REUNIÓN CIENTÍFICA RED HERACLES 2010

Granada, 13-15 Diciembre 2010

AGENDA

Lunes 13 de Diciembre

Llegada a Granada durante el día. HOTEL VINCCI GRANADA (a cinco minutos caminando de la Facultad de Medicina) Av. Constitución, 18 18012 Granada **Excursión a la Alhambra y centro de Granada.**
Cena Informal Red Heracles **21:30 – Café-Pub El Granero**, Plaza Poeta Luis Rosales S/N, (cerca Pza. Isabel Católica)

Martes 14 de Diciembre

REUNIÓN CIENTÍFICA HERACLES.

Lugar de la Reunión:

Facultad de Medicina
Salón de Seminarios A
Avenida Madrid 11
Granada

10:00–11:00	***COFFEE WELCOME***	***1h***
11:00 – *13:00*	***Reunión de Jóvenes Investigadores*** *(ver OD adjunta al final)*	***2h***
11:00– *13:00*	***Reunión de IPs*** *(1 Jefe de Grupo + 1 ó 2 acompañantes)*	***2h***

13:00–14:00	***COMIDA FRÍA***

14:00– *14:30*	*Evaluación de la Red. J Marrugat*	***30min***

Martes 14 de Diciembre (cont)

Mesa sobre BASES HTA (Línea 1) **Moderador: Miguel Ángel Valverde**		
14:30– *15:30*	*Conferencia invitada Línea 1* *Prof. Ralf Köhler. "KCa channels and cardiovascular disease"*	***45min + 15min (discusión)***

15:30– *17:00*	*- Ponencias Línea 1*	***1h 30min***
	1. UNICA-UPF & LDFAO-GRIB **Anabel Fernández: *MAXIK CHANNEL-DEPENDENT EFFECTS OF TUNGSTATE IN HETEROLOGOUS EXPRESSION SYSTEM AND IN THE VASCULATURE*.** **Summary:** Tungstate (WO_4^{2-}) is able to reduce blood pressure in spontaneously hypertensive rats although its mechanism is not well understood. We have evaluated the impact of tungstate on BK channels, which are key regulators of vascular tone regulation. Electrophysiological studies of heterologously expressed BK channels and vascular contractility in mouse models were run to determine the impact of tungstate in the vasculature.	*20min + 10min (discusión)*
	2. ULEC/IMIM & FIIJT **Carla Lluis: USE OF A MULTI-LOCUS GENETIC RISK SCORE IN IMPROVING THE ASSESSMENT OF CARDIOVASCULAR RISK** **Summary:** Cardiovascular risk functions are currently used as a screening tool in primary prevention. However, the sensitivity of the risk functions is low. In the last years several genetic polymorphisms associated with coronary heart disease (CHD) have been identified. The aim of this study is to assess whether the inclusion of genetic information in risk functions improves their predictive capacity.	*20min + 10min (discusión)*
	3. UNICA-UPF & NEUROMAR **Ernest Palomer: VASCULAR NITROTYROSINATION PATHOPHYSIOLOGY IN ISCHEMIC CONDITIONS** **Summary:** Identification of a biomarker for stroke is critical for its correct treatment, which depends on rapid and accurate diagnosis. After a stroke, the damaged, ischemic tissue produces nitric oxide (NO) and reactive oxygen species, such as superoxide anion, which reacts with NO to produce peroxynitrite, a harmful and highly reactive agent that irreversibly nitrates tyrosine residues of proteins. We have exploited this pathophysiological trait to evaluate a biomarker with biological plausibility.	*20min + 10min (discusión)*
17:00– *18:30*	*Reunión monográfica Estudio PROCELL* 1. *Calendario de actuaciones* 2. *Artículos* 3. *Otros*	***1h 30m***

CENA HERACLES
21:00 – Hotel VINCCI

Miércoles 15 de Diciembre

Mesa sobre FACTORES REMODELADO CARDIOVASCULAR Y TERAPÉUTICA (Línea 2)

Moderador: Mª Teresa Pérez

9:00–10:00	*Conferencia invitada Línea 2* *Dr. Vicente Andrés. "Remodelado cardiovascular: un punto de encuentro HERACLES-RECAVA"*	***45min + 15min (discusión)***
10:00–12:30	*- Ponencias Línea 2*	
	1. HCUV-SERCAR **Clara Bonanand: INFLUENCE OF COMORBIDITIES ON ONE-YEAR OUTCOMES IN NON-ST-SEGMENT ELEVATION ACUTE CORONARY SYNDROME** **Summary:** Objective: To investigate the comorbidities with prognostic influence in non-ST elevation acute coronary syndrome (NSTEACS). Methods: The study group consisted of 1017 (derivation cohort, H Clínic València) and 652 (validation cohort, Hospital Clínic Barcelona) patients. Comorbid conditions, including risk factors and components of the Charlson comorbidity (ChCI) and coronary artery disease (CAD) specific indices, were collected. The main outcome was 1-year mortality. Results: After adjusting for 4 variables related to NSTEACS characteristics (base model), 5 comorbidities predicted mortality: renal failure, dementia, peripheral artery disease, prior heart failure and prior myocardial infarction. A simple comorbidity index (SCI) was developed using these variables. All 3 models including either the SCI, ChCI or CAD-specific index showed higher discriminative ability than the base model (7.31%, 5.59% and 4.31%, respectively; p<0.001), without differences among them. The strength of the association between the SCI and mortality was similar in the validation cohort. Conclusions: Renal dysfunction, dementia, peripheral artery disease, prior heart failure and prior myocardial infarction are the comorbidity predictors of mortality in NSTEACS. A simple index using these variables proved to be as accurate as the more complex comorbidity indices.	*20min + 10min (discusión)*
	2 .UCM **Ricardo Caballero/Eva Delpón: PHARMACOLOGICAL MODULATION OF CARDIAC INWARD RECTIFIER CHANNELS.** **Summary**: Both increase and decrease of cardiac inward rectifier current (IK1) are associated with severe cardiac arrhythmias. Flecainide, is an antiarrhythmic drug very effective in the cardioversion of atrial fibrillation while exhibits ventricular proarrhythmic effects. We characterized the electrophysiological and molecular basis of the flecainide-induced increase of the current generated by Kir2.1 channels (IKir2.1). Flecainide increases outward IKir2.1 generated by homotetrameric Kir2.1 channels by decreasing their affinity for intracellular polyamines, which reduces the inward rectification of the current. Flecainide interacts with the HI-loop of the cytoplasmic domain of the channel, Cys311 being critical for the effect. This explains why flecainide does not increase IKir2.2 and IKir2.3, since Kir2.2-2.3 channels do not exhibit a Cys residue at the equivalent position. We also demonstrated that incubation with flecainide increases expression of functional Kir2.1 channels in the membrane, an effect also determined by Cys311. Our results provide noteworthy clues about the structural determinants of the C-terminus cytoplasmic domain of Kir2.1 channels involved in the control of gating and rectification.	*20min + 10min (discusión)*
	3. HCSC & ICSCM **Javier Modrego Martín: EFFECTS OF PLATELETS ON THE PROTEIN EXPRESSION IN AORTIC SEGMENTS. A PROTEOMIC APPROACH** **Summary:** It is well known that disturbances in vascular function contribute to the development of the cardiovascular diseases. Vascular reactivity has been Healthy vascular wall represents a non-adhesive and non-thrombotic surface that inhibits platelet activity while under inflammatory conditions, as it occurs in arterial-related ischemic events, the antithrombotic properties of the vascular wall shift towards a prothrombotic state favouring platelet activation. We have analyzed whether platelets may modified the expression of proteins in the vascular wall using an in vitro model by coincubating human platelet rich plasma (PRP) with control and tumour necrosis factor-α (TNF-α)-preincubated bovine aortic segments. Two-dimensional electrophoresis (2 DE), mass spectrometry and Western blot analysis were used. The expression of proteins associated with the cytoskeleton and energetic metabolism was determined in the aortic segments. In control healthy vascular wall, only the expression of cytoskeleton-related proteins was modified by PRP. However, when PRP was coincubated with TNF- pre-stimulated aortic segments a lower number of cytoskeleton-related proteins were modified by PRP. In control segments, PRP modify energetic-related proteins associated with oxidative stress. In TNF- preincubated aortic segments the presence of PRP modified both the level of expression of key-step glycolytic-related proteins and their activity. This work suggests that crosstalk between platelets and the vascular wall is bidirectional and platelets regulated in the vascular wall the expression of proteins associated with cytoskeleton and energetic metabolism.	*20min + 10min (discusión)*

11:30-12:00	***COFFEE BREAK***	***30min***

12:00–*12:30*	**4. IBGM-UVA & CARDIO-IDIBAPS** **Pilar Cidad: CONTRIBUTION OF KV1.3 CHANNELS EXPRESSION TO THE PROLIFERATIVE RESPONSE OF VASCULAR SMOOTH MUSCLE CELLS: MOLECULAR DETERMINANTS** **Summary:** Phenotypic switch of vascular smooth muscle cells involves changes in the expression of membrane receptors and ion channels. Our previous work using in vivo and in vitro animal models of vascular smooth muscle cell proliferation demonstrated that functional expression of Kv1.3 channels associates with increased proliferation. In the present work we have explored if this association is a conserved feature across vascular beds from different species and we have investigate some of the possible mechanisms linking Kv1.3 expression and cell proliferation. These results can contribute to the development of new therapies for the prevention and treatment of unwanted vascular remodelling.	*20min + 10min (discusión)*

Mesa sobre DISFUNCION ENDOTELIAL (Línea 3)
Moderador: Juan Tamargo

12:30–*14:20*	*- Ponencias Línea 3*	***1h** 50min*
	1. NKRI & ULEC-IMIM **Miguel López-Botet: ACUTE CORONARY DISEASE AND CAROTID PLAQUE THICKNESS ARE ASSOCIATED TO AN INCREASED EXPRESSION OF THE LILRB1 RECEPTOR BY HUMAN NK AND T CELLS** **Summary:** A population-based case-control study was designed comparing the expression of NKG2A, NKG2C and LILRB1 NK cell receptors (NKR) from patients studied within 72 h after acute myocardial infarction (AMI), and from individuals without clinical evidence of cardiovascular disease; in the latter, the relationship between NKR expression and carotid intima-media thickness (CIMT) was also assessed. Seropositivity for cytomegalovirus was associated to increased proportions of circulating NKG2C+ and LILRB1+ NK and T cells, confirming previous reports. By contrast, only LILRB1+ cells were found increased in patients with acute coronary disease, independently of age, sex, conventional vascular risk factors and seropositivity for HCMV. Remarkably, higher LILRB1 expression levels in NK and T cells significantly correlated with carotid plaque thickness in a cohort of control individuals. These observations support a possible link of infectious burden with overt and subclinical atherosclerosis.	*20min*
	2. NEUROMAR & NKRI **Jose Enrique Martínez Rodríguez: INNATE IMMUNE RESPONSE IN CAROTID ATHEROSCLEROSIS: INSIGHTS INTO THE INFECTIOUS BURDEN HYPOTHESIS.** **Summary:** The combined activity of past and chronic infections over the immune system may collaborate in the atherosclerotic inflammatory process and increase the risk of vascular complications. Based on the evidences that some chronic infections may modulate the natural killer receptors expression on lymphocytes, it is evaluated their potential use as biomarkers of high-risk carotid atherosclerotic plaques based on clinical, ultrasonographic and pathological data from a prospective series of patients.	*20min + 10min (discusión)*

	3. NEUROMAR & HEMATO-IDIBAPS **Elisa Cuadrado: VON WILLEBRAND FACTOR LEVELS AND THE RISK OF STROKE RECURRENCE** **Summary:** The aim of the study is to determine if plasmatic levels of vW factor can predict the risk of stroke recurrence in two scenarios: In patients with transitory ischemic attacks (TIA) of any etiology and in patients with cryptogenic strokes. The end point of the study is the diagnosis of a new stroke or TIA during a minimum follow-up of six months. In cryptogenic group detection of Atrial fibrillation during follow-up is also considered and end point. Plasmatic levels of vWF are measured from plasma samples obtained during the first 24h after the symptoms onset. The study is still ongoing and is carried out in collaboration with HEMATO-IDIBAPS.	*20min + 10min (discusión)*
	4. HEMATO IDIBAPS **Carolina Caballo / Maribel Diaz-Ricart: CONTRIBUTION OF UREMIA AND SUBSTITUTIVE THERAPIES IN THE DEVELOPMENT OF ENDOTHELIAL DYSFUNCTION IN PATIENS WITH CHRONIC KIDNEY DISEASE: IMPACT OF PERITONEAL DIALYSIS** **Summary:** Deficient hemostasis coexists with accelerated atherosclerosis in patients with chronic kidney disease. The high incidence of aterothrombotic events has been associated with endothelial dysfunction. Although most of the studies have been carried out in hemodialysis patients, the contribution of the uremic state and the substitutive therapies has been often disregarded. We have explored potential biomarkers and the mechanisms involved in the development of endothelial damage in three groups of patients with chronic kidney disease: i) under conservative treatment (predialysis), ii) after at least a month on hemodialysis, and iii) patients on peritoneal dialysis. Results point out to a potential role of the transcription factor NFkappaB	*20min + 10min (discusión)*

14:20–15:20	***COMIDA FRÍA***	

15:20- *16:20*	*- **ENTREGA DE PREMIOS GENDIAG:*** *a la mejor publicación de HERACLES 2009 * y* *a la mejor publicación de HERACLES 2009 de un JOVEN INVESTIGADOR ** *- Presentación de los resultados de la mejor publicación HERACLES* *15'* *- Presentación de los resultados de la mejor publicación de un JOVEN investigador HERACLES* *15'* *- Clausura*	***1h***

* Las bases de los premios aparecen en la nueva página web HERACLES: www.redheracles.net

AGENDA REUNIÓN JÓVENES INVESTIGADORES HERACLES

(Granada, diciembre 2010)

Introducción – Dr Jaume Marrugat

11:00–*11:20*	*Seguimiento desde la última reunión y próximos pasos para el Grupo de Jóvenes Investigadores – Ana Paula Dantas*
11:20–*12:05*	*- Ponencias*
	- Ponencia 1 (10 min+5min discusión) – *Irene López - Hemato-IDIBAPS* *"Líneas de investigación en el grupo HEMATO-IDIBAPS"*
	- Ponencia 2 (10 min +5min discusión) – *Manuel Sánchez Santos - UGR* *"Chronic antihypertensive effects of the PPAR-β agonist"*
	- Ponencia 3 (10 min +5min discusión) – *Laura Novensa - Cardio-IDIBAPS* *"Murine model to study cardiovascular damage by aging and menopause"*
12:05–*12:20*	*Discusión General y Elección de Nuevo Representante*
12:20–*10:00*	*Otros temas*