5% choledocholithiasis, 19.4% malignant obstructive jaundice (47.4% pancreatic origin, 31.4% cholangiocarcinoma, 10.3% ampuloma, 10.3% malignant extrinsic compression of other origin), 6.1% benign stenosis, 1% biliary fistula. 23.5% had undergone an ERCP before. 15.3% had biliary stent previously placed and 28.6% required placement of a biliary stent for the first time. Post-ERCP complications: 1% pancreatitis and 2% hemorrhage. Average hospital stay 5.5 days. Global detection of Helicobacter spp in bile samples17.3%, with 94.2% of them being H. Pylori. Helicobacter was isolated in 17.7% of the malignant lesions. We did not find an association between Helicobacter in bile and neoplasia p> 0.05. On the other hand, there is a statistically significant association between neoplasia and diabetes p = 0.006, absence of cholecystectomy p = 0.015, prothrombin activity value p = 0.0001, bilirubin value at admission p = 0.0001 and hemoglobin value at admission p = 0.02.
Conclusions: A significant percentage of Helicobacter spp have been detected in bile. We did not find association between Helicobacter spp and bile tract malignancies, although the small sample size could be related to the lack of association obtained. We have found an association between analytical alterations on admission and neoplasia, as well as the presence of diabetes and the absence of cholecystectomy.

Ic. Mutational status of mesenchymal stromal cells in myelodysplastic synfromes patients

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Scientific Program: Cancer (Oncology and Oncohematology)
Keywords: Myelodysplastic syndromes, Mesenchymal stromal cells, Next Generation Sequencing.

Abstract: Mesenchymal stromal cells (MSC) represent a key component of the microenvironment. It has been shown that MSC cells derived from myelodysplastic syndromes (MDS) patients are functionally incorrect displaying chromosomal abnormalities, aberrant cytokine secretion or deregulation of gene expression profile. However, little is known about the mutational profile of MSC in MDS.
Here, applying the targeted next generation sequencing (NGS) we analyzed mutational profile of MSC of 58 MDS patients, and we compared it with the genetic alterations of their hematopoietic counterparts, evaluating their possible role as well in MDS pathogenesis.
NGS analysis revealed that 60.3% of patients carried mutations in hematopoietic progenitor cells (HPC) while MSC alterations were presented in 13.8% MDS cases. Ninety-six mutations of 107 detected (89.7%) were founded in HPC, affecting 40 genes. The genes most frequently mutated in HPC were TET2 (31%), followed by SF3B1 (17.2%), SRSF2 (13.8%), TP53 (13.8%) and DNMT3A, EZH2, RUNX1, STAG2 (10.3% each). The remaining 11 of the 107 mutations were founded in MSC (10.3%) and affected 10 genes without any specific mutational pattern. Six of ten genes affected (60%) MSC were common with the mutated genes in HPC. Another 4 genes (40%) were exclusive for MSC. MSC mutations were always different to their HPC counterpart as well to MSC mutations of other patients. The median number of alterations per patient was 1 (0-7) in the case of HPC and 0 (0-4) in MSC. The 51% of HPC mutations have been previously described (83.7% in haematological cancer), while almost all MSC mutations have not (except ETV6, p.R105G). All the clinical, biological and overall survival characteristics of MDS patients with and without MSC mutations were similar.
Therefore, our study demonstrated that MSC from MDS patients can harbor mutations in myeloid-related genes, however they are occasional and different to mutations in HPC of the same patient.

Id. Improvement of "off-the-shelf" allogeneic CAR-T cells

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Scientific Program: Cancer (Oncology and Oncohematology).
Keywords: Immunotherapy; CAR T cells; CRISPR-Cas9; HLA; TCR; T lymphocytes subpopulations.

Abstract: Therapy based on T cells expressing chimeric antigen receptors (CAR T cells) is a novel treatment for lymphoid neoplasms, which has already proven promising results. However, several improvements on this strategy are currently being carried out. In first place, in order to avoid difficulties in obtaining the necessary number of autologous T cells, the use of allogenic off the shelf products is being considered and tested. On the other hand, several clinical trials involving CAR T cells have been impacted by T cell intrinsic dependent factors mainly associated with T cells phenotypes. CAR T cells enriched for naïve and central memory subsets generate CAR products with greater in vivo persistence, and so, with a more robust effect. With this in mind, we expected to generate universal allogenic CAR-CD19 T cells, with a defined phenotype.
In our study we are generating universal off the shelf CAR T cells, by the disruption of B2M and TCR loci with the CRISPR-Cas9 system, with the aim of generating a double knock-down CAR T cell to avoid both rejection and graft versus host disease. This approach is combined by the selection of a specific T cells subset with an enhanced antitumoral activity and higher in vivo persistence. The efficiency of the gene editing approach is being assessed by PCR and and Synthego's ICE tool, while the sorted T cell subsets with specific memory or stem cell memory are under study through different flow cytometry approaches.
To sum up, gene editing of CAR-T lymphocytes by TCR and B2M loci disruption, in combination with the isolation of T lymphocytes subsets are two in vitro procedures developed with a translational objective to improve the clinical results of CAR-T cells infusions in patients with refractory or relapsing B neoplasms.

Ie. Immunotherapy as the newest treatment for pediatric cancer

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Keywords: Children, Immunotherapy, neoplasms.

Abstract: Introduction. Cancer is one of the leading causes of death in childhood, being in first place B-cell acute lymphoblastic leukemia and brain tumors. In the last decade, advances in cancer diagnosis and treatment have increased the survival of children. However, its side effects and the difficulty of healing of refractory and recurrent neoplasms are still present. Immunotherapy emerges as a rising form of cancer treatment that promises to solve these problems.
Objective. To identify the actuality of immunotherapy treatments in pediatric cancer, their side effects, and barriers to overcome them and achieve maximum effectiveness.
Material and methods. A systematic review in the following databases, PubMed, Scopus, Cochrane, and Web of Science with a five-year limitation of the search, was carried out. The documents included followed the PRISMA principles.
Results. Twenty studies have been included, most of them, precisely 70%, were developed in the United States. Of the total, 35% classified as “general” the other 35% corresponding to “hematological malignancies,” and finally, 30% has been classified under the term of “solid tumors. The primary therapies correspond to monoclonal antibodies and adoptive cell therapy, being in both of them the primary side effect, the cytokine release syndrome.
Conclusions. Immunotherapy treatments in the pediatric population reduce side effects compared to usual treatments, but they are not free from these effects. The future of these treatments is promising, although the further investigation still requires.

If. Culture of circulating tumor cells from patients with hepatocellular carcinoma for the isolation of cancer stem cells

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Keywords: Hepatocellular carcinoma, cancer stem cells, circulating tumor cells, liquid biopsy.

Abstract: The cancer stem cells (CSCs) theory is acquiring more experimental evidence in the progression of hepatocellular carcinoma (HCC). It has been proposed as an explanatory mechanism for the events involved during metastasis, tumor recurrence or even resistance to therapy. This theory presents the tumor as an organized tissue with a CSC population that shares similar characteristics to regular stem cells. CSCs have self-renewing features and are capable of differentiating into tumor cells of varying phenotypes with less or limited proliferative potential, partly accounting for the heterogeneous clinical presentation of HCC. However, CSCs theory is still difficult to accept because CSCs subpopulations are always hard to identify and trace.
Liquid biopsy is a non-invasive method that allows the extraction and isolation of several tumor byproducts present in blood samples. This methodology has been successfully used to identify and recover circulating tumor cells (CTCs) from peripheral blood in cancer patients, which are thought to come from the tumor. Different studies have proved the presence of cells with stem cell-like properties within this population of CTCs. Due to the self-renewal capacity attributed to CSCs, they can generate tumor-derived spheroids in the appropriated culture conditions. Here, we have used two different strategies to get CSCs from peripheral blood samples from HCC patients undergoing transarterial chemoembolization: (1) positive selection of CTCs by using an anti-EpCAM-based immunomagnetic methodology and the IsoFlux® system; and (2) a negative selection protocol based on CD45 expression. The obtained cell population was cultivated in ultra-low adherence conditions to favor the growth of CSCs. Regardless of the blood CTC count, we have failed to obtain spheres of CSCs in any of the patients analyzed to date. Maintaining CSC cultures from human blood samples is a complicated task because of the minimal presence of these cells in blood and required culture conditions.

Ig. Quantitative proteomic analysis reveals a key role of splicing machinery in hepatocellular carcinoma

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Keywords: hepatocellular carcinoma; proteomics; SWATH; splicing; RBM3; TCERG1

Abstract: Hepatocellular carcinoma (HCC) is the sixth cancer type in incidence and the fourth in mortality but the molecular events underlying its development and progression are still to be fully elucidated. Since proteomic approaches represent unbiased, high throughput methods to detect tumour-specific alterations with clinical application, we performed herein the first quantitative proteomic analysis in an ample, representative and well-characterized cohort of HCC samples/patients. Thus, the nuclear and cytosolic protein composition from hepatic tissues of a cohort of HCC patients (n=43; tumor vs. non-tumor adjacent tissues) was determined by SWATH-MS and the results analysed by IPAR to perform pathways and regulators enrichment and activation analysis. Elements of the most relevant pathways were selected to validate their dysregulation in other HCC cohorts and to evaluate their diagnostic potential and their relationship with progression. In vitro proliferation assays after silencing specific targets were performed in three HCC cell-lines (HepG2, Hep3b and SNU-387). The proteomic analysis identified cytosolic (n=507) and nuclear (n=925) tumour-dysregulated proteins, which were mostly related to cellular metabolism, immune response and cancer-related cellular functions, as well as dysregulated upstream regulators such as FXR and C/EBP. Remarkably, mRNA splicing appeared strongly dysregulated and the alteration of 15 key components of the splicing machinery was confirmed in several retrospective and in silico HCC cohorts. Among them, PTBP1, RBM3 and TCERG1 showed a high diagnostic potential, individually or in combination with others, were related to aggressiveness parameters and invasive capacity, and/or their silencing (using specific siRNAs) decreased the proliferation of HCC-derived cell lines. Therefore, this study provides novel insights into the molecular alterations underlying HCC development and progression, demonstrating the alteration of key cellular processes, including splicing. Indeed, key splicing factors such as PTBP1, RBM3 and TCERG1 may represent novel diagnostic biomarkers or potential therapeutic targets in HCC.

Chronic and Inflammatory diseases

IIa. Association of Gut Dysbiosis with Radiographic and Enthesis Involvement, Disease Activity and Duration in Axial Spondyloarthritis. Data from CASTRO Registry

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Scientific Program: Chronic and Inflammatory diseases.
Keywords: Spondylarthritis, disease activity, enthesitis, microbiome.

Abstract: Objectives: To determine the alterations in the gut microbiota in AxSpA patients. To evaluate whether gut microbiota in AxSpA patients are associated with radiographic and enthesis involvement or disease activity.
Methods: Cross-sectional study of 33 patients with AxSpA (according to ASAS criteria) and 7 sex-age matched healthy donors (HDs). Disease activity variables such as C-reactive protein and erythrocyte sedimentation rate (ESR) were measured. The enthesis affectation was evaluated using the Madrid Sonographic Enthesitis Index (MASEI). Gut microbiota was evaluated using the Ion Torrent S5 platform and the sequences were processed using the QIIME2 analysis platform. Chi-square and Mann-Whitney tests were used for qualitative and quantitative variables. Significant differences were considered p <0.05.
Results: AxSpA patients and HDs did not show significant differences in βand βdiversity. A significant increase in Coprococcus comes in AxSpA patients compared to HDs (p=0,003) was found. Also, we observed that patients had a non-significant tend to differ from HDs in the families Bacteroidaceae and Bifidobacteriaceae and the genera Bacteroides, Bifidobacterium and Dialister.
Family Brucellaceae (p=0.037), species such as Alistipes finegoldii (p=0.018), Alistiper putredins (p=0.034) and Paraprevotella clara (p=0.034) and a βdiversity indicator (Shannon index) were significantly decreased and family Peptostreptococcaceae (p=0.002) was increased in patients with active disease (Ankylosing Spondylitis Disease Activity Score >2.1) versus inactive patients.
Moreover, families Peptostreptococcaceae (p=0.025) and Streptococcaceae (p=0.029) were significantly increased in patients with pathological enthesis ultrasonography (MASEI >17) versus patients with normal enthesis.
Finally, patients with radiographic AxSpA had an increase in family Erysipelotrichaceae (p=0.048), genus Rhuminococcus (p=0.024) and species Rhuminococcus gnavus (p=0.010) versus non-radiographic AxSpA. Further, positive correlation was observed between genus Roseburia (p=0.005) and species Roseburia faecis (p=0.008) with disease duration.
Conclusions: 1) AxSpA patients had a significant alteration of the gut microbiota. 2) These alterations are associated with disease activity and duration, and enthesis and radiographic involvement.

IIb. Nurses-led interventions on the management of chronic obstructive pulmonary disease patients in hospital setting. Systematic review and meta-analysis

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Scientific Program: Chronic and Inflammatory diseases.
Keywords: Nurse, family nurse, community nurse, respiratory nurse, COPD, primary care, secondary care, empowerment.

Abstract: Introduction/Objectives: Chronic obstructive pulmonary disease (COPD) is a chronic disease; however, an adequate follow-up of the disease can soothe the symptoms, improve quality of life and reduce mortality. In the field of hospital assistance, nursing is of great importance in follow-up. The objective was to synthesize the available evidence on the nurses-led interventions on the management of COPD patients in hospital setting.
Method: A systematic review and meta-analysis was carried out in the Medline, Embase and Lilacs databases. The search terms were used: “hospital nurs*”, “respiratory nurs*”, “chronic obstructive pulmonary disease*”, “asthma”, “chronic bronchitis*”, “emphysemas”; adapting the search to each database. Observational (case-control studies, cohorts, cross-sectional studies) and intervention studies (randomized or not), published between 01/01/2009 and 02/29/2020, and in which exist a nursing intervention in COPD patients in the hospital setting were included.
Results: 4322 references were identified, 17 of them met the inclusion criteria. The results of the included articles focused on the improvement of the quality of life, physiological aspects adn the empowerment of the COPD patient. Although the instrument used to determine outcomes differed, it seems to exist a positive effect of health education on smokers [differences of means: 1.09 (CI 95%: -2.11-4.28); I2=89%] and hospital admissions [differences of means: -0.33 (CI 95%: -0.89-0.23); I2=0%].
Conclusion: Health education carried out by nursing in hospital setting improves the physical state of the adult smoker patient with COPD. Also, there is a reduction in hospital admissions. Even though, it is necessary to carry out prospective studies evaluating similar outcome in order to improve the analytical heterogeneity observed.

IIc. " Measuring Spinal Mobility Using an Inertial Measurement Unit System: A Validation Study in Axial Spondyloarthritis"

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Scientific Program: Chronic and Inflammatory diseases.
Keywords: axial spondyloarthritis; spinal mobility; inertial measurement unit

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Abstract: Background: Portable inertial measurement units (IMUs) are beginning to be used in human motion analysis. These devices can be useful for the evaluation of spinal mobility in individuals with axial spondyloarthritis (axSpA).
Objectives: The objectives of this study were to assess (a) concurrent criterion validity in individuals with axSpA by comparing spinal mobility measured by an IMU sensor-based system vs. optical motion capture as the reference standard; (b) discriminant validity comparing mobility with healthy volunteers; (c) construct validity by comparing mobility results with relevant outcome measures.
Methods: A total of 70 participants with axSpA and 20 healthy controls were included. Individuals with axSpA completed function and activity questionnaires, and their mobility was measured using conventional metrology for axSpA, an optical motion capture system, and an IMU sensor-based system. The UCOASMI, a metrology index based on measures obtained by motion capture, and the IUCOASMI, the same index using IMU measures, were also calculated. Descriptive and inferential analyses were conducted to show the relationships between outcome measures.
Results: There was excellent agreement (ICC > 0.90) between both systems and a significant correlation between the IUCOASMI and conventional metrology (r = 0.91), activity (r = 0.40), function (r = 0.62), quality of life (r = 0.55) and structural change (r = 0.76). This study demonstrates the validity of an IMU system to evaluate spinal mobility in axSpA. These systems are more feasible than optical motion capture systems, and they could be useful in clinical practice.

IId. Aortic valve infiltrating pro-inflammatory cells in aortic stenosis patients

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Scientific Program: Chronic and Inflammatory diseases.
Keywords: Aortic Stenosis, Cardiovascular disease, inflammation, immunopathology

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Abstract: Aortic valve stenosis (AS) is a frequent cardiac disease in the elderly and is characterized by valvular calcification, fibrosis and inflammation, however its pathogenesis is not well known. AS has been traditionally considered a passive chronic degenerative process due to the accumulation of damage with age. Nevertheless, recent studies suggest that AS is similar to atherosclerosis, being an active inflammatory process. Particularly, it has been suggested that several immune cell types, present in the valve infiltrate, might contribute to its degeneration and to the progression towards stenosis. However, the valve inflammatory infiltrate has not been well characterized in any study regarding AS. Up to date there is no other treatment for the valve stenosis other than the replacement of the valve itself. Therefore, the characterization of the cells implicated in the inflammatory processes of the valvular stenosis is of outmost importance in order to develop new therapies for AS patients.
Here we present the first results of a recently developed protocol for the phenotypic characterization of aortic valve infiltrating cell populations in AS patients.

IIe. A mHealth based brief psychological intervention in self-efficacy for improving subjective self-management of the disease on patients with cardiovascular disease: A randomized, controlled, prospective trial.

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Scientific Program: Chronic and Inflammatory diseases.
Keywords: Cardiovascular disease; Self-efficacy; mHealth, Brief psychological intervention

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Abstract: Cardiovascular disease diagnosis implies a lot of changes in a person's life. An effective adherence to treatment, as well as, the incorporation of health-related habits and the acceptance of the disease are crucial for a healthy psychological functioning after diagnosis. Self-efficacy is known to be an important and trainable factor for improving self-management of chronic diseases, considered as an emerging essential aspect for intervening in health. Objective: This study aimed to promote self-efficacy in cardiovascular disease patients through a mHealth based brief psychological intervention. Method: A two-arm randomized controlled prospective trial study was carried out comparing an experimental group with a treatment as usual (TAU) group. The study sample (N = 42) were patients with cardiovascular disease diagnosis. The experimental condition received a psychoeducational session of 1 hour about self-efficacy, and a later, 2-weeks mHealth based self-efficacy intervention. The study variables were self-efficacy for managing chronic and cardiovascular disease. Five different time points were assessed over a period of 1.5 month: at baseline, after the psychoeducational session, after the mHealth intervention and at 2- and 4- weeks of follow-up. Results: After the psychoeducational session, the experimental group exhibited a better self-efficacy for managing the chronic disease. Also, it was found a better cardiac management self-efficacy in the experimental group over time and compared to the TAU group after mHealth intervention. Finally, the experimental group showed a higher self-efficacy for managing chronic disease compared to the TAU group in all evaluations. Conclusions: mHealth based brief psychological intervention in self-efficacy seems to be a good and an affordable alternative for improving the engagement in the management of the cardiac disease. Training in self-efficacy on cardiovascular patients could imply a better adjustment to the disease, and therefore, could help to reduce cardiac risk and to promote a better quality of life.

IIf. Role of Nox4 in acute kidney injury associated to massive intravascular hemolysis

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Keywords: intravascular hemolysis, AKI, Nox4, oxidative stress

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Abstract: Massive and recurrent intravascular hemolysis is associated to acute kidney injury (AKI). AKI is characterized by loss of kidney function due to development oxidative stress, inflammation and cellular death. NADPH oxidase 4 (Nox4) is the principal source of reactive oxygen spices (ROS) in the kidney. We aim to investigate the role of Nox4 in AKI associated to intravascular hemolysis.
We performed an experimental model of massive intravascular hemolysis by intraperitoneal administration of phenylhydrazine (200mg/kg) in wild type and Nox4 knockout mice. Animals were sacrificed 24h and 72h after induction of intravascular hemolysis. In other experiment, the Nox4 inhibitor GKT137831 (10 mg/kg) was injected intraperitoneally 24h prior to induction of hemolysis and mice were sacrificed 72h later. In both animal models, we collected urine, serum and kidneys to quantify renal function, oxidative stress, inflammation and cell death. We also performed in vitro experiments in murine tubular epithelial cells (MCT) and murine podocytes. We used the Nox4 inhibitor GKT137831 in cells stimulated with Hb and heme to identify the molecular mechanisms involved in Nox4 pathological effects.
Our results show that induction of hemolysis promoted loss of renal function (increased creatinine and BUN plasma levels), higher expression of the tubular injury marker NGAL, increased oxidative stress (HO-1, Ferritin, MDA, 4HNE) pro-inflammatory IL-6 expression, podocytes injury marker (Nephrin) and tubular cell death (TUNEL), mainly at 72h after hemolysis induction. Importantly, these pathological effects were reduced in Nox4 Knockout mice or mice treated with the Nox4 inhibitor GKT137831. In cultured tubular cells and podocytes stimulated with Hb and heme, the pre-treatment with GKT137831 reduced oxidative stress. We concluded the important role of Nox4 in the induction of AKI associated to massive intravascular hemolysis. Moreover, the inhibition of Nox4 may be a potential therapeutic target to prevent loss of renal function in patients with intravascular hemolysis.

IIg. Importance of planification and analysis of risk factors of primary failure of arterio-venous fistula

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Keywords: Arterio-Venous Fistula, hemodialysis, primary failure

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Abstract: Arterio-Venous internal fistula (FAVi) is the vascular access princess in patients with Chronic Kidney Disease (CKD) which need hemodialysis (HD) as renal replacement therapy. Primary failure, early thrombosis or non-adequate maturation are frequent complications in this kind of patients. The objective of the study was to analyze factors that can be implicated on primary failure of FAVi . FAVis done in two different centers belong to Hospital Universitario Reina Sofía, between 2017 and 2019. Demographics and biochemical parameters were recorded at the time of intervention (hemoglobin, calcium, phosphorous, parathyroid hormone (PTH), albumin, C reactive protein (PCR), cholesterol, triglycerides, ferritin and glomerular filtration) and comorbidities (hypertension, diabetes mellitus, obesity, peripheric vascular disease, ischemic cardiopathy and tobacco). In one of the two centers, surgeon make an echographic evaluation of vascular tree previous to intervention of FAVi.
A total of 264 FAVi were performed. 70% of patients had advanced CKD, 18% were on HD program and 3% were kidney transplant receipt. Mean of age was 65 years and 59% of male were present. A total of 34 FAVi presented failure. We did not find statistical differences on existing diabetes, statin treatment, antiaggregant or anticoagulant therapy, obesity, peripheric vascular disease, ischemic cardiopathy, previous central venous catheter and biochemical parameters at the moment of intervention between FAVi with or without failure. Primary failure was significantly more frequent in smoker patients and in patients without hypertension ($p<0.05$). FAVi performed in the center without echographic evaluation, primary failure was significantly higher than in the other center.
In conclusion, primary failure is a frequent complication, it is important to identify risk factors for decrease the incidence. An adequate planification with doppler previous to surgery is imperative to obtain the higher success with the FAVi.

IIh. Klotho plays a key role in early and long-term protection against acute kidney injure induced by rhabdomyolysis

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Scientific Program: Chronic and Inflammatory diseases.
Keywords: kidney, AKI, klotho, fibrosis, oxidative stress, inflammation, myoglobin, rhabdomyolysis

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Abstract: Acute kidney injury (AKI) is a common complication of rhabdomyolysis. This syndrome is characterized by the breakdown of the skeletal muscle and the release of muscular cell content to the bloodstream. Once filtered by the kidney, myoglobin (Mb) causes oxidative stress, inflammation, and tubular cell death. Klotho is an anti-aging protein mostly expressed by the kidney. In addition to its functions in the regulation of mineral metabolism, Klotho protects from renal injury during AKI.
We performed an experimental model of rhabdomyolysis in C57BL/6J mice by intramuscular injection (10 ml/kg) of 50% glycerol. Mice were sacrificed 3 and 6 hours or 1, 3, 7 and 30 days after glycerol administration. In another experiment, mice were injected intraperitoneally with 0.1 mg/kg recombinant mouse Klotho, or vehicle (PBS) 30 minutes before and 1, 3 and 5 days after glycerol injection. Blood, urine, and renal samples were collected. In addition, we carried out studies in murine tubular cells (MCTs) to study the molecular mechanisms involved in Klotho regulation.
Rhabdomyolysis induces an early decrease of Klotho, in line with augmentation of creatinine concentration, kidney inflammation and tubular injury. Moreover, patients with rhabdomyolysis also showed lower plasma Klotho levels and increased FGF23 plasma concentration than healthy individuals. Klotho protein expression remained reduced one month after rhabdomyolysis-induction, in line with long-term renal fibrosis and macrophage accumulation. Exogenous Klotho administration ameliorated renal function and reduced cell death, oxidative stress, and tubular damage 24h after glycerol injection. In the same line, Klotho administration during AKI reduced renal fibrosis and macrophage infiltration one month later. Antioxidant therapies with N-acetylcysteine (NAC) and sulforaphane, a Nrf2 inducer, reverted Mb-mediated Klotho decrease in MCT. Our findings are the first to demonstrate lower renal and soluble Klotho expression in rhabdomyolysis-induced AKI, both during the acute phase and the long-term consequences. We also provide novel mechanisms involved in Klotho regulation and the potential therapeutic use of Klotho in patients with this syndrome.

IIi. Protective behavioral strategies on alcohol consumption and the moderating role of drinking-group gender composition

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Scientific Program: Chronic and Inflammatory diseases.
Keywords: protective behavioral strategies; alcohol consumption; group composition; gender differences

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Abstract: Background. There is international concern about the negative consequences for health related to young people's alcohol consumption. Peer relationships can play a positive and protective role to cope with risky behaviors associated with alcohol consumption. Objective. This study investigated the influence of protective behavioral strategies (PBS) on alcohol consumption and the moderating role of drinking-group gender composition and drinking-group size. Methods. The sample comprised 286 youths (mean age = 23.49; SD = 2.78; 67.5% female). Participants reported their protective behavioral strategies, their alcohol consumption and the size (overall mean = 7.44; SD = 3.83) and gender composition (62.58% mixed; 19.93% all-female; 9.8% all-male) of their social drinking groups. The mean sizes of mixed, all-female, and all-male groups were 8.27, 5.34, and 6.2, respectively. Results. Data showed that women consume less alcohol and use more protective strategies than men, particularly those strategies directed at avoiding negative consequences. Furthermore, the number of men in a group influences protective strategies and consumption, therefore drinking-group gender composition moderates the relationship between protective strategies and alcohol consumption. The more protective strategies that young adults use, the lower their alcohol consumption. This relationship is moderated by the size of the group. Conclusion. Strategies to prevent risky drinking behavior should focus on both PBS shared by drinking-group members and the training in individual PBS associated with drinking behavior. Finally, taking into account the relationship between drinking-group gender composition and protective behavioral strategies for alcohol consumption, a positive protector role for individual and group habits in relation to alcohol consumption is discussed.

IIj. Palliative care experience of healthcare personnel and primary caregivers: a systematic review

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Scientific Program: Chronic and Inflammatory diseases.
Keywords: spiritual care, palliative care, accompaniment, interventions.

Abstract: Background: Healthcare personnel play an essential role in how their patients prepare for the dying moment. An accompaniment to the patient and the family is essential, allowing them to settle their affairs and death to be accepted as a natural process and live in peace, thus humanizing the dying process (Pichardo García et al. 2010).
Objectives: To synthesize the scientific production related to experiences and/or perception of healthcare personnel and primary caregivers in palliative care units regarding spiritual accompaniment.
Method: A systematic review was carried out. The search for articles was carried out in various electronic databases: PubMed, ProQuest and Cochrane between the months of May and June 2020. Period 2015-2020. The search was carried out with the following Keywords: spiritual care, palliative care, accompaniment, interventions. Observational studies and qualitative studies, published in Spanish and English in the last 5 years were included.
Results: Four articles met the inclusion criteria. Of the included studies, healthcare personnel were dissatisfied due to the slow diffusion of research in palliative care because of the existing biomedical model. They referred to the existing resistance in the matter, by the culture and they saw in a very positive way, the role of palliative care in chronic diseases. Regarding the main or family caregivers, it was evident that they had little information on palliative care. They declared that they had a good relationship with health personnel, valuing their presence, availability and open dialogue. They also highlighted the great importance of health personnel in accompaniment and psychological support.
Conclusion: There is reduced evidence on the perceptions and / or experiences of health personnel and main caregivers in the spiritual approach carried out in palliative care units. Palliative care training and research is essential for both healthcare staff and primary caregivers of patients.

IIk. Effects of components of milk on oxidative damage and dysbiosis in multiple sclerosis based on the latter's experimental model "Autoimmune encephalomyelitis"

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Scientific Program: Chronic and Inflammatory diseases.
Keywords: Bacterial lipopolysaccharide, Casein, Experimental Autoimmune Encephalomyelitis, Glutathione redox system, Lactose, Multiple Sclerosis.

Abstract: Experimental autoimmune encephalomyelitis (EAE) in rats closely reproduces multiple sclerosis (MS), a disease characterized by neuroinflammation and oxidative stress, that also appear to extend to other organ compartments. The origin of MS is a matter for discussion but it would seem that altering certain bacterial populations present in the gut may lead to a proinflammatory condition due to the bacterial lipopolysaccharides (LPS) in the so-called brain-gut axis. The casein and lactose in milk confer anti-inflammatory properties and immunomodulatory effects.
Twenty male Dark Agouti rats were divided in control rats, EAE rats and EAE rats to which casein and lactose were administered. Fifty-one days after casein and lactose administration, the rats were sacrificed and different organs studied. In the latter, products derived from oxidative stress were studied (lipid peroxides and carbonylated proteins) as well as the gluthatione redox system, various inflammation factors (total nitrite, Nuclear Factor-kappa B p065, the Rat Tumour Necrosis Factor-β and the LPS values.
Casein and lactose administration improved the clinical aspect of the disease at the same time as reducing inflammation and oxidative stress, exerting its action on the gluthatione redox system.

III. A serum magnesium concentration lower than 2mg/dl predicts mortality in chronic kidney disease patients. A propensity score matching study

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Keywords: serum magnesium, chronic kidney disease, mortality

Abstract: Introduction: Decreased serum magnesium may be associated with mortality and vascular calcifications. There is limited information on the impact of low magnesium (mg) in CKD stage 4 patients. We aimed to evaluate whether serum mg levels are associated with mortality in a matched population of CKD patients.
Methods: Patients were stratified into tertiles according to serum mg (T1<2.0 mg/dl, T2 = 2.01-2.39 mg/dl and T3>2.4 mg/dl). For survival analysis, we used log-rank tests to compare Kaplan-Meier (KM) probability of death curves and performed uni- and multivariable Cox regression analysis. Given the comparable survival among patients in T2 and T3, serum mg below or above 2 mg/dl were used to further perform propensity score matching (PSM) to minimize any potential confounding and selection biases between tertiles. We used the derived propensity scores to match the groups in a 1:1 ratio. Further, it was performed survival analysis with the matched population.
Results: This study included 1002 patients evaluated in the advanced-CKD outpatient clinic from 2009 to 2018. During the study follow-up, 158 died, 84 from T1, 34 from T2, and 35 from T3. KM showed that patients from T1 had a worse survival as compared with T2 and T3 (p<0.001; Figure 1A). Multivariate Cox proportional hazard showed that patients with mg <2 mg/dl had a higher mortality risk (HR 1.61, CI 1.05–2.46) as compared to the other groups. After matching, it was obtained an adjusted population of 343 patients with mg <2 mg/dl and 343 with higher concentrations of mg. Survival analysis with PSM-adjusted cohorts showed that patients with mg <2 mg/dl had a worse survival compared to T2 and T3 (log-rank p=0.01; HR 1.73, CI 1.02–2.36, p=0.44; Figure 1B)
Conclusion: In appropriately-matched patients, a serum mg <2 mg/dl predicts mortality.

IIm. Role of endothelial microvesicles released by p-cresol on endothelial dysfunction

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Scientific Program: Chronic and Inflammatory diseases.
Keywords: Endothelial cells, endothelial dysfunction, endothelial microvesicles, p-cresol, microRNA, uremic toxins.

Abstract: Protein bound uremic toxins, such as p-cresol, cannot be effectively removed by conventional dialysis techniques and are accumulated in plasma, thus contributing to progression of both chronic kidney disease (CKD) and cardiovascular disease (CVD). Pathological effects of uremic toxins include activation of inflammatory response, endothelial dysfunction and release of endothelial microvesicles. To date, the role of p-cresol in endothelial microvesicles formation has not been analyzed. The aim of the present study was evaluate the effects of endothelial microvesicles released by p-cresol (PcEMV) on endothelial dysfunction. An in vitro model of endothelial damage mediated by p-cresol was proposed to evaluate the functional effect of PcEMV on the endothelial repair process carried out by endothelial cells and microRNA (miRNA) that could be involved in this process. We observed that p-cresol induced a greater release of microvesicles in endothelial cells. these microvesicles altered regenerative capacity of endothelial cells, decreasing their capacity for cell migration and their potential to form vascular structures in vitro. Moreover, we observed increased cellular senescence and a deregulation of miRNA-146b-5p and miRNA-223-3p expression in endothelial cells treated with endothelial microvesicles released by p-cresol. in summary our data show that microvesicles generated in endothelial cells treated with p-cresol (PcEMV) interfere with the endothelial repair process by decreasing the migratory capacity, the ability to form new vessels and increasing the senescence of mature endothelial cells. these alterations could be mediated by the upregulation of miRNA-146b-5p and miRNA-223-3p

IIn. Quality of life in patients with chronic kidney insufficiency that start dialysis

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Keywords: Quality of life; Renal Dialysis; Renal Replacement Therapy; Chronic Renal Insufficiency

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Abstract: OBJECTIVE: To assess the impact of the start of hemodialysis (HD) on health-related quality of life (HRQOL) at the beginning and three months, as well as its relationship with anxious/depressive symptoms and medical-clinical variables.
PATIENTS AND METHODS: Prospective longitudinal study in patients with end-stage chronic kidney disease (CKD) who started HD. HRQL was evaluated using the KDQOLTM-36 and Euroqol-5D questionnaires while collecting socio-demographic and medical-clinical variables.
RESULTS: Statistically significant differences were described in the symptom problems list (t14=5,11; p<0,001) and in the visual analogue scale (VAS) (z=1,89; p=0,002). Furthermore, in patients with anxious/depressive symptoms at the beginning, significant differences were found in the mental component summary (MCS) (t7=2,84; p=0,025) and the burden of kidney disease (t7=2,45; p=0,044). A negative correlation was found between changes during the first three months of HD in physical component summary (PCS) and phosphorus (r=-0,59; p=0,021) and between erythropoietin dose and EVA score (rho=-0,58; p=0,023).
CONCLUSIONS: An improvement in HRQL is found three months after the onset of HD, which results statistically significant in the symptom problems list and VAS. Those who start HD with anxious/depressive symptoms achieve a remarkable improvement, reaching values close to those who do not suffer from them. There is a negative correlation in the changes produced in the first three months of HD between phosphorus and PCS levels and also between erythropoietin dose and EVA.

IIñ. ASAS Health Index in patients with spondyloarthritis and its association with disease activity and disease burden including fibromyalgia

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Keywords: ASAS-HI, spondyloarthritis, fibromyalgia.

Abstract: Objectives: Several studies have shown that disease activity and functionality have an impact on the quality of life in patients with Spondyloarthritis (SpA), evaluated with the ASQoL questionnaire. The ASAS Health Index (ASAS-HI) questionnaire, a tool that measures the impact of the disease on the health in these patients, has been recently validated. However, there are still no studies evaluating the utility of this questionnaire in daily clinical practice. Therefore, the objective of this study is to evaluate the association of ASAS-HI with disease activity and disease burden in patients with SpA.
Methods: This is an observational, cross-sectional and single-centre study from the Córdoba AxSpA Task force, Registry and Outcomes (CASTRO) in which 126 consecutive patients with SpA were included. Scores related to disease activity (BASDAI and ASDAS), functionality (BASFI), structural damage, mobility, health and the presence of concomitant fibromyalgia (FM) were obtained from all patients. The ASAS-HI questionnaire was considered as the main outcome (scale from 0 to 17). Pearsonβs correlation coefficient was used to evaluate the association of the different continuous variables with each other. Studentβs t-test was used to compare the ASAS-HI between different subgroups of patients (men vs. women, ASDAS>2,1 vs. ASDAS≤2,1 and fibromyalgia + vs. fibromyalgia-). Finally, a multivariate linear regression was performed to determine which factors explain the variability of ASAS-HI in these patients.
Results: Among the 126 patients included, 83 (65.9%) were men, with a mean age of 45.1±12.3 years and a mean disease duration of 18.7±14.5 years. The mean ASAS-HI score in all patients was 4.6±3.9, showing a βstrongβpositive linear correlation (r>0.60) with BASDAI and BASFI, and βmoderateβpositive (r=0.40 to 0.60) with Global VAS and ASDAS (Figure 1). Patients with FM showed a significantly higher ASAS-HI score compared with patients without FM (9.5±3.2 vs 3.7±3.4, respectively). In addition, patients with high disease activity (ASDAS>2,1) showed a higher mean score in ASAS-HI compared with those with low activity (ASDAS≤2,1) (5.8 ± 3.8 vs 2.0 ± 2.4, p<0,001).
Finally, multiple linear regression showed that 57,4% (R2=0,574) of the ASAS-HI variability is explained by the presence of concomitant FM (β= 2.23, 95%IC 0.73 to 3.80, p=0.004), BASDAI (β= 0.62, 95%IC 0.25 to 0.97, p=0.001) and BASFI (β= 0.57, 95%IC 0.26 to 0.88, p=0.001).
Conclusions: In our study, the impairment of the quality of life in patients with SpA was mainly associated with a high disease activity (BASDAI) and worsening functionality (BASFI). Moreover, FM can coexist with SpA, worsening the quality of life of these patients and therefore impacting the scores on questionnaires used for evaluation of the patients and PROs. This could influence therapeutic decisions. In the same way, in clinical practice scenarios, for patients with SpA who score high on the different questionnaires, we must rule out the presence of concomitant FM, especially in women."

IIo. New cut-off point for waist circumference to predict metabolic syndrome in older women

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Scientific Program: Chronic and Inflammatory diseases.
Keywords: Anthropometry, Diagnosis, Geriatrics, Metabolic syndrome, Primary Care, Rural Health.

Abstract: Background and Objectives: Metabolic Syndrome (MetS) is more prevalent in the elderly and needs to be diagnosticated by at least three variables. One such variable is waist circumference (WC), which in the case of men and women must be greater than 102 cm and 88 cm, respectively. The main objective is to know which cut-off point of the waist circumference most accurately predicts metabolic syndrome in older people according to gender.
Research Desing and Methods: A study of MetS prevalence was made at the Lucena health center. The anthropometric variables analyzed were: body mass index, waist circumference (WC), waist-height ratio, body fat percentage, and waist-hip ratio. A crude and adjusted binary logistic regression was performed, and operator-receptor curves were obtained for determining the predictive capacity of those variables.
Results: The prevalence of the MetS in older women was 53.2%. Although the cutting point of the WC was 102.75 cm in older men, very close to the official cutting point with sensibility=86.8%, specificity=61.3%, and Youden Index=0.48. For older women, the WC of 93.25 cm was shown to be the cut-off point with the greatest predictive value in older women with sensibility=82.9%, specificity=62.7%, and Youden Index=0.46.
Discussion and Implications: The cut-off point for the WC in men is similar in the general population to that in the elderly, with a value of 102 cm. However, in the case of older women, the cut-off point with the highest predictive capacity is 93.25 cm, compared to the official 88 cm. A new cutting point in older women for the WC should be valued.

IIp. Homelessness, an invisible health problem?

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Keywords: Homeless people; Disease; Discrimination; Nursing

Abstract: Objectives: Determining the main health problems homeless people are exposed to in Cordoba; as well as studying the possible relation between homelessness and health. Identifying the role that Nursing can play within this population group.
Material and methods: Cross-sectional study. Through a simple random sampling without replacement, between the homeless people who spent the night in an Organization shelter for social interest purposes and also those who received assistance on the street with the night care device in Córdoba between October 2019 and Included on March 2, 2020. The number of homeless people who participated in the study was 62.
Results: 52 homeless people suffered from a serious or chronic diagnosed illness, 79% acknowledged that their state of health was deficient or bad. Significant relations were found between suffering from an illness and having been assaulted, insulted and deceived ($p<0.05$), having been admitted to hospital in the last year ($p<0.05$), having a recognised disability ($p<0.05$), having stopped eating at some time during the day in the last week ($p<0.05$) and having emigrated or changed location ($p<0.05$). In turn, there was no evidence of relation with the variables: insomnia, tobacco, alcohol or drugs. The whole group stated that they had suffered some type of discrimination since they had been homeless.
Conclusions: Homelessness predisposes to health problems and discrimination, especially if you are a woman. Nursing is key to the follow-up of this population.

IIq. Detection of early pulmonary damage in patients with severe mental illness

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Scientific Program: Chronic and Inflammatory diseases.
Keywords: Pulmonary damage, Chronic Obstructive Pulmonary Disease, Severe Mental Ilness, Schizophrenia, Bipolar Disorder, Tobacco, Spirometry

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Abstract: People with severe mental illness (SMI) have a reduction of their life expectancy of at least 20 years. The main causes are cardiovascular and respiratory diseases (preventable natural deaths). With consumption rates similar to those of the general population 50 years ago, smoking is the highest preventable risk factor for premature mortality in SMI. Smokers with SMI: start smoking earlier, develop higher dependency levels and have a qualitatively more intense smoking habits (they smoke faster and deeper). The hypothesis is that these patients might develop greater lung damage and earlier than general population. This damage may be explained due to tobacco smoking, which is the main risk factor. Furthermore, smoking makes the mental illness worse. Smoking cessation could recover 10 life years.

IIr. The role of the plasma exchange in Anti-Glomerular Basement Membrane Disease

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Keywords: Anti-glomerular basement membrane disease, plasma exchange

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Abstract: INTRODUCTION: Anti-glomerular basement membrane (GBM) disease is characterized by the presence of circulating and deposited antibodies directed against basement membrane antigens and usually leads to rapidly progressive glomerulonephritis. The concurrence of ANCA is common. Treatment aims to rapidly remove pathogenic autoantibody, typically with the use of plasma exchange, along with steroids and cytotoxic therapy. In this study, we aimed to assess clinical features and outcomes in a large cohort of patients with this disease and the efficacy of the treatment in these patients.
METHODS: This is a retrospective multicentric observational study including 48 patients from 14 nephrology departments belonging to the Spanish Group for the Study of Glomerular Diseases with biopsy proven anti-GBM disease (positive glomerular linear IgG staining detected by immunofluorescence) +/- positive serum anti-GBM antibodies detection during the years 1999-2019. ANCA positive patients (double positive) also were included. Demographic, clinical and analytical variables were evaluated at the time of the biopsy.
ESRD development (dialysis or renal transplant) were evaluated. Clinical course in those patients who received a renal transplant was observed during the follow-up.
RESULTS: The mean (SD) age was 59 (±19) years. In total, 13 patients (27%) had pulmonary hemorraghe. The creatinine at the time of the biopsy was 6.9 (4.54-11.03) mg/dl. 88% required dialysis on admission. The average percentage of crescents in each renal sample was 76 (+/-26.76)%. In 94% of patients kidney biopsy sample immunofluorescence for IgG showed linear deposits along the glomerular basement membrane. Forty-four patients (91%) undergo plasma exchange and the majority received immunosuppression treatment that in most cases included steroids and cyclophosphamide. 41 patients (85.4%) developed ESRD, in most cases occurs in the initial phase of the disease. Twelve patients (25 %) died in the follow up. Seven patients (14.6%) remained free of dialysis in the follow-up with a mean serum creatinine of 1.99 (+/-0.73) mg/dl. In Kaplan-Meier analysis, kidney survival at 1 and 2 years was 27% and 20,5% respectively. Fourteen patients (29.2 %) underwent a renal transplant in the follow-up, the median creatinine in transplantation was 1,3 (0,9-2) mg/dl. No patients exhibited evidence of relapse in the graft.
CONCLUSIONS: Anti-glomerular basement membrane disease is a poor prognosis entity. Plasma exchange treatment seems not improve renal prognosis. Patients with antiGBM disease who undertaked a renal transplant, exhibited evidence of relapse in the graft".

IIs. Endoscopic findings not associated with portal hypertension in patients with liver cirrhosis undergoing screening endoscopy

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Keywords: Esophagogastroduodenoscopy. Liver cirrhosis. Portal hypertension. Peptic ulcer disease.

Abstract: Background: Patients with liver cirrhosis undergo endoscopic screening to detect esophageal varices. The aims of our study were to describe the prevalence of endoscopic lesions unrelated to portal hypertension in patients with cirrhosis and to identify the risk factors for their development.
Methods: Cross-sectional, unicentric study including a consecutive cohort of patients with liver cirrhosis who underwent an upper gastrointestinal endoscopy to screen for esophageal varices within a 5-year period (2013-2018). Patients under 18 were excluded.
Results: 379 patients (22.2% women, mean age: 57.5±11.4 years) were included in the analysis. Alcohol (54.6%, n=207) was the most common cause of cirrhosis, followed by the viral hepatitis C infection (14.2%, n=54). Main Child-Pugh stage was 6.8±2.1 and MELD was 11.7±5. Fifty-eight percent of patients were active or previous smokers. The prevalence of endoscopic lesions unrelated with portal hypertension was 39.6% (n=150): 15.8% erosive gastritis, 4% peptic ulcer, 12.7% duodenitis, 13.5% oesofagitis and 10% hiatal hernia. We observed peptic disease (erosive gastritis, duodenitis and/or peptic ulcer) in 96 patients, among whom urease was obtained in 54 cases (56.2%). Positive urease rate was 44.4%. The presence of endoscopic lesions unrelated to portal hypertension was not influenced by age (p=1), gender (p=0.28) nor liver function (MELD p=0.71, Child-Pugh p=0.54). Smoking habit showed a trend towards increased prevalence of endoscopic lesions unrelated to portal hypertension (43.2% vs 34.6%; p=0.09), which reached statistical significance for peptic ulcer (6.4% vs 0.6%, p=0.005) and peptic duodenitis (17.3% vs 6.3%; p=0.002). The prevalence of endoscopic lesions unrelated to portal hypertension in alcoholic cirrhosis and/or smoking history was as high of 43% (n=101).
Conclusions: Among cirrhotic patients, a history of smoking and/or alcohol consumption is associated with increased prevalence of endoscopic lesions unrelated to portal hypertension, being some of them severe. Endoscopic surveillance should be more exhaustive in this subset of patients.

IIt. Assessment of the relationship between cardiovascular risk and structural damage in patients with axial spondyloarthritis

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Keywords: Axial spondyloarthritis, cardiovascular risk, structural damage, carotid intima media thickness, disease activity.

Abstract: Introduction: Spondyloarthritis (SpA) is a group of chronic inflammatory disorders that present different but related phenotypes including ankylosing spondylitis (AS) (currently known as radiographic axial spondyloarthritis (r-axSpA)). This disease is related to the presence of some comorbidities, being the most common in these patients osteoporosis and cardiovascular (CV) involvement, especially atherosclerosis. Objectives: To evaluate the association of cardiovascular (CV) risk and subclinical atherosclerosis with radiographic structural damage in patients with axial spondyloarthritis (axSpA).
Methods: Cross-sectional study including 114 patients axSpA from the SpA registry of Córdoba (CASTRO) and 132 age- and sex-matched healthy controls (HCs). Disease activity and the presence of traditional CV risk factors were recorded. The presence of atherosclerotic plaques and carotid intima media thickness (cIMT) were evaluated through carotid ultrasound and the SCORE index was calculated. Radiographic damage was measured through modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). The association between mSASSS and SCORE was tested using generalized linear models (GLM), and an age-adjusted hard cluster analysis was performed to identify different phenotypes dependent on the subclinical CV risk.
Results: Increased traditional CV risk factors, SCORE and the presence of carotid plaques were found in axSpA patients compared to the HCs. The presence of atherosclerotic plaques and levels of SCORE were associated with radiographic structural damage. The GLM showed that the total mSASSS was independently associated with the SCORE adjusted for age, tobacco and C-reactive protein. Hard cluster analysis identified two phenotypes of patients. Patients from cluster 1, characterized by the presence of plaques and increased cIMT, had a higher prevalence of CV risk factors and SCORE, and more structural damage than cluster 2 patients.
Conclusions: Radiographic structural damage is closely associated with increased CV risk: higher SCORE levels in axSpA patients were found to be independently associated with mSASSS after adjusting for age, CRP and tobacco.

Infectious and Immunological diseases. Organ transplantation

IIIa. Enterocytozoon bieneusi in Iberian pigs and wild boar in Mediterranean ecosystems from Spain: are they a potential source of zoonotic infection?

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Keywords: Enterocytozoon bieneusi; immunosuppressed; zoonotic; emergent; wildlife; Iberian pigs.

Abstract: Microsporidia is a phylum of obligate emergent intracellular protist-like fungi pathogens that infect a broad range of hosts including vertebrates and invertebrates. Enterocytozoon bieneusi is the most common cause of microsporidiosis in humans, affecting primarily immunosuppressed patients but also reported in immunocompetent individuals. Epidemiological information on the presence and molecular diversity of E. bieneusi in livestock and wildlife in Spain is limited. Therefore, the occurrence of this zoonotic microsporidia was investigated in sympatric extensively reared Iberian pigs (n = 186) and free ranging wild boars (n = 142) in the province of Córdoba, Southern Spain. Forty-two Iberian pigs (22.6%) and three wild boars (2.1%) were found E. bieneusi positive by PCR. In Iberian pigs, occurrence of E. bieneusi was significantly higher in sows than in fattening pigs (31.6% vs. 11.4%; p = .001). Five genotypes were identified in Iberian pigs, four previously reported (EbpA, PigEb4, O, Pig HN-II) and a novel genotype (named PigSpEb1), while only two genotypes were identified in wild boars, EbpA and novel genotype PigSpEb1. All five genotypes identified belong to Group 1 suggesting zoonotic potential. This study constitutes the first report on the occurrence and molecular characterization of E. bieneusi in Iberian pigs and wild boars. The identification of two genotypes with zoonotic potential in sympatric Iberian pigs and wild boars suggests that E. bieneusi can be potentially transmitted between those two hosts, but also implies that they may act as natural sources of microsporidia infection to other hosts including humans.

IIIb. Are wild lagomorphs a source of Hepatitis E virus transmission for humans?

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Scientific Program: Infectious and Immunological diseases. Organ transplantation.
Keywords: Genotype 3, hepatitis E virus, public health, zoonosis, Iberian hare, wild rabbit.

Abstract: In recent decades, cases of autochthonous hepatitis E (HE) have sharply increased in European countries where foodborne transmission is considered the main route of HE virus (HEV) transmission. Although rabbits are considered the main reservoir of the zoonotic HEV-3ra subtype, information on the role of wild lagomorphs in the epidemiology of HEV remains scarce. The aim of this study therefore was to assess the circulation of HEV in European wild rabbits (Oryctolagus cuniculus) and Iberian hares (Lepus granatensis), the most important lagomorph species in Spanish Mediterranean ecosystems. Liver samples from 372 wild rabbits and 78 Iberian hares were analyzed using a broad-spectrum RT-PCR that detects HEV genotypes 1 to 8. None of the 450 lagomorphs tested (0.0%; IC95%: 0.0-0.8%) were positive for HEV infection. To the best of our knowledge, this is the first study to assess HEV circulation in wild rabbits in Spain and the first to evaluate HEV infection in Iberian hares. Our results indicate absence of HEV circulation in wild rabbits and Iberian hares in southern Spain during the study period, which suggests that the risk of transmission of HEV from wild lagomorphs to other species, including humans, is low.

IIIc. Hepatitis E virus in people living with HIV: first report of HEV-3ra infection in Spain

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Scientific Program: Infectious and Immunological diseases. Organ transplantation.
Keywords: Hepatitis E virus; Emerging; HIV; Emergence; HEV-3ra; Rabbit; Zoonotic.

Abstract: Hepatitis E (HE) is an emerging infectious disease that affects more than 20 million people annually around the world. In Europe, although most cases are related to HEV genotype 3, an important number of new viral zoonotic strains have emerged. These isolates have been described in a high proportion of patients with chronic hepatitis, suggesting that those patients with underlying immunosuppression could be more susceptible to these emerging strains of HEV. The objective of our study was to assess the prevalence and incidence of HEV in people living with HIV (PLWH) in a Spanish national cohort. A retrospective longitudinal study was conducted including 845 PLWH recruited in the cohort of adult HIV-infected patients of the AIDS Research Network in follow-up at 28 Spanish hospitals in 2014 and 2015. All samples were tested for anti-HEV IgG and IgM antibodies and for HEV-RNA. Samples with detectable HEV viral loads were genotyped. At baseline, 101 patients were positive for HEV IgG antibodies (11.9%), none had HEV IgM antibodies, and two presented HEV RNA (0.23%). Forty-two seroconverted for IgG, supposing a cumulative incidence of 5.7%. One subject was positive for IgM (0.13%), and two showed detectable HEV RNA (0.27%). Phylogenetic analyses were carried out in three samples. Two sequences belong to subtype 3f whereas one was the emergent and zoonotic sutbype HEV-3ra, whose main reservoir is rabbit. Our results showed the potential risk of zoonotic transmission of this emerging subtype in Spain.

IIId. Risk Factors for 90-day all-cause mortality in asymptomatic KPC-KP rectal carriers: the impact of the KPC-KP gut load

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Scientific Program: Infectious and Immunological diseases. Organ transplantation.
Keywords: Colonization, bacterial load, Klebsiella pneumoniae carbapenemase-producing Klebsiella pneumoniae (KPC-KP), mortality.

Abstract: Introduction: Mortality related to KPC carbapenemase-producing Klebsiella pneumoniae (KPC-KP) has become a major public health problem. Increased relative abundance of specific bacterial taxa in the gut microbiota (bacterial load) and bacteremia has been reported in high-risk patients. We aimed to evaluate the impact of KPC carbapenemase-producing Klebsiella pneumoniae (KPC-KP) load on 90-day mortality.
Materials/methods: Observational, prospective cohort study enrolling asymptomatic KPC-KP rectal carriers from January 2018 to March 2020. KPC-KP gut load measured on day 0 (basal load), and monthly thereafter by quantitative real-time PCR (percentage of copies of blaKPC relative to 16S rRNA genes in rectal swab samples). Primary study end point: 90-day mortality. To analyze variables associated with 90-day mortality, we adjusted a Cox regression model, stratifying by presence of bacteriemia. Non-significant variables in bivariate Cox regression were removed, as long as the rest of coefficients in the model were not significantly altered, and proportional hazard assumption was confirmed.
Results: 80 patients included (58% female, median age 84, range 74-88) with several comorbidities (44% diabetes mellitus, 21% chronic renal disease, 18% tumor, 15% recurrent urinary tract infections). 85% hospitalized at enrollment [median length of hospital stay (LOHS) 16 days, range 9-28]. Crude 90-day mortality: 41.3%. In univariate Cox regression, 13 variables were associated with time to death, including KPC-KP basal load, both as continuous variable (HR 1.04%, 95% CI 1.02%-1.07%) and dichotomized (cut-off 7%, HR 2.6%, 95% CI 1.2%-5.6%). Stratifying by bacteremia, the final Cox regression model included the following 3 variables: age (HR 1.07, 95% CI 1.03-1.11, p=0.004), basal KPC-KP load (HR 1.03, 95% CI 1.00-1.06, p=0.027), and LOHS (HR 3.13, 95% CI 1.45-6.78); and showed a concordance index of 0.743.
Conclusions: In this population, KPC-KP basal load was associated with 90-day crude mortality, with a 3% increased risk of death per increased unit of basal load.

IIIe. COVID-19 infection and digestive symptoms. Analysis of an outpatient geriatric population

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Keywords: COVID-19, diarrhea, geriatrics, fever, symptoms.

Abstract: We analyzed the COVID19 positive cases found in a nursing home.
Patients: 147 residents were followed during March and April 2020.
Results: COVID19 infection was detected in 71 people (48,3%) by PCR and/or rapid test for specific antibodies and 39,4% (IC 95%: 28,0-51,7) of them were asymptomatic. 77,4% (IC95%: 66,0-86,6) of the positive patients were women and the mean age was 84.1 years old (DE=11,3). Diarrhea was the most frequent symptom (50%), followed by cough (41,9%) and fever (40,5%). Diarrhea was detected on the first day in 90,4% of cases. In 33,3% (IC95%: 19,5-49,5), diarrhea was associated with other symptoms and in 16,6% (IC95%: 6,9-31,3) it coursed isolated. The average duration of the symptoms were 11,7 days. 30,2% (IC95%: 17,1-46,1) of patients required hospital admission and 16,2% (IC95%: 6,8-30,7) of them died by respiratory complications or sepsis
Conclusions: Gastrointestinal symptoms could be frequent in COVID19 infection and even be the first manifestation of the disease. These group of patients presented a lower proportion of complications and fatality than usual.

IIIf. Analysis of quality of life in patients with simultaneous kidney pancreas transplantation

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Keywords: Pancreas, Kidney, Diabetes, transplant.

Abstract: Background: Simultaneous Kidney pancreas transplant (PKT) is considered the best treatment for selected patients with type 1 diabetes mellitus (DM1) and end-stage renal disease. The evolution in the latest surgical techniques and the improvement in immunosuppressive protocols have allowed us to offer considerable survival benefits in patients with T1DM who receive a PKT transplant, however, the impact on quality of life has been poorly studied.
Methods: Comparative cross-sectional study to evaluate the quality of life in 50 patients transplanted simultaneously with pancreas and kidney (SPK) between 2013-2019 in our program and 50 patients with T1DM on insulin treatment and preserved renal function (n = 100). Transplanted patients with dysfunction of any of the grafts were excluded. The Health Related Quality of Life (HRQL) was evaluated with the SF-36 survey. To assess satisfaction with diabetes treatment, the DTSQ-s questionnaire was used. The surveys were carried out by telephone with oral consent.
Results: There were no differences in the baseline characteristics of both groups. The SPK group presented higher scores for the General Health, Physical Function, Physical Role, Vitality, Social Function, Emotional Role and Mental Health scales, the differences being statistically significant (P <0.05). The SPK group presented a higher perception of Body pain (P <0.001). Satisfaction with treatment (DTSQ-s questionnaire) was significantly higher in the SPK group compared to DM1 patients (33.90 ± 2.28 vs. 27.75 ± 8.45; 6.15 [3.18- 9.11]; P <0.001). The perceived episodes of hypoglycemia and hyperglycemia were significantly lower in the SPK group (p <0.001).
Conclusions: SPK transplantation shows greater satisfaction with treatment, less impact of diabetes on quality of life and an improvement in quality of life compared to insulin treatment in type 1 diabetic patients. SPK transplant patients they present a higher perceived body pain.

IIIg. The determinant factors of the hemodynamic and cryopreserved pulmonary homograft dysfunction implanted during the ross surgery in pediatrics patients

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Keywords: Pediatric patients, Ross Procedure, Pulmonary homograft, Pulmonary stenosis, Reintervention.

Abstract: Cryopreserved pulmonary homograft is currently the treatment of choice for reconstructing RVOT in Ross's intervention, with pulmonary homograft stenosis being the main complication in the early and late postoperative period, although the factors involved, as well as its clinical implications, are still unknown. Long-term follow-up of patients is excellent in terms of overall survival and event-free, with the "risk of reoperation" being low.
The purpose of this study was to evaluate the outcome and risk factors for implant failure in pediatric patients who underwent pulmonary position homograft placement for right ventricular outflow tract obstruction and to know the most prevalent hemodynamic factors in the dysfunction of cryopreserved pulmonary homografts implanted in pediatric Ross surgery.
An observational, descriptive, longitudinal, retrospective, and Unicenter study (Reina Sofía University Hospital, Córdoba) Corresponding to a series of pediatric patients operated by Ross procedure from 1997 to November 2020 inclusive, including patients undergoing Ross-Konno surgery was performed.
Adverse events related to pulmonary homografts, such as PHS and/or the need for reintervention techniques during the follow-up interval, will be collected.
For statistical analysis, data will be analyzed with the SPSS® version 25 statistical package. Measurements will be expressed as mean ± standard deviation. For univariate analysis, we will use the χ^2 test, the Fisher Exact test, and the Student-t-test.
The comparison of the demographic data and the pre- or post-operative data between the groups will be done with the use of an unpaired t-test. The accepted p-statistic value is <0.05 as significant, with 95% confidence intervals and 80% statistical power. The Kaplan-Meier analysis will be used to represent the probability of the absence of stenosis and homograft reintervention at various time points. As the main limitation, we would have the characteristic of being an observational study. The project has been approved by the Provincial Committee of Ethics.

IIIh. Identification and classification of HEV strains circulating in Spain

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Scientific Program: Infectious and Immunological diseases. Organ transplantation.
Keywords: HEV-PCR, phylogenetic analysis, genotype 3

Abstract: Background/Objective: The hepatitis e virus (HEV) is one of the leading causes of acute hepatitis worldwide. The aim of our study was to identify and classify the strains of HEV circulating in our environment.
Materials and methods: Prospective study in which we included samples of patients with acute HEV infection diagnosed in Spanish hospitals from February 2018 to May 2019. The diagnosis of infection was established by positive IgM and/or detectable viral load of HEV. A serum sample was required in all cases identified for HEV viral load determination in our laboratory. In patients with detectable viral load, sequencing of the ORF2 region (420nt) of the viral genome was performed to identify the genotype. Phylogenetic analyses were performed, including sequences similar to those identified by BLAST, as well as the strains proposed as standard by Smith and collaborators.
Results: Thirty-six patients were included in this study, 28 of which had serum samples for viral RNA detection. The RNA was amplified in 17 patients, obtaining sequencing results in 11 patients. All strains were consistent with genotype 3 and subtype f. By phylogenetic analysis, two viral chains with a homology greater than 99% were identified, having been isolated in 2 patients from different provinces (Seville and Cordoba), with a temporality between cases of 4 days.
Conclusions: Our study identifies and classifies circulating strains of HEV in Spain. It is necessary to establish a surveillance system to evaluate the circulation of these strains, as well as their possible transmission route.

IIIi. First molecular characterization of the hepatitis E virus in humans in Cameroon: Confirmation of the HEV outbreak in Touboro, North-Cameroon

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Scientific Program: Infectious and Immunological diseases. Organ transplantation.
Keywords: Cameroon; hepatitis E virus; genotype; outbreak

Abstract: Background/Objective: Hepatitis E virus is a major causative agent of acute viral hepatitis in many regions of the world including Africa. In Cameroon, there is no published molecular study on HEV in humans. However, based on serological assays, the first outbreak of HEV was detected in North-Cameroon. The objective of this study was to determine the molecular characterization of HEV that circulated during this period.
Material and methods: A retrospective study design was used to select serum samples among those collected during the outbreak period. IgM positive samples available in sufficient volumes (200 µL) to amplify HEV RNA were selected. RNA was extracted, and then amplified by a real-time RT-PCR assay, followed by a nested RT-PCR assay for sequencing and phylogenetic analysis.
Results: Overall, 24 samples were selected and HEV RNA was amplified by real-time RT-PCR in 20 samples. Amongst these, 12 samples were positive for HEV RNA by nested RT-PCR and yielded good sequencing products. Phylogenetic analysis showed that 10 samples clustered with HEV genotype 1 (subtype 1e) and 2 samples clustered with HEV genotype 3 (subtype 3f).
Conclusions: This study fills the gap of knowledge on the molecular epidemiology of HEV in Cameroon and confirms the first report of hepatitis E outbreak in North-Cameroon. Despite these findings, much still remains to be done to understand the epidemiology of this infection in Cameroon.

IIIj. Hepatitis C viral kinetics in peripheral blood mononuclear cells cannot predict viral relapse: A case-control pilot study

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Keywords: HCV, PBMCs, viral relapse, DAA.

Abstract: Background/Aim: The success rate of hepatitis C virus (HCV) therapy has increased significantly with the use of direct-acting antivirals (DAA). However, a proportion of patients experience a viral relapse despite achieving an undetectable serum viral load at the end of therapy. There is evidence of HCV replication in peripheral blood mononuclear cells (PBMC) which has been associated with HCV occult infection, but has not been studied as a possible predictor of viral relapse. Therefore, the objective of our study was to analyze whether the viral kinetics of HCV in PBMCs during IFN-free DAA treatment could be a useful tool to predict viral relapse.
Materials and methods: This is a case-control study, in patients who had a confirmed viral relapse which were defined as cases, and those who achieved sustained viral response were controls.
Results: The detection of HCV RNA in serum and PBMCs was determined in both groups of patients at baseline, 4, 8, and end of treatment. Four of 326 patients had a viral relapse, and then 12 controls were selected and included in this study. Serum HCV viral kinetics followed a linear pattern during treatment, although the pattern of HCV viral kinetics in PBMCs was irregular and independent of success to treatment.
Conclusions: Our study suggest that the determination of HCV RNA in PBMCs is not useful for predicting which patients may experience viral relapse after treatment with an IFN-free regimen.

IIIk. High lateral resolution MALDI mass spectrometry imaging of peptides in formalin-fixed paraffin-embedded (FFPE) cutaneous leishmaniasis lesions

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Keywords: MALDI mass spectrometry imaging, Cutaneous leishmaniasis (CL), Topical treatment, High lateral resolution.

Abstract: Cutaneous leishmaniasis (CL) is a vector-borne disease produced by the infection of Leishmania parasites (1). Lesions are characterized by skin nodules and ulcers with raised edges and several epidermal and dermal alterations with intense inflammatory cell-reaction and dermal infected macrophages (2 y 3). There is not an ideal treatment and search for new drug alternatives is a priority. Topical treatment constitutes an available approach; however, its effectivity could be affected by drug: CL lesions interactions (4). In order to explore the spatial-distribution of CL molecules (5), the aim of this work was to standardize a mass spectrometry imaging (MS-Imaging) workflow on formalin-fixed and paraffin-embedded (FFPE) biopsies in order to establish and to compare (with non-infected skin) changes in the distribution of peptides. L. (Viannia) braziliensis-infected BALB/c mice were sacrificed and biopsies were processed by FFPE. Different sections were performed, dewaxed and mounted on indium tin oxide (ITO) slides. Two different types of matrices: βcyano-4-hydroxycinnamic acid (CHCA) and 2,5-dihydroxybenzoic acid (DHB) were tested. The parameters used for the acquisition and possible applications of this workflow were also suggested. The protocol used in this study displayed some interesting peptides profiles on FFPE skin sections from CL lesions produced by L. (V.) braziliensis with high reproducibility and lateral resolution (spatial).

IIIl. Should we pay special Interest to c3 deposit in membranous nephropathy?

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Keywords: C3 staining, Membranous nephropathy, complement system, spontaneuos remission

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Abstract: Background and Aims: Membranous nephropathy (MN) is the most common cause of biopsied nephrotic syndrome in adults. Recently, it has been reported that the pathogenesis of MN may be associated with an activation of the complement system. The pathway of activation is not clearly established. The intensity of C3 deposition could be a good marker of this activation in MN as has been shown in other diseases (IgA nephropathy, crescentic GN). The aim of this study is to evaluate clinical-pathological data in a cohort of patients with MN and the significance of glomerular C3 staining as a possible predictor of renal outcomes.
Method: We analysed patients with idiopathic MN biopsied in our department between January 2000 and December 2019, excluding those who had no material for IF (n = 115). The patients were divided into positive (87 cases) and negative (28 cases) based on glomerular C3 deposition. We assessed the clinical and histological characteristics and the percentage of spontaneous remission (SR) and end-stage renal disease (ESRD).
Results: A total of 115 patients with MN were followed with a median follow-up of 65 (25-161) months. We found no differences in baseline characteristics between both groups, with the exception that patients with C3 deposit had less albumin at the time of biopsy that negative patients [2.4 (2-2.9) vs 2.8 (2.3-3.1) g/dl, P=0.011)].
Patients with C3-negative had a higher percentage of SR than patients with C3-positive (75 vs 24%, P = 0.000) and less need for immunosuppressive treatment (18 vs 56%, P =0.001). At the most recent follow-up, C3-positive group had higher creatinine [1.42 (0.8-1.7) vs 0.97 (0.71-1) mg/dl, P=0.045] and proteinuria [1.64 (0.08-3.2) vs. 0.62 (0.05-0.79) g / 24h, P = 0.039]. Regarding histology, we found no differences in glomerular sclerosis, tubular atrophy and interstitial fibrosis. The renal survival analysis showed no statistically significant differences between both groups (P = 0.091). We analysed a subgroup of patients (n = 23) with antibodies against the phospholipase receptor on blood at the time of the biopsy (13/23 were positive). 84% of this positive group presented C3-positive in the renal biopsy vs 25% of the C3-negative group (P =0.008).
Conclusion: Patients without C3 staining show a higher rate of SR and less need for immunosuppressive treatment than patients with C3-positive.
These results would support the theory that complement activation in this entity can play an important role.
It is possible that these patients with negative C3 deposit represent a MN with evolution to SR and in these patients and that these patients do not need immunosuppressive treatment.

IIIm. Stable mutants are involved in heteroresistance to colistin in isolates of Klebsiella pneumoniae clinical origin producing OXA-48

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Keywords: Klebsiella pneumoniae, heteroresistance, colistin.

Abstract: Background: Heteroresistance (HR) can be related to the emergence of persisters (organisms can survive the lethal action of antibiotics without a change in their minimum inhibitory concentration (MIC)) or the selection of stable mutants (stable increment of MIC). The objective of this study is to evaluate if clinical isolates of Klebsiella pneumoniae producing the carbapenemase OXA-48 and susceptible to colistin, express HR to colistin.
Materials/methods: Three OXA-48 clinical isolated from different patients were evaluated. MICs of colistin were determined by standardized broth microdilution (BMD; CLSI-EUCAST guidelines). Colistin HR was determined by population-analysis-profiling (PAP), performing bacterial counts on solid media with increasing concentrations of colistin (up to 64 mg/L), incubating the plates for 48h-5d-7d. Up to 8 colonies of 4xMIC, 16xMIC and maximum concentration with bacterial growth [MAX] were selected from PAP. Bacteria were subcultured twice in antibiotic-free medium and BMD were again subsequently performed.
Results: The three isolates corresponded to ST323, ST147 and ST15. All isolates were susceptible (BMD) to colistin (MIC: 0.5 mg/L). PAP indicated that all isolates contained colistin-heteroresistant subpopulations with colonies growing up to 32 (2 isolates) or 64 mg/L (1 isolate). In all isolates, the organisms grown at 16xMIC and [MAX] were stable mutants (MIC: 16-128 mg/L). In the ST15 isolate, three colonies on the plates containing only 2 mg/L (4xMIC) of colistin were persisters.
Conclusions: Heteroresistance of OXA-48 producing K. pneumoniae can mainly generate subpopulations of stable mutants, but it can also be related to the emergence of persisters at low supra-MIC of colistin.

IIIn. Lack of cytomegalovirus (CMV)-specific cell-mediated immune response using QuantiFERON-CMV assay in CMV-seropositive healthy volunteers: fact not artifact

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Scientific Program: Infectious and Immunological diseases. Organ transplantation.
Keywords: Cytomegalovirus; CMV-specific cell-mediated immunity; IFNG release; lymphocyte proliferation; QuantiFERON-CMV assay; FASCIA assay

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Abstract: Rationale: The QuantiFERON-CMV assay measures cell-mediated immunity against cytomegalovirus (CMV-CMI), which is particularly useful in individuals susceptible to CMV infection such as transplant patients. A positive QF result identifies patients that are better protected against CMV infection. However, the significance of a negative QF result in CMV-seropositive individuals needs to be clarified.
Objective: To evaluate whether CMV-seropositive healthy individuals with a negative QF result show an impaired proliferative response against CMV lysate or this humoral/cellular discordance in CMV-seropositive individuals is an artifact of the QF assay related to the type of stimulus.
Methods: In this work, CMV-CMI was analyzed in healthy virus carriers using the QF assay, and, in parallel, the Flow-cytometric Assay of Specific Cell-mediated Immune response in Activated whole blood (FASCIA). FASCIA assay measures T-cell proliferation using CMV lysate as stimulus whereas QF assay use a mix of peptides.
Results: A total of 93 of healthy subjects were enrolled. Thirteen out of 71 CMV-seropositive healthy volunteers (18,3%) showed humoral/cellular discordance using QF assay (CMV+QF-). Interestingly, with FASCIA assay CD4+ and CD8+ T-cell proliferations were lower in CMV+QF- than in CMV+QF+ individuals. Furthermore, CMV+QF- volunteers had a lower level of anti-CMV IgG than CMV+QF+ subjects.
Conclusions: Discordant CMV+QF- volunteers can be defined as low responder individuals since they show a lower CMV-specific humoral and cellular immune responses in comparison to CMV+QF+ individuals. Immune discordance shows the high heterogeneity of immunity to CMV in healthy subjects.

Nutrition, Endocrine and metabolic diseases

IVa. Longitudinal Changes in physical activity behavior pattern from childhood to adolescence: GENOBOX follow-up study

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Keywords: Childhood, obesity, physical activity, pubertal status, sedentary time.

Abstract: Longitudinal changes of physical activity (PA) from childhood into adolescence have not been accurately described yet. The aim is to evaluate the changes of PA in a cohort of children from the prepubertal to pubertal period. 213children with a longitudinal follow up were selected. In both periods, anthropometric and PA changes, assessed by accelerometry, in time and intensity were evaluated. Sedentary behavior increased about 50%, while all PA intensities declined from the pre-pubertal to pubertal period. Light PA was the major contributor, decreasing about 30%. Boys were more active than girls in both periods, but they showed a higher decline in PA, especially moderate-to-vigorous physical activity (MVPA). The proportion who reached the recommendation of 60 min of MVPA fell to 35% in boys and 10% in girls. Children with obesity or overweight had lower MVPA than those with normal-weight in the pre-pubertal period, but no differences were found in the pubertal period. This study shows a decrease of PA and an increase of sedentarism in the transition from childhood to adolescence, particularly in girls. Regardless of body weight, adolescents tend to be less active. Therefore, it is necessary to implement measures at these stages to reduce sedentary lifestyle and at least maintain optimal? physical activity levels. Therefore, prevention programs should be implemented to achieve optimal physical activity and low levels of sedentarism during infancy taking into account the differences found by sex.

IVb. Congenital malformations of urinary tract: evolution to chronic renal disease

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Keywords: CAKUT, Glomerular filtration rate, Chronic renal failure.

Abstract: Aim of the study. Congenital anomalies of kidney urinary tract (CAKUT) constitute a relevant group of diseases in clinical practice because of their high prevalence in children and because they are the main cause of chronic kidney disease (CKD) in pediatric population. Recent advances in the knowledge of its pathogenesis and clinical manifestations contributes to improve the clinical outcome of these patients. Our goal is to know the characteristics of children with CAKUT in our centre and the prevalence of CKD, identifying the factors associated with the occurrence of kidney damage.
Methods. A retrospective, descriptive, analytical and cross-sectional study was carried out. It included the patients treated in the Pediatric Nephrology outpatient clinic at the Reina Sofía University Hospital from January 1, 2018 until December 31, 2018. Epidemiological,clinical and analytical variables were analyzed and the possible risk factors for progression of renal damage as well.
Main Results.685 patients with 827 renal units with CAKUT were included with a mean age of 9.98 ± 5.12 years. 62.2% were male and the mean follow-up since the diagnosis of CAKUT was 9.95 ± 5.09 years. 58.8% were non-obstructive dilations, the most frequent group followed by renal dysplasia, obstructive dilations and number and position abnormalities. The most frequent malformation was the VUR. Left side was more frequently affected (47.5%). 55% of the diagnoses were prenatal. A total of 172 patients were surgically treated, mostly for VUR. The first choice treatment e was endourological and the reintervention rate reached 20%. One in 7 children had CKD (86% stage 2), at a mean age of 13.8 ± 4.6 years. Male sex, bilaterality and proteinuria were associated with CKD.
Conclusions. The study and knowledge of the epidemiological and clinical characteristics of children with CAKUT and the factors associated with CKD help us to individualize the clinical follow-up of these patients by adapting diagnostic tests and health resources.

IVc. Cluster Analysis of Physical Activity Patterns, and Relationship with Sedentary Behavior and Healthy Lifestyles in Prepubertal Children: Genobox Cohort

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Scientific Program: Nutrition, endocrine and metabolic diseases.

Keywords: Exercise; obesity; Mediterranean diet; cardiovascular diseases.

Abstract: Sedentary habits during childhood are associated with adverse health outcomes. The aim of this work was to cluster lifestyle behaviors and metabolic biomarkers to establish different patterns in children. Their physical and sedentary activities were evaluated by accelerometry, and questionnaires that included lifestyle behaviors, such as adherence to a Mediterranean diet, anthropometry and blood biochemical markers. Cluster analysis was performed to establish different groups based on physical activity levels. A total of 489 children were finally selected. Cluster 1 included children with a mostly sedentary state, whereas Cluster 3 included the most active children and Cluster 2 included children that did not fit into either the sedentary or the highly active groups. In Cluster 3, 56% of children were in a sports club, and a lower percentage used electronic devices in their rooms compared to the other groups. Cluster 1 children exhibited higher insulin, HOMA-IR and triacylglycerides with respect to the other groups. No differences were found regarding adherence to a Mediterranean diet. The choice to practice an extracurricular sport could be an influencing factor to increase exercise and ensure an active lifestyle in children. Reducing or limiting screen time mainly in children's rooms could contribute to an active lifestyle.

IVd. Automated method for determination of acylcarnitines in serum by SPE-LC-MS/MS

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Scientific Program: Nutrition, endocrine and metabolic diseases.
Keywords: Carnitines, LC-MS/MS, Serum, SPE, MRM, Sample preparation.

Abstract: Acylcarnitines are derivatives of fatty acids and carnitine produced by esterification, that possess important biological functions for human body. Among them, regulation of fatty acids β oxidation and fatty acid transport across the mitochondrial membrane. A deregulation of these processes involves an accumulation of acylcarnitines in the mitochondria and transfer to the cytosol and, then, to the blood, which produces acidemias. Moreover, acylcarnitines are related to different pathologies such as cardiovascular and peripheral arterial diseases and male infertility, among others. In this research, an automated analytical method based on solid phase extraction on-line coupled to liquid chromatography with tandem mass spectrometry detection (SPE-LC-MS/MS) was developed for quantitative determination of carnitine and 50 lineal acylcarnitines (from saturated and unsaturated fatty acids) in serum. On-line SPE was performed by using miniaturized cartridges (10 mm length x 2 mm inner diameter) based on ionic exchange to enhance the retention/elution efficiency of acylcarnitines. This arrangement allows to reach high levels of sensitivity, precision and selectivity because the automation of the analytical process, the preconcentration of the analyte in the SPE step, a good chromatographic separation and the determination by tandem mass spectrometry. The volume of serum needed is 10 µL, which is diluted with milli-Q water before direct injection of 100 µL. For these reasons, the method is especially suited for implementation in clinical studies demanding for high-throughput analysis.

IVe. Disruption of circadian rhythms as a cardiometabolic risk factor in subjects with established coronary disease: from CORDIOPREV study

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Scientific Program: Nutrition, endocrine and metabolic diseases.
Keywords: Disruption circadian rhythm, cardiometabolic risk factor, chronotype, cardiovascular disease.

Abstract: The objective of this work was to assess the relation between chronotype and disruption of circadian rhythm with cardiometabolic risk in subjects with established coronary disease. In a cohort of 857 subjects from the CORDIOPREV study, we determined the chronotype using morningness-eveningness questionnaire by Horne and Ostberg and we classified the subjects such as mornings, indeterminate and evenings. At the beginning of the study and every year in the first four years of the study lipids, PCR and homocysteine levels were measured. In addition, we assessed lifestyle factors using food, physical activity and sedentarism validated questionnaires. The prevalence of metabolic syndrome was calculated in these subjects. Interestingly, we found that evenings subjects had higher levels of triglycerides ($p<0.01$), protein C reactive (PCR) (p 0.02) and homocysteine ($p <0.01$), and lower levels of high-density cholesterol (HDL) (p 0.04) comparing with mornings subjects. Moreover, the prevalence of metabolic syndrome was higher in evening subjects compared with mornings subjects (OR 1.58, p 0.01). Additionally, evening subjects were less active spending less time doing physical activity ($p<0.01$) and spending more sitting time ($p <0.01$) compared with morning subjects. In this regard, the disruption of circadian rhythm has been established as a risk factor in the development and progression of cardiovascular disease. Chronotypes determine the individual's circadian preference, allowing to classify the people as evenings or mornings depends on the diurnal or nocturnal preferences. The evening chronotype has been linked to a predisposition of disruption of circadian rhythm. These subjects have usually worse lifestyle habits, with consumption of unhealthier diet than morning subjects and with a sedentary behaviour. This work provides novel evidence on a large cohort about that evenings subjects with established coronary disease have higher cardiometabolic risk than morning subjects. This new knowledge has the potential to become a valuable tool in order to do an individualized lifestyle approach in patients at very high cardiovascular risk.

IVf. Pharmacogenetic activation of anorexigenic POMC neurons of the arcuate nucleus reveals a predominant stimulatory action on the reproductive axis: Implications for reproductive dysfunction in conditions of malnutrition and obesity

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Keywords: Reproduction, POMC, DREADDs, Metabolism

Abstract: Reproduction is an energy-demanding function regulated by complex neuroendocrine circuits, including those processing metabolic information regarding nutrient availability and body energy depots. POMC neurons, located in the hypothalamic arcuate nucleus (ARC), are key components of these circuits, with a dominant anorexigenic (satiety) effect. However, while activation of POMC neurons occurs in conditions of nutrient availability/energy excess, required for proper reproductive function, the predominant role of this neuronal population in the reproductive axis remains ill-defined. This is mainly due to the fact that these neurons release neurotransmitters with opposite effects on the reproductive axis, with βMSH, CART and glutamate being stimulatory, and βendorphin and GABA inhibitory.
The objective of this work was to develop a protocol for in vivo activation of ARC POMC neurons, to evaluate the consequences of such neuronal activation on the reproductive axis. For this purpose, we used virogenetic/pharmacogenetic tools to induce the expression of the activator DREADDs (Designer Receptors Exclusively Activated by Designer Drugs), hM3Dq, selectively in ARC POMC neurons, for its subsequent stimulation by the specific ligand, clozapine-n-oxide (CNO).
Pomc-Cre mice, expressing Cre recombinase under the POMC promoter, were bilaterally injected in the ARC with viral vectors harboring Cre-dependent hM3Dq constructs, to enable selective expression of activatory DREADDs in ARC POMC neurons. Peripheral CNO administration to induce DREADD-mediated neuronal activation evoked a significant increase in the circulating LH levels, as subrogate marker of central activity of the reproductive axis. Activation of POMC neurons evoked also the expected decrease in food intake. Our data document a major stimulatory role of ARC POMC neurons in the control of the reproductive axis. These results open the possibility that dysregulation of POMC neurons, as seen in conditions of metabolic unbalance, from malnutrition to obesity, might have causative, as well as therapeutic, implications for forms of infertility linked to metabolic distress.

IVg. Congenital ablation of Tacr2 reveals distinct and overlapping roles of NK2R signaling in the control of reproductive axis

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Scientific Program: Nutrition, endocrine and metabolic diseases.
Keywords: Tachykinins, tachykinin receptors, Tacr2, Neurokinin A, puberty, reproduction, gonadotropins, sex behavior, neuroendocrinology

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Abstract: Tachykinin (TAC) signaling is an important element in the control of reproduction. TAC family is mainly composed of substance P (SP), neurokinin A (NKA) and NKB, which bind preferentially to the receptors, NK1R, NK2R and NK3R, respectively. While most studies on the reproductive roles of TAC have focused on NKB/NK3R, and to a lesser extent SP/NK1R, the relevance of NK2R, encoded by Tacr2, remains poorly characterized.
We address herein the physiological roles of NK2R signaling in the regulation of the reproductive axis by characterizing a novel mouse line with congenital ablation of Tacr2. Activation of NK2R evoked acute LH responses in control mice, analogous to those of agonists of NK1R and NK3R. Despite absent expression of NK2R, Tacr2-/- mice displayed only partially reduced LH responses to a NK2R agonist; yet, these responses were totally abrogated in Tacr2-/- males after concomitant blockade of NK3R. Tacr2-/- mice displayed normal pubertal timing. Yet, in adulthood, LH pulsatility was partially altered in Tacr2-/- females, with suppression of basal LH levels, but without changes in the number of LH pulses. In addition, trends for increase in breeding intervals were detected in Tacr2-/- mice. However, null animals of both sexes were fertile, with no changes in estrous cyclicity or sex preference in social behavioral tests.
In conclusion, stimulation of NK2R elicited LH responses in mice, while congenital ablation of Tacr2 partially suppressed basal and stimulated LH secretion, with moderate reproductive impact. Our data support a distinct role of NK2R in the control of the gonadotropic axis, with partially overlapping functions with other tachykinin receptors. Our data pave the way for exploring for the eventual pathophysiological role of NK2R signaling, as well as the potential use of NK2R analogs, in reproductive disorders linked to deregulated LH secretion, such as polycystic ovary syndrome (PCOS).

IVh. Dissecting the roles of KNDy-derived kisspeptins in the control of reproduction and metabolism

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Scientific Program: Nutrition, endocrine and metabolic diseases.
Keywords: Reproduction, metabolism, Kisspeptin, KNDy neurons.

Abstract: Kiss1 neurons, which produce kisspeptins, have emerged recently as indispensable regulators of puberty and fertility, acting primarily by stimulating hypothalamic GnRH neurons. In addition, kisspeptins have been proposed to participate in the control of other bodily functions, including weight homeostasis and metabolism; yet, the relevance of the later remains contentious. A prominent population of Kiss1 neurons is located in the arcuate nucleus (ARC), where Kiss1 neurons co-express two other neuropeptides: Neurokinin B (NKB; encoded by Tac2) and Dynorphin (Dyn); hence, this population has been named KNDy neurons. However, NKB-only and Kiss1-only neurons are also found in the ARC, but the relative contribution of the different subsets of Kiss1 neurons to the control of reproductive function and metabolism, remains unexplored. To define the precise roles of KNDy-born kisspeptins, we report the generation and characterization of the first mouse line with conditional ablation of Kiss1 in Tac2-expressing neurons, namely the TaKKO mouse.
TaKKO mice of both sexes displayed a substantial decrease of ARC Kiss1 mRNA and kisspeptins expression, while Tac2 mRNA levels remained unaltered. Despite this drop of Kiss1/kisspeptins, puberty onset occurred at normal timing. However, especially in females, gonadal weights were markedly decreased in 2-month-old TaKKO mice, together with a reduction in basal LH levels, suggesting the perturbation of the reproductive axis. This was further supported by our analyses in 6- and 12-month-old TaKKO female mice, which displayed overt irregularities in ovarian cyclicity and decreased fecundity. Additionally, our metabolic analyses suggest that the ablation of Kiss1 in KNDy neurons leads to changes in body composition and modest changes of glucose and insulin tolerance, mainly noticed in males. Altogether, our data suggest that KNDy-born kisspeptins are dispensable for puberty onset but required for maintenance of reproductive and metabolic homeostasis in adulthood; deregulation of this system may lead to infertility and/or metabolic alterations.

IVi. Lipoprotein particle profile in peripheral artery disease: from the CORDIOPREV study

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Scientific Program: Nutrition, endocrine and metabolic diseases.
Keywords: Peripheral artery disease, lipoproteins, NMR metabolomics, ankle-brachial index.

Abstract: Atherogenic dyslipidaemia has been associated with risk of coronary artery disease. Standard lipid panels measure overall cholesterol concentration within lipoproteins but are unable to provide lipid concentration or size of lipoproteins. Techniques such as nuclear magnetic resonance (NMR) spectroscopy can provide quantitative molecular data on lipoprotein subclasses, their lipid concentration and composition. Peripheral artery disease (PAD) is an atherosclerotic occlusive disease of the lower extremities that can be diagnosed with the ankle-brachial index (ABI). PAD risk factors include smoking, diabetes mellitus, high blood pressure or high cholesterol levels, among others. The objective of this research work has been to compare lipoprotein particle profile in coronary heart disease patients from the CORDIOPREV study with and without peripheral artery disease. NMR metabolomics was used to quantify particle concentration and lipid composition of lipoprotein subclasses from plasma samples. Obtained results showed that patients with an ABI <0.9 showed fewer large and medium HDL particles, lower concentration of HDL, HDL2 and HDL3 cholesterol, smaller HDL particle diameter, lower concentration of ApoA1, phosphatidylcholine and sphingomyelins (all FDR-adjusted p-values <0.05). With the results found in this work we aim to develop a regression model to define the HDL particle profile associated with the presence of peripheral artery disease in coronary heart disease patients to find biomarkers of atheroprotective HDL function, and to provide insight into the physiopathology of the disease.

IVj. Obstetric and neonatal results in women candidates for low intervention after trial of labour after cesarean (TOLAC)

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Scientific Program: Nutrition, endocrine and metabolic diseases.
Keywords: Vaginal birth after cesarean; Trial labor; Natural childbirth; Newborn.

Abstract: Introduction: The cesarean section rate in developed countries is around 21% (SEGO, 2017), while the WHO recommends rates between 10-15% (WHO, 2015). Vaginal birth after cesarean section (VBAC) is an important procedure to decrease the rate of cesarean sections.
Objectives: To analyse the obstetric and neonatal results of women undergoing TOLAC.
Methods: Descriptive and analytical study carried out in a third level Hospital in southern Spain with medical records of women with and without previous cesarean section candidates for low intervention labor. A systematic and random sampling was performed. Single-term, in cephalic presentation and low-risk births during 2015-2017 were included. Obstetric and neonatal variables were analysed and compared between women with and without a history of cesarean section.
Results: Of the total of 416 deliveries, 40 had a history of cesarean section. The mean age was 31.2 (±5.6) years, being higher in women with a previous cesarean section (33.7±4.4). VBAC's success rate was 57.5%. Women with a previous cesarean section had a higher risk of another cesarean section (OR 8.8; p<0.001), births at ≥ 41 weeks (OR 2.2; p=0.029) and labor induction (OR 2.5; p=0.005), and lower rate of epidural analgesia (p=0.024) and use of oxytocin (p=0.029). For children, Apgar score <9 at 5 minutes were higher (p=0.002), higher birth weight (p = 0.006), lower rate of early breastfeeding (p=0.009) and lower rate of skin-to-skin contact (p<0.001). No significant differences were found in umbilical cord pH, Apgar <7 at 1 and 5 minutes, hospitalizations in neonatology or advanced resuscitation.
Conclusions: TOLAC was associated with an increased risk of cesarean section, induction of labor, delivery after 41 weeks of gestation, and less use of oxytocin and epidural analgesia. There appears to be no significant risks for newborns of mothers with a history of cesarean section.

IVk. Influence of diet and physical activity in workers' health loss

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Scientific Program: Nutrition, endocrine and metabolic diseases.
Keywords: nutrition, physical activity, worker's health promotion, temporal incapacity

Abstract: Background: Some lifestyles have been associated with the loss of health in workers, such as poor nutrition and sedentarism.
Main objective: To identify some lifestyles associated with the loss of health in workers.
Methods: A longitudinal and observational study was conducted carried out during 2015-2017. A total of 240 workers were studied from check-up health in Córdoba (Spain). The outcome variable was the loss of health measured through of the duration length (in days) of episodes of illness or occupational accident. The predictive variables were: age, gender, worksite, tobacco and alcohol consumption, physical activity (IPAQ) and, Mediterranean diet adherence (MDA). An adjusted multiple linear regression was performed.
Results: 177 men (73.8%) and 63 women (26.2%) were studied. The total average age was 50.2 (SD=7.9) years. 104 men (58.8%) and 25 women (39.7%) suffered any episode of illness or occupational accident ($p<0.05$). 4.6% of the workers obtained a sedentary-low PA and 59.2% showed an adequate MDA. According to the worksite, the average duration for the white-collar workers was 29.5 days, 74.5 for blue collar workers (BCW) and 47.8 days for police and firefighters ($p<0.05$). Workers who did a high PA obtained an average of 36.3 days for 64.4 days in workers with low-moderate. The MDA did not obtain significant association with duration of illness or occupational accident.
Conclusions: Along with the worksite, physical activity has been the lifestyle most associated to the loss of health in workers.

IVl. Influence of two healthy models on the degree of atherosclerosis in coronary heart disease patients: from the CORDIOPREV study

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Scientific Program: Nutrition, endocrine and metabolic diseases.

Keywords: Carotid intima-media thickness, Mediterranean diet, secondary prevention, cardiovascular disease, dietary intervention

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Abstract: Background: Lifestyle and diet affect cardiovascular risk, although there is currently no consensus about the best dietary model for the secondary prevention of cardiovascular disease (CVD). Our main objective was to evaluate the effectiveness of two healthy dietary patterns (low-fat versus Mediterranean diet) in reducing CVD progression (assessed by intima-media thickness of both common carotid arteries (IMT-CC)) in coronary heart disease (CHD) patients.

Methods: From the total 1002 CHD participants, 939 patients completed the evaluation of IMT-CC at baseline and were randomized to follow a Mediterranean diet (35% fat, 22% MUFA, <50% carbohydrates) or a low-fat diet (28% fat, 12% MUFA, >55% carbohydrates). The IMT-CC measurements, carotid plaque number and height were repeated after 5 and 7 years.

Results: Mediterranean diet induced IMT-CC regression at 5 years (-0.027 ± 0.008 mm; $p < 0.001$), which was maintained at 7 years (-0.031 ± 0.008 mm; $p < 0.001$) compared to baseline. The Mediterranean diet did not modify the carotid plaque number but did produce a higher reduction on carotid plaque height compared to the low-fat diet ($p < 0.05$). The low-fat diet did not reduce IMT-CC, carotid plaque number or height.

Conclusions: Our data show that long-term consumption of a Mediterranean diet, but not a low-fat diet, was associated with a reduction in CVD progression, determined by reduced IMT-CC and carotid plaque height. These findings support the clinical benefits of the Mediterranean diet in the context of secondary cardiovascular prevention.

IVm. Changes in atherosclerosis-related miRNA expression after intervention with two healthy diets in patients with cardiovascular disease

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Scientific Program: Nutrition, endocrine and metabolic diseases.
Keywords: microRNA, atherosclerosis, Mediterranean diet, low fat diet, cardiovascular disease

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Abstract: Background: Cardiovascular disease prevention and treatment are top priorities in healthcare. Most cardiovascular disease is caused by atherosclerosis, a chronic thickening and inflammation of the carotid intima-media. Diet plays a key role in the prevention of atherosclerosis and cardiovascular disease. Previous studies have demonstrated the role of miRNAs in atherosclerosis-related mechanisms. Our aim was to study the modulation by diet of miRNAs involved in the progression and regression of carotid intima-media thickness (cIMT) as a risk factor in the development of atherosclerosis in patients with established cardiovascular disease.
Materials and Methods: The present study included 240 patients from the CORDIOPREV study: 120 with the most extreme progression of cIMT after 5 years of low fat (LFHCC) or Mediterranean (Med) dietary intervention (n= 59 and 61, respectively), and 120 patients with the most extreme regression of cIMT (n= 58 and 62, respectively). cIMT was measured bilaterally with high-resolution B-mode Doppler echography. Intracellular levels of miRNAs from peripheral blood mononuclear cells at baseline and at year 5 were determined through the OpenArray platform. Statistical analyses were performed by repeated measures ANOVA.
Results: Our results showed an increase in the expression of miR-365 in patients with progression of the cIMT after the intake of LFHCC diet and in patients with regression of the cIMT after the intake of the Med diet (both $p<0.05$). The expression of miR-221 increased in patients with cIMT progression after intake of LFHCC diet and in patients with cIMT regression after intake of the Med diet (both $p<0.05$). The Mediterranean diet induced increased expression of miR-210-5p in patients who showed regression of the cIMT after the intervention period ($p=0.048$)
Conclusion: Dietary intervention could regulate the expression of miRNAs directly involved in mechanisms associated with atherosclerosis development in patients with cardiovascular disease.

IVn. Microscopic study of obesity: interaction networks between organelles

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Scientific Program: Nutrition, endocrine and metabolic diseases.
Keywords: Adipocytes; obesity; lipid droplets; fibrosis; insulin resistance; inflammation

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Abstract: Introduction: Smith-Lemli-Opitz syndrome (SLOS) is an autosomal recessive rare disorder caused by mutations in the DHCR7 gene, affecting the synthesis of the 7-dehydrocholesterol reductase enzyme, resulting in low plasma cholesterol levels. These low levels lead into clinical manifestations, shaping a typical phenotypic pattern. This can be influenced, among other factors, by both the genotype and effectiveness of treatment over time. The purpose of this study is to compare two SLOS diagnosed patients with different prognosis related to genotype and phenotype.
Methods: Serum cholesterol and 7-8 dehydroxycholesterol (DHC) metabolites levels were followed-up every six months during the last ten years in two SLOS paediatrics patients. In order to evaluate their progression in relation with their phenotype and response to treatment, patients are being treated with cholesterol supplementation.
Results: Each patient has a completely different evolution despite a precocious diagnosis during infancy. A 20 year-old-patient has a severe phenotypic pattern without any response to cholesterol supplementation, with low cholesterol and high 7-8DHC serum levels. In contrast, an 8 year-old-patient has a successful response to treatment although he has one of SLOS most common mutations related to a severe phenotype since born. In this case, cholesterol levels increase and 7-8DHC levels decrease as time goes on. This fact indicates that these levels are related to the clinical prognosis. For this reason, an adequate control of serum cholesterol and metabolites are necessary to propose individualized and personalized treatments. In addition, the genotype in the SLOS has an impact in both the clinical manifestations and chances of success in patients on a diet supplement with cholesterol, even in cases with severe spectrum.
Conclusion: Treatment should be individualized according to the biochemical control of serum cholesterol and sterols levels. Both the phenotypic pattern and prognosis can be predicted depending on the evolution of the biochemical markers.

IVñ. Smith-Lemli-Opitz Syndrome: Phenotypic pattern and prognosis after 10 years of treatment

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Scientific Program: Nutrition, endocrine and metabolic diseases.
Keywords: syndrome, Smith-Lemli-Opitz, hypocholesterolemia, sterols

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Abstract: Introduction: Smith-Lemli-Opitz syndrome (SLOS) is an autosomal recessive rare disorder caused by mutations in the DHCR7 gene, affecting the synthesis of the 7-dehydrocholesterol reductase enzyme, resulting in low plasma cholesterol levels. These low levels lead into clinical manifestations, shaping a typical phenotypic pattern. This can be influenced, among other factors, by both the genotype and effectiveness of treatment over time. The purpose of this study is to compare two SLOS diagnosed patients with different prognosis related to genotype and phenotype.
Methods: Serum cholesterol and 7-8 dehydroxycholesterol (DHC) metabolites levels were followed-up every six months during the last ten years in two SLOS paediatrics patients. In order to evaluate their progression in relation with their phenotype and response to treatment, patients are being treated with cholesterol supplementation.
Results: Each patient has a completely different evolution despite a precocious diagnosis during infancy. A 20 year-old-patient has a severe phenotypic pattern without any response to cholesterol supplementation, with low cholesterol and high 7-8DHC serum levels. In contrast, an 8 year-old-patient has a successful response to treatment although he has one of SLOS most common mutations related to a severe phenotype since born. In this case, cholesterol levels increase and 7-8DHC levels decrease as time goes on. This fact indicates that these levels are related to the clinical prognosis. For this reason, an adequate control of serum cholesterol and metabolites are necessary to propose individualized and personalized treatments. In addition, the genotype in the SLOS has an impact in both the clinical manifestations and chances of success in patients on a diet supplement with cholesterol, even in cases with severe spectrum.
Conclusion: Treatment should be individualized according to the biochemical control of serum cholesterol and sterols levels. Both the phenotypic pattern and prognosis can be predicted depending on the evolution of the biochemical markers.

IVo. Impact of families who have children with chronic diseases

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Scientific Program: Nutrition, endocrine and metabolic diseases.
Keywords: Pediatric chronic diseases; Family; Health Impact Assessment; Surveys and Questionnaires

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Abstract: Objective: To synthesize current and relevant information on the impact suffered by families who have children with chronic diseases.
Material and method: Systematic review of the scientific literature carried out in Medline (through Pubmed) and CINAHL (through EBSCO) using the modified PRISMA criteria. It was limited to published articles in the last decade in English or Spanish. The search ended on May 1, 2020. To assess the methodological quality of the included studies, the critical assessment tools used by the Joanna Briggs Institute in its Systematic Reviews were used. For the synthesis of information a content analysis was performed.
Results: Finally, a total of 25 articles were selected. The daily management of children with chronic diseases requires correct treatment of the disease and the possible complications or risks that it implies. The recognition of this reality is especially burdensome for many parents, since their desire to maintain the safety and well-being of their child, at all times, can end up causing states of stress and anxiety. Another important aspect in terms of impact is related to the sociability of the child (and families), social interactions play a fundamental role in child development, especially those that take place within the school context. This situation is lived with great anguish, causing the social isolation of the whole family and affecting the working life of the parents, and even the idea of not having more children.
Conclusions: the chronic illness of the child produces an impact on the entire family unit that affects all dimensions of her life (personal, family, social and economic) although it is the social dimension that is most affected.

IVp. Circulating miRNA profiling for improved molecular diagnosis of obesity-induced hypogonadism in men

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Scientific Program: Nutrition, endocrine and metabolic diseases.
Keywords: MiRNAs, testosterone, molecular diagnosis, male hypogonadism

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Abstract: Obesity-induced hypogonadism (OIH) is a complex condition at the crossroads of reproductive and metabolic disease. Overweight is a risk factor for central hypogonadism, which results in low testosterone levels, with potential impact on reproductive/sexual health. In turn, decreased testosterone levels impact on the course of metabolic disease, favoring the progression of glucose intolerance and obesity. Yet, the pathophysiological basis and even the clinical relevance of OIH remain unsolved. Our recent evidence suggests that microRNAs are involved in the control of the reproductive axis, and our studies in preclinical models evidence that altered hypothalamic expression of specific miRNAs contributes to the genesis of OIH and might be target for intervention. Notably, miRNAs are also detectable in plasma, where they have been proposed as biomarkers of a wide range of conditions. Yet, no information about altered miRNA levels in OIH is available.
To evaluate whether OIH in men is associated with dysregulated levels of miRNAs in circulation, we applied high-throughput analysis, using NanoString technology, to plasma samples obtained in a cohort of 272 obese men, with and without hypogonadism/low testosterone. The cohort was categorized in four groups as follows: eugonadal (n= 99; Testosterone: 107.06 ± 29.4 (SD) ng/mL; mean HOMA-index= 2.34), eugonadal with insulin resistance (n= 107; T: 96.37 ± 23.9 ng/mL; HOMA-index= 6.5), hypogonadal (n= 27; T: 58.03±9.2 ng/mL; HOMA-index= 2.5), and hypogonadal with insulin resistance (n= 43; T: 56.19 ± 9.5 ng/mL; HOMA-index= 7.4). Unbiased analyses in representative plasma samples of each group (n=9) allowed us to select a group of five miRNA candidates (anonymized due to patent protection) with differential expression in the OIH groups. We are currently validating these targets by qPCR in a larger sample of each cohort group (n=25). We expect that these analyses will permit to identify a molecular signature of deregulated miRNAs in OIH, which may help to better diagnose and stratify obese patients, suffering or not low testosterone and insulin resistance.

IVq. Clinical evolution in pediatric patients with eating disorders

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Scientific Program: Nutrition, endocrine and metabolic diseases.
Keywords: Eating disorders, anorexia nervosa, bulimia nervosa, children.

Abstract: Objectives. There is a striking increase in eating disorders in pediatric patients, with little information about their characteristics. Therefore, the purpose of this study is to evaluate the clinical profile of children with anorexia nervosa by evaluating the factors related to the appearance of the disease, its evolution and prognosis, considering the differences with the adult population. It will be analyzed whether the healthcare process used determines the final result and how to improve the current therapeutic approach for these patients.
Material and methods. A retrospective, observational and descriptive study of pediatric patients diagnosed with eating disorders, anorexia nervosa type, derived from the Children's Mental Health Unit to the Metabolism Unit of the Reina Sofía University Hospital due to its severity was developed for 10 years. A clinical evaluation that included a physical and anthropometric examination was performed. Body composition by bioimpedanciometry as well as a nutritional assessment in each visit, and blood biochemical tests were realized. Demographic and other variables related to diagnosis, initial evaluation, evolution and treatment were also collected. A descriptive statistical analysis was performed with SPSS.
Results. The symptoms of children were similar to those of adolescents and adults referred to in the literature, but more often presented as incomplete forms. The sex ratio was 3: 1 for girls compared to boys. The mean age of onset was 11.3 years (in boys: 10 years) and the evolution time before diagnosis had an average of 6.6 months (younger in girls: 2.4 months). In the first evaluation, a serious deterioration in health status was observed. The average weight lost before the first consultation was 10.4 kg and 43% of the patients had a lower weight than P10. After a mean follow-up of 17 months, normalization of eating patterns, psychosocial, interpersonal and occupational functioning and restoration of normal growth were achieved.
Some alteration in the biochemical parameters was detected in 47% of the patients and 58% presented altered hormonal levels. Furthermore, 85% manifested changes in psychosocial functions and comorbidities such as depression and anxiety (65% required specific pharmacological treatment). Regarding treatment, 100% were prescribed a personalized nutritional plan, 60% received a nutritional supplement and only 5% of the total required feeding by nasogastric tube at some point in the process.
Conclusions. The profile in children with anorexia nervosa presents a more equitable distribution by sex and cases with lower ages than expected, a shorter time of evolution before diagnosis, a lower deterioration of the health status in the first medical evaluation, as well as a shorter duration of the disease in relation to the typical pattern described in the literature in this disease. Therefore, the better prognosis in this child sample could be explained by the closer intervention and follow-up of the multidisciplinary team, together with the early mediation of the parents and the greater dependence of these patients on their caregivers that increases the adherence to treatment, as well as greater plasticity in the response to psychological treatment. This analysis will allow us to make proposals for improvement in the eating disorders care process in our environment.

IVr. Role of miRNAs in the cellular aging of patients with cardiovascular disease

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Scientific Program: Nutrition, endocrine and metabolic diseases.
Keywords: Cardiovascular Disease, miRNAs, Oxidative Stress, Cellular Aging, Telomere.

Abstract: Background: According to the WHO, the death rate from chronic age-related diseases (cardiovascular diseases, diabetes) will increase significantly. The development of these diseases is related to cellular aging. Recent studies indicate that microRNAs play an important role in the development of diseases such as CVD, obesity and DMT2. Our aim was to study the role of miRNAs in the cellular aging and its relationship with biological processes involved in the development of the diseases in patients with cardiovascular disease.
Materials and Methods: The present study includes 400 subjects who participated in the CORDIOPREV study. Parameters of oxidative stress and aging were determined. Expression of 17 miRNAs was also analyzed by real time PCR in a subpopulation of 240 subjects at baseline and after 5 years of follow-up. ANOVA for repeated measured were performed by SPSS software.
Results: Our results showed that subjects with higher carbonylated proteins levels have low miR-126 levels after 5 years of follow-up ($p = 0.015$). Subjects with higher levels of SOD showed an increase of miR-143 expression ($p = 0.002$) after follow-up period. Also, subjects with lower LPO levels showed an increase of miR-133 expression ($p = 0.004$) after the intervention. In turn, an increase in miR-145 expression was observed in subjects with higher GSSG levels ($p = 0.002$) after the follow-up period. Finally, miR-145 expression decreased in subjects with short telomeres after the follow-up period compared to baseline ($p = 0.023$).
Conclusion: Epigenetic factors such as miRNAs are involved in cellular aging by the regulation of biological processes such as oxidative stress in patients with cardiovascular disease.

IVs. The treatment with PTH improve the cutaneous wound healing in diabetic rats

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Scientific Program: Nutrition, endocrine and metabolic diseases.
Keywords: PTH, wound healing, Endothelial progenitor Cells, HUVEC, diabetes

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Abstract: Background: Diabetic chronic wounds are a complication of diabetes and a major clinical problem with a high socioeconomic burden. Diabetics have less progenitor cells mobilization, and this decreases the healing capacity. Furthermore, prolongation of the inflammatory phase and increased oxidative stress produces an unfavorable microenvironment for tissue regeneration. The parathyroid hormone (PTH) is secreted by the parathyroid glands and plays an important role in the metabolism of calcium and phosphorus. While continuous high levels of PTH favor the bone loss, its intermittent application is used as anabolic treatment in osteoporosis. PTH can promote angiogenesis and endothelial progenitor cells mobilization (EPC). Furthermore, its receptor, PTH1R, has been found in endothelial cells, fibroblasts, and epithelial cells. Considering the above, we have studied its possible effect on the healing of skin wounds in diabetics.
Methods: Dorsal skin wounds have been made in diabetic rats, which have been treated with 60 µg/Kg/day. The speed of healing has been studied by photographs and the mobilization of EPC in blood at times 0, 3, 7 and 14 days. In the last time, they were sacrificed, and wound samples were taken for histological analysis and serum for factor determinations by elisa and assays of viability, migration and angiogenesis in HUVEC.
Results: PTH treatment accelerated wound closure compared to untreated rats. In the early stages of healing, the treated rats showed a greater mobilization of EPC, but not significant. Histologically, the values were like that of the non-diabetic control rats. Serum from diabetic rats increased HUVEC migration, viability, and angiogenesis, but not significantly.
Conclusion: Although we have not obtained significant changes in several parameters, probably due to the low number of animals analyzed, our results suggest that intermittent administration of PTH could be a possible therapeutic strategy for the treatment of chronic cutaneous ulcers in diabetics.

IVt. Approach to the effectiveness of educational and psychoeducational interventions for the improvement of HbA1c levels. A systematic review

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Keywords: T1D, diabetes, psychoeducational intervention, HbA1c, metabolic diseases, review, multidisciplinary, motivation

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Abstract: Type 1 diabetes is a chronic autoinnmune disease that can produce other serious health pathologies and that some forecasts present it as the seventh leading cause of death in 2030. This context forces us to react to the different possibilities to improve the control of the disease at early ages that reduce other complications. In recent years, studies have been carried out on the efficiency and effectiveness of educational or psychoeducational interventions in diabetics with contradictory results. In this situation, with the aim of finding scientific evidence on the effectiveness of these interventions for metabolic control, a systematic review has been developed in accordance with PRISMA's guidelines and the research question designed with the PICO strategy. The inclusion criteria were: children and adolescents with type 1 diabetes who carried out any type of educational or psychoeducational intervention, the existence of a control or comparator that allowed us to appreciate the effect of the intervention and that the variable considered was HbA1c levels. Scientific publications in English of the last 10 years have been used from the Medline (Pubmed), Cochrane, PsycINFO and PsycARTICLES databases.
The search, after eliminating duplications, resulted in 869 scientific publications, of which 21 were selected for analysis. 13 of them verified a significant improvement in HbA1c levels at some point in the study with respect to the baseline, compared with the levels obtained in the control group or with the interaction of a psychosocial variable included in the study. The educational perspective shows a heterogeneous implementation of multiple strategies for the development of the interventions that allow us to group the strengths of each for the future design of another. In line with other reviews, although there are favorable indications, we cannot determine that the educational or psychoeducational intervention is effective by itself.

Active ageing and Fragility

Va. Predictive value of early warning scales on admitted patients: a systematic review

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Scientific Program: Active ageing and fragility.
Keywords: Early warning score, mortality, nursing, patient safety, systematic review

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Abstract: Background: Admitted patients are exposed to a variety of risks such as the possibility of sudden deterioration. Quick recognition of deterioration is duty of the health care professionals but it is specially nurses' duty. To support a rapid recognition, many scores have been developed; these scores are known as early warning scores.
Purpose: The aim of the study was to know the predictive value of early warning scores in terms of mortality and intensive care unit admission.
Methods: Search strategy was conducted in April 2018 and used following databases: PubMed, Scopus, SciVerse and Web of Science. Papers were filtered from 2008 to 2018 with full text in English and Spanish. Quantitative and qualitative research papers that examined the predictive capacity of early warning scores in admitted adults were included. Quality assessment, data extraction, and analysis were carried out by two reviewers on all included studies.
Results: Nine observational studies were included; studies were developed in Europe and Africa and included 38506 participants in total, the number of participants in each study ranged from 65 to 32149. The selected studies showed the predictive effect of early warning scores in in-hospital mortality, transfer to intensive care units and hospital stay. The most frequently used vital signs were: hearth rate, systolic blood pressure, temperature, breathing rate, and conscious level
Conclusions: Findings suggest that early waning scores are powerful tools as mortality predictors as well as for the detection of critical patients. However, the literature is contradictory about the relationship between length of stay and early waning score values, therefore, further research is needed to clarify if there is a relationship.

Vb. Presence of comorbidities in people with advanced dementia: a descriptive study

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Scientific Program: Active ageing and fragility.
Keywords: Dementia, comorbidity, aged.

Abstract: Introduction: The ageing population that we are currently witnessing brings with it the emergence of pathologies clearly linked to age, such as hypertension and musculoskeletal disorders, among others. Furthermore, advanced age is considered a risk factor for neurodegenerative pathologies such as Alzheimer's disease. The presence of both situations in the elderly could lead to a decrease in their quality of life as well as a more complex approach to both dementia and different comorbidities.
Objective: To know the proportion of people with advanced dementia who present comorbidities, to identify the most prevalent pathologies in these patients and describe the distribution of these according to gender.
Methods: Descriptive cross-sectional observational study. The study population consisted of 100 people with advanced dementia who scored between 5-7 on the Global Deterioration Scale and whose legal guardian/representative signed the informed consent to participate in the present study. Data collection was performed by completing an ad-hoc questionnaire after reviewing the patient's medical history.
Results: 91% of people with advanced dementia were diagnosed with another pathology, specifically 92.31% of women and 86.36% of men. In particular, 63% of these had hypertension, 30% dyslipidemia and 21% type 2 diabetes mellitus. Regarding the distribution of these pathologies according to sex, 65.38% of women were hypertensive compared to 54.55% of men, 20.51% of women had diabetes compared to 22.73% of men and 28.21% of women were diagnosed with dyslipidemia compared to 36.36% of men. On the other hand, with respect to mental disorders, it is worth noting that 34% had a medical diagnosis of depression (37.18% of women and 22.73% of men) and 15% of anxiety (16.67% of women and 9.09% of men). Similarly, musculoskeletal diseases were relatively frequent, since 28% of these subjects had osteoarthritis (30.77% of women and 18.18% of men) and 16% osteoporosis (20.51% of women and none man).
Conclusions: The presence of comorbidities in older people with advanced dementia is common. Specifically, cardiovascular risk factors and depression are clinical entities of great predominance in this group, which interferes decisively in the cognitive deterioration in older people. Therefore, an appropriate approach to these pathologies could generate substantial benefits for the cognitive function.

Vc. Individual circadian preference, shift work, and risk of medication errors: A cross-sectional web survey among Italian midwives

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Scientific Program: Active ageing and fragility.
Keywords: Circadian rhythm; Chronotype; Midwives; Morningness-Eveningness Questionnaire (MEQ); Near misses; Nurses; Rhythms desynchronization; Risk of medication errors; Shift work; Sleep.

Abstract: Background: A series of desynchronizing factors, including shiftwork, may play crucial role in disrupting the individual organization of circadian rhythms and could expose health care professional to the risk of medication errors.
Objective: To explore the possible association between chronotype and risk of medication errors and chronotype in Italian midwives.
Design: A cross-sectional study with a web-based survey design (on Google Forms).
Setting: A questionnaire was used to collect data in 2019. This comprised three main components: (1) demographic information, previous working experience (years), actual working schedule (shiftwork, daywork); (2) individual circadian preference (chronotype), either calculated by Morningness-Eveningness Questionnaire, MEQ (19 items), and self-evaluated; (3) self-perception of risk of medication error (based on the seven rights rule, 7R).
Results: Midwives (N = 401, 98.8% women, range age 22-64) responded 'yes, at least once' to the question dealing with self-perception of risk of medication error in 48.1% of cases. Cluster analysis showed that perception of risk of medication errors was associated with class of age 31 - 35 years, shift work schedule, working experience 6 - 10 years, and Intermediate-type MEQ score.
Conclusions: Perception of the risk of medication errors is present in near one out of two midwives in Italy. In particular, younger midwives with lower working experience, engaged in shiftwork, and belonging to an Intermediate chronotype, seem to be at higher risk of potential medication error. Further research is needed, since early morning hours seem to represent highest risk frame for female healthcare workers, and shiftwork is not always aligned with individual circadian preference. Assessment of individual chronotype in healthcare personel, could represent easy and inexpensive method to identify subjects at higher risk of circadian disruption.

Vd. Effect of MSC-derived extracellular vesicles in hypoxia on cell viability and differentiation

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Keywords: Exosomes, hypoxia, HUVEC, MSC, cell differentiation

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Abstract: Background: Mesenchymal stem cells (MSC) are capacity to differentiate into diverse cellular lineages. This and their anti-inflammatory and immunosuppressive activities, have made them an interesting therapeutic tool in cellular therapy and regenerative medicine. For instance, strategies that activate osteoblast differentiation in MSCs and inhibit adipocyte differentiation, can be used to promote bone regeneration and the treatment of bone pathologies. The therapeutic effect of stem cells is partially mediated by extracellular vesicles secreted by them, such as exosomes. Hypoxia preconditioning for MSCs can be used to elevate the levels of paracrine effectors in exosomes. In this study, we investigate the effect of exosomes derived from human MSCs cultured under hipoxic and normoxia conditions on osteoblastogenesis and adipogenesis.
Methods: Exosomes were isolated from MSC grown in normoxia or hypoxia (3% 02) during 48h, by ultrafiltration and size exclusion chromatography, and characterized and quantified by electron microscopy, dynamic light scattering (DLS) and Western Blot. We examined the effects of exosomes on proliferation, migration, chemotaxis, and angiogenesis of MSCs and Human Umbilical Vein Endothelial Cells (HUVECs).
We also evaluate the effect of exosomes on the differentiation of MSC into osteoblast and adipocytes.
Results: Exosomes increased proliferation and migration of MSCs, but not in HUVEC. There were no differences between normoxia and hypoxia. HUVEC Angiogenesis increased with exosomes. In osteoblast-induced MSCs, exosomes, mainly those derived from hypoxia, increased the mineralization and expression of osteoblastic genes. However, in MSCs induced to adipocytes, they had no significant effects on fat vesicle formation and adipogenic gene expression.
Conclusion: Exosomes derived from human MSCs in hypoxia have the capacity to induce osteoblastogenesis without affecting adipogenesis, so they could potentially be used in therapies for bone regeneration and treatments for bone pathologies such as osteoporosis.

Ve. Alterations of mitochondrial metabolism and autophagy markers in mouse skeletal muscle by aging and overexpression of CYB5R3.

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Scientific Program: Active ageing and fragility.
Keywords: Cytochrome b5 reductase, aging, mitochondrial metabolism, longevity and skeletal muscle.

Abstract: Aging is defined as a gradual decline of the normal physiological functions of an organism and is considered as the most important risk factor for most chronic diseases. Nowadays, there is great interest in identifying enzymes which promote healthy aging and increase longevity. Cytochrome b5 reductase-3 (CYB5R3), which catalyzes electron transfer from NADH to cytochrome b5 and also to alternative electron acceptors as plasma membrane coenzyme Q or several exogenous compounds, increases longevity, improves mitochondrial function, decreases oxidative damage and protects against induced cancer in transgenic mice. We are interested in elucidating how CYB5R3 overexpression extends longevity and have focused our efforts towards the study of markers related to mitochondrial metabolism (mitochondrial complexes, mitochondrial dynamics and biogenesis) and autophagy in young and old mice of wild-type and CYB5R3-overexpressing phenotypes. Mice were fed with standard chow for 3 months and then transferred to an AIN93M diet during 4 or 21 months. Once the corresponding intervention period was completed, mice were sacrificed. We focused our studies on hindlimb skeletal muscle, a model of a postmitotic tissue which plays a relevant role in aging. CYB5R3 was highly overexpressed in skeletal muscle, indicating that this tissue is a suitable model to study the direct effects of CYB5R3 overexpression in the cellular physiology. CYB5R3 levels were not affected by aging in skeletal muscle. CYB5R3 overexpression in old mice tends to increase the levels of mitochondrial complexes, which could be related with the prevention of mitochondrial dysfunction associated with aging. Besides, CYB5R3 overexpression could also counteract the decline in autophagy seen in aging. Optimization of mitochondrial physiology and autophagy thus emerge as key mechanisms related with the antiaging effect of CYB5R3 overexpression. Moreover, our data suggest that therapies aimed on increasing CYB5R3 levels or activity might be feasible antiaging approaches at any age.

Vf. Social support in southern Spain. Preliminary data from an intervention study

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Scientific Program: Active ageing and fragility.
Keywords: Social support, loneliness, ageing, social networks

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Abstract: Background: Demographic and social changes are leading to growth of the population (Bivand et al. 2017). The social support available to older people in the final stage of life affects their health (Gustafsson et al. 2017). Social support refers to social networks and can be defined as help from family, friends, neighbours and other members of the community (Arias Astray & Barrón López, 2008).
Aim: To know the situation of social support of a population in southern Spain, before an individual intervention.
Methods: Observational study carried out on 139 people over 65 in southern Spain, who are being cared for by the Spanish Red Cross. Prior to an individual intervention, sociodemographic and data related to socio-familiar, social support and loneliness status were collected between the months of November 2019 and March 2020.
Results: The mean age of the study population was 80.7 ß.6 years old. 71.2% were widowed, 61.9% considered themselves to be from a low social class and 87.1% were women. 69.1% of the sample claimed to live alone, half of them having been in this situation for more than 5 years. Half claimed to have a good relationship with the family and only a third indicated having a good health condition. However, 12.3% showed a low perceived social support, 1.4% socio-familiar risk was detected and 48.2% were in a situation of loneliness. Low perceived social support was associated with socio-familiar risk (OR: -0.17; CI95%: -1.17- -0.33) and with loneliness (OR: 0.76; CI95%: 0.94-1.22).

Vg. Consumption of a Mediterranean diet on risk factors related to mild cognitive development

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Scientific Program: Active ageing and fragility.

Keywords: Mild cognitive impairment, Mediterranean diet, Advance glycation end products

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Abstract: Higher adherence to the Mediterranean diet (MD) may protect from Alzheimer disease (AD), but its association with mild cognitive impairment (MCI) has not been well explored.

Our aim was to investigate the association of a MD rich in virgin olive oil (supplemented or not with probiotics) to influence MCI development, by neuropsychological test by a randomized crossover study which included 47 men and women with MCI. These patients followed three dietary intervention period of 24 weeks each: 1.- WHO's recommended diet; 2.- MD+placebo and 3.- MD+Probiotic capsule (109 CFU of Lactobacillus rhamnosus and Bifidobacterium longum). Diets were named as WHOd, MD_A and MD_B because double-blind was not open yet. Biochemical analysis, dietary consumption, serum advanced glycation end products (AGEs) and neuropsychological test were determined and analysed at baseline and after each diet. Results with p-value<0.05 were consider statistically significant.

Results showed that blood pressure (both systolic (SBP) and diastolic (DBP)) decreased independently of the diet consumed. However, glycemia and HDL-cholesterol level only decreased after WHOd consumption, compared to pre-intervention. Dietary AGEs were reduced independently of the diet consumed. Serum CML (carboxymethyl-lysine (AGEs)) levels decreased after MD_B compared with WHOd. Regarding neuropsychological test, VOSP-PS (VOSP progressive silhouettes) were improved independently of the diet consumed, FCSRT-interferences were enhanced in those who followed MD vs preintervention, although VOSP-PD (VOSP position discrimination) decrease only with WHOd but not in MD. Significant correlations between dietary AGEs and BP or glycemia and serum CML levels correlated with SBP. VOSP-PS were correlated with serum CML levels, VOSP-PD with SBP and dietary AGEs and FCSRT-interferences with SBP (all $p < 0.05$).

In conclusion MD was associated with a reduction on BP, serum and dietary AGEs which could be related with an improvement or determent of MCI development.

Vh. Sexual dimorphism of mitochondrial complexes, autophagy markers and nutritional sensors in skeletal muscle and liver for transgenic mice overexpressing NADH-cytochrome b5 reductase

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Scientific Program: Active ageing and fragility.
Keywords: CYB5R3, sexual dimorphism, skeletal muscle, liver

Abstract: Higher adherence to the Mediterranean diet (MD) may protect from Alzheimer disease (AD), but its association with mild cognitive impairment (MCI) has not been well explored.
Our aim was to investigate the association of a MD rich in virgin olive oil (supplemented or not with probiotics) to influence MCI development, by neuropsychological test by a randomized crossover study which included 47 men and women with MCI. These patients followed three dietary intervention period of 24 weeks each: 1.- WHO's recommended diet; 2.- MD+placebo and 3.- MD+Probiotic capsule (109 CFU of Lactobacillus rhamnosus and Bifidobacterium longum). Diets were named as WHOd, MD_A and MD_B because double-blind was not open yet. Biochemical analysis, dietary consumption, serum advanced glycation end products (AGEs) and neuropsychological test were determined and analysed at baseline and after each diet. Results with p-value<0.05 were consider statistically significant.
Results showed that blood pressure (both systolic (SBP) and diastolic (DBP)) decreased independently of the diet consumed. However, glycemia and HDL-cholesterol level only decreased after WHOd consumption, compared to pre-intervention. Dietary AGEs were reduced independently of the diet consumed. Serum CML (carboxymethyl-lysine (AGEs)) levels decreased after MD_B compared with WHOd. Regarding neuropsychological test, VOSP-PS (VOSP progressive silhouettes) were improved independently of the diet consumed, FCSRT-interferences were enhanced in those who followed MD vs preintervention, although VOSP-PD (VOSP position discrimination) decrease only with WHOd but not in MD. Significant correlations between dietary AGEs and BP or glycemia and serum CML levels correlated with SBP. VOSP-PS were correlated with serum CML levels, VOSP-PD with SBP and dietary AGEs and FCSRT-interferences with SBP (all $p < 0.05$).
In conclusion MD was associated with a reduction on BP, serum and dietary AGEs which could be related with an improvement or determent of MCI development.

Vi. Understanding the decision-making process about the place of care in old age: a systematic review of qualitative studies

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Scientific Program: Active ageing and fragility.
Keywords: Decision-making, older people, place of care, systematic review

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Abstract: Objectives: To understand the decision-making process on the place of care of the older people.
Design: Systematic review of qualitative studies.
Methods: A systematic review of six databases was conducted from the outset until November 29, 2017. The entire review and analysis process was conducted by peers, consulting a third reviewer in cases where there were discrepancies. We included all articles addressing the decision-making process on the place of care of older people (people aged 65 and over), already experienced by participants, while excluding articles due to technical, methodological and thematic criteria. Finally, an analysis of the quality of the studies finally included was made, and a study of their contributions to the results of the review was also carried out. More details on the methodological aspects of the review can be found in the published review protocol1.
Results: The search strategy yielded 498 articles. 46 articles met the inclusion criteria, but only 44 articles addressed how participants experience the decision-making process. The experiences were multiple and diverse, finding both positive and negative experiences for different group of participants. Negative experiences were the most frequently mentioned.
Conclusions: This systematic review shows the variability in the way of experiencing the decision-making process on the place of care in old age through the great number and diversity of experiences expressed by the participants in this process. The knowledge of these aspects will help to facilitate and improve the way in which this decision-making is carried out.
PROSPERO registration number CRD42018084826.
Bibliography:
1. Serrano-Gemes G, Serrano-del-Rosal R, Rich-Ruiz M. Decision-making on the location of care of the elderly:protocol for a systematic review of qualitative studies. BMJ Open 2018;8(10): e022411. doi:10.1136/bmjopen-2018-022411”

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