SCIENTIFIC MEETING HERACLES NETWORK 2011

Barcelona, December 15-16, 2011
IMIM-PRBB

AGENDA

Thursday, December 15

10:30 **11:30**	COFFEE / WELCOME Room: **XIPRE (1st floor)**	**60min**
11:30 13:00	**Meeting of the HERACLIDES Investigators** Room: **XIPRE (1st floor)**	**90min**
11:30 13:00	**Meeting of PIs** (agenda in Appendix 2) Room: **CÓRSEGA-SARDENYA (1st floor)**	**90min**
13:15 14:00	Evaluation of the Network - J Marrugat Room: **CONFERENCE HALL. PRBB**	**45min**
14:00 **15:00**	LUNCH	**60min**

Thursday, December 15 (cont.)

ENDOTHELIAL DYSFUNCTION PANEL

CONFERENCE HALL. PRBB

Moderator: Juan Tamargo

15:00 16:00	Invited Lecture, ENDOTHELIAL DYSFUNCTION IN CARDIOVASCULAR DISEASE: A ROLE FOR INFLAMMATION-DRIVEN OXIDATIVE STRESS? Prof. Javier Díez	**45min + 15min (discussion)**
16:00 17:00	Papers: ENDOTHELIAL DYSFUNCTION	**1h**
	1. CARDIO-IDIBAPS **Ana Paula Dantas: EFFECTS OF ESTROGEN AND RALOXIFENE ON VASCULAR INFLAMMATION: A MATTER OF TIMING**.	15min + 5min (discussion)
	2. UCM **Marta González de la Fuente: EFFECTS OF BETA-ADRENOCEPTOR STIMULATION ON HUMAN ATRIAL K+ CURRENTS.**	15min + 5min (discussion)
	3. FICUV & HCUV-SERCAR **Carlos Bueno Betí: ISOLATION, CULTURE AND LATE ENDOTHELIAL PROGENITOR CELL FUNCTIONAL CHARACTERIZATION FROM PATIENTS WITH ACUTE CORONARY SYNDROME.**	15min + 5min (discussion)
17:15 18:15	**Transferencia de conocimiento: la experiencia de crear una SPIN-OFF** **Dra. Celia Sánchez-Ramos** **Prof. Titular UCM** **Directora de la EBT : *Alta Eficacia Tecnología*** Room: **CONFERENCE HALL. PRBB**	**1h**
18:15 18:45	Monograph Meeting: COLMAH (*Colección de Muestras Arteriales de HERACLES*) Room: **CÓRSEGA-SARDENYA (1st floor)**	**30min**
18:45 19:45	Monograph Meeting: PROCELL Study Room: **CÓRSEGA-SARDENYA (1st floor)**	**1h**

HERACLES NETWORK DINNER

Friday, December 16

MOLECULAR MECHANISMS OF ARTERIAL HYPERTENSION PANEL

CONFERENCE HALL. PRBB

Moderator: Miguel Ángel Valverde

9:00 10:00	Invited Lecture, MOLECULAR MECHANISMS OF ARTERIAL HYPERTENSION **Prof. Anna Dominiczak**	**45min + 15min (discussion)**
10:00 11:00	Papers: MOLECULAR MECHANISMS OF ARTERIAL HYPERTENSION	**60min**
	1. HCSC & ICSCM & UCM	
	José Javier Zamorano León: PROTEOMIC CHANGES RELATED TO "BEWILDERED" CIRCULATING PLATELETS IN THE ACUTE CORONARY SYNDROME.	15min + 5min (discussion)
	2. UGR & UCM	
	Rosario Jiménez Monleón: EPICATECHIN LOWERS BLOOD PRESSURE, RESTORES ENDOTHELIAL FUNCTION AND DECREASES OXIDATIVE STRESS, ENDOTHELIN-1 AND NADPH OXIDASE ACTIVITY IN DOCA-SALT HYPERTENSION.	15min + 5min (discussion)
	3. HEMATO-IDIBAPS & CARDIO-IDIBAPS	
	Irene López-Vilchez: INTERNALIZATION OF TISSUE FACTOR BY PLATELETS PROMOTES REVERSIBLE CYTOSKELETAL ASSEMBLY THROUGH ACTIVATION OF RHOA AND PI3-KINASE. EFFECTS OF INHIBITORY STRATEGIES.	15min + 5min (discussion)
11:00 **11:30**	**COFFEE BREAK**	**30min**

Friday December 16 (cont.)

CLINICAL AND INFLAMMATION RESEARCH PANEL

Moderator: Mª Teresa Pérez

CONFERENCE HALL. PRBB

11:30 12:30	Invited Lecture, CA2+ SIGNALING AND VASCULAR REMODELING **Prof. Mohamed Trebak**	**45min + 15min (discussion)**
12:30 13:30	Papers: CLINICAL AND INFLAMMATION RESEARCH	**90min**
	1. NEUROMAR & ULEC/IMIM	
	Carolina Soriano Tárraga: EPIGENETICS OF ISCHEMIC STROKE.	15min + 5min (discussion)
	2. ULEC/IMIM	
	María Grau Magaña: DERIVATION AND VALIDATION OF A SET OF 10-YEAR CARDIOVASCULAR RISK PREDICTIVE FUNCTIONS IN 11 POPULATION SPANISH COHORTS: THE FRESCO STUDY.	15min + 5min (discussion)
	3. HCUV-SERCAR:	
	Clara Bonanad Lozano: RANDOMIZED COMPARISON BETWEEN INVASIVE AND CONSERVATIVE STRATEGIES IN PATIENTS WITH NON-ST-SEGMENT ELEVATION ACUTE CORONARY SYNDROME AND COMORBIDITIES.	15min + 5min (discussion)

13:30 14:30 **GENDIAG AWARDS CEREMONY:**

Best Publication, HERACLES 2010

Best HERACLIDES (YOUNG INVESTIGATOR) Publication, HERACLES 2010

- Presentation of the results of the best HERACLES publication — 15min
- Presentation of the results of the best HERACLIDES INVESTIGATOR publication — 15min
- Closing

14:30 15:30 **LUNCH**

ENDOTHELIAL DYSFUNCTION PANEL

CARDIO – IDIBAPS:

1. Speaker: Ana Paula Dantas
   Title: Effects of Estrogen and Raloxifene on vascular inflammation: a matter of timing.
   Abstract: Our studies aims to determine the role of aging on vascular function and how time since menopause affects the vascular modulation by estrogen and Raloxifene. To address this issue, the effects of estrogen on key regulators of vascular function have been studied in a murine model of aging as well as in arteries from postmenopausal women. To this point, we have established that aging alters estrogen-mediated effects on the modulation of inflammatory and prooxidative biomarkers in women. For some markers aging can be associated to a switch from a beneficial anti-inflammatory action by estrogen, at earlier stages of menopause, to a pro-inflammatory profile after 5 year past its onset. How aging affects estrogen responses and to what extent these changes can modify the risk for cardiovascular disease remains unknown, but our data strongly suggest that timing to start hormone replacement therapy should be taken into account when deciding the best therapy to treat postmenopausal women.

UCM:

2. Speaker: Marta González de la Fuente
   Title: Effects Of Beta-Adrenoceptor Stimulation On Human Atrial K+ Currents
   Abstract: The electrophysiological effects of β-adrenergic stimulation on atrial myocytes obtained from patients in sinus rhythm (SR) and chronic atrial fibrillation (CAF) have not been compared until yet, even when it has been proposed that β-adrenergic stimulation has profound influence in the genesis and maintenance of atrial fibrillation. Therefore, we analyzed the effects produced by isoproterenol (Iso, 1 nM), a β-adrenoceptor agonist, on the transient outward (Ito), the ultrarapid (IKur) and the slow delayed rectifier (IKs) K+ currents recorded in human atrial myocytes obtained from SR and CAF patients.

FICUV:

3. Speaker: Carlos Bueno Betí
   Title: Isolation, culture and late endothelial progenitor cell functional characterization from patients with acute coronary syndrome
   Abstract: Fifty patients from PROCELL study with acute coronary syndrome (ACS) were recruited. The number of total circulating endothelial cells (CEC) and endothelial progenitor cells (EPC) was assessed by flow cytometry by analyzing the expression of CD31, CD146, CD34 and KDR markers in fresh blood samples taken at days 0, 7, 30 and 180 after ACS. Mononuclear cell (MNC) were isolated from peripheral blood samples and cultured until first colonies of endothelial progenitor cells appeared. Then, EPC functional parameters were studied in terms of adhesion, growth curve, proliferation, vasculogénesis and apoptosis.

MOLECULAR MECHANISMS OF ARTERIAL HYPERTENSION

HCSC:

1. Speaker: José Javier Zamorano León
   Title: Proteomic Changes Related To “Bewildered” Circulating Platelets In The Acute Coronary Syndrome
   Abstract: Acute coronary syndromes (ACS) are associated with platelet activation. The aim of the present study was to study the protein expression level associated with glycolysis, oxidative stress, cytoskeleton and cell survival in platelets obtained during an acute coronary syndrome. Platelets from 37 coronary ischemic patients, divided into patients admitted within 24 hours after the onset of chest pain, (ACS group; n=14) and patients with stable coronary ischemic disease (CAD, n=23), were analyzed using proteomics. The expression levels of proteins involved in cellular cytoskeleton (F-actin capping, b-tubulin, a-tubulin isotype 1 and vimentin), glycolysis pathway (glyceraldehyde-3-phosphate dehydrogenase and three pyruvate kinase isotypes) and cellular related anti-oxidant system (three catalases isotypes and manganese superoxide dismutase) as even the activity of glutathione-S transferase were significantly reduced in platelets from ACS patients compared to CAD patients. Moreover, reduction in the expression of proteins associated with cell survival such as heat shock protein 71 and proteasome subunit beta type 1 were also observed in ACS platelets compared with CAD platelets. In summary, these results suggest the existence of circulating antioxidant, cytoskeleton and glycolytic-“bewildered” platelets during the acute phase of a coronary event.

UGR:

2. Speaker: Rosario Jiménez Moleón
   Title: Epicatechin Lowers Blood Pressure, Restores Endothelial Function And Decreases Oxidative Stress, Endothelin-1 And Nadph Oxidase Activity In Doca-Salt Hypertension.
   Abstract: We studied the effects of chronic treatment with epicatechin on blood pressure, endothelial function and oxidative status in DOCA-salt induced hypertension. Rats were treated for five weeks with (-)-epicatechin 2 or 10 mg kg-1day-1. The high dose of epicatechin prevented both the increase in systolic blood pressure and proteinuria induced by DOCA-salt. Plasma endothelin-1 and malondialdehyde levels and urinary isoprostaglandin F2□ excretion, were increased in animals of DOCA group, and reduced by epicatechin10 mg kg-1 treatment. Aortic superoxide levels were enhanced in DOCA-salt group and abolished by both doses of epicatechin. However, only epicatechin10 mg kg-1 reduced the raise in aortic NADPH-oxidase activity and p47phox and p22phox gene overexpression found in DOCA-salt animals. Epicatechin increased the transcription of Nrf2 and Nrf2 target genes in aortas from control rats. Epicatechin also improved the impaired endothelium-dependent relaxation to acetylcholine and increased the phosphorylation of both Akt and eNOS in aortic rings. In conclusion, epicatechin prevents hypertension, proteinuria and vascular dysfunction.

HEMATO IDIBAPS:

3. Speaker: Irene López Vilchez
   Title: Internalization of tissue factor by platelets promotes reversible cytoskeletal assembly through activation of RhoA and PI3-Kinase. Effects of inhibitory strategies
   Abstract: Platelets can internalize and store tissue factor-rich microvesicles from placental origin (pTF), event enhanced by serotonin (5-HT). There is limited knowledge on the mechanisms involved in the uptake, redistribution and functional expression of TF by platelets. The mechanisms implied in the uptake and traffic of pTF by platelets have been investigated focusing on the role of RhoA, PI3-kinase, the 5-HT transporter (SERT), and changes in the cytoskeletal organization. Effects of inhibitory strategies to block GPIIbIIIa (Reopro), the scavenger receptor GPIV (anti-CD36), the SERT (S-Citalopram), and PI3-kinase (Wortmannin) were evaluated.

CLINICAL AND INFLAMMATION RESEARCH

NEUROMAR:

1. Speaker: Carolina Soriano Tárraga
   Title: Epigenetics of ischemic stroke
   Abstract: Ischemic stroke is a heterogeneous multifactorial disorder, among the leading causes of mortality and long-term disability in the western world. Epidemiological data provides evidence for a genetic component to the disease, but its epigenetic involvement is still largely unknown. Epigenetics mechanisms, such as DNA methylation, regulate high-order DNA structure and gene expression. Global methylation changes over time, and has been suggested its association with aging processes and with modulation in risk of suffering different pathologies. Analysis of global DNA methylation may provide information about the disease, its prognosis and about the effect of vascular risk factors. We will measure global DNA methylation by luminometric methylation assay (LUMA) on DNA blood samples of 800 ischemic stroke patients and 800 controls. Preliminary case results will be ready for early December. Changes in global DNA methylation may enhance risk factors effect and anticipate events onset. It could provide evidence of an epigenetic component in ischemic stroke.

ULEC/IMIM:

2. Speaker: María Grau
   Title: Derivation and validation of a set of 10-year cardiovascular risk predictive functions in 11 population Spanish cohorts: the FRESCO Study
   Abstract: Cardiovascular risk functions determine the probability to present a cardiovascular event in the future, based on a series of individual characteristics typically sex, age and risk factor profile. The aim of FRESCO project is to present a set of simple, incremental functions to predict CHD and stroke events at 10 years with classical and non-laboratory cardiovascular risk factors that could be implemented in the electronic medical records, particularly, but not necessarily only, in primary care or in preventive medicine settings where cardiovascular risk is typically screened.

HCUV-SERCAR:

3. Speaker: Clara Bonanad Lozano
   Title: Randomized comparison between invasive and conservative strategies in patients with non-ST-segment elevation acute coronary syndrome and comorbidities
   Abstract: The guidelines of clinical practice, based on the randomized studies, recommend an invasive strategy in non-ST elevation acute coronary syndrome (NSTEACS). However, patients with comorbidities are excluded from the randomized studies and the observational registries show that patients with comoribidities undergo fewer cardiac catheterizations. Our aim is to investigate the benefit of the invasive strategy in patients with NSTEACS and comorbidities.
   Patients hospitalized with NSTEACS, older than 70 years and with significant comorbidities, will be included. The latter will be defined as at least 2 of the following: peripheral artery disease, cerebral vascular disease, dementia, chronic pulmonary disease and chronic renal failure. The included patients will be randomized to an invasive (routine coronary angiogram) or conservative (coronary angiogram only if recurrent or inducible ischemia) strategy. All patients will receive medical treatment according to current recommendations.
   The main outcome will be death, reinfarction or readmissions by cardiac cause at one-year follow-up. Our hypothesis is that an invasive strategy will improve prognosis in patients with NSTEACS and comorbidities.

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HERACLIDES INVESTIGATORS MEETING

Barcelona, December 15, 2011

Room: XIPRE

11 30h – 13 00h

AGENDA

1. Introducción - Ana Paula Dantas

2. Presentación de Grupos de Investigación

2.1 FICUV - Carlos Bueno

2.2 HCUV-SERCAR - Clara Bonanad

2.3 HEMATO-IDIBAPS - Irene Lopez-Vilchez

2.4 IBGM-UVA - Pilar Cidad

2.5 NKRI-IMIM - Aura Muntasell

2.6 UCM - Ricardo Gómez

2.7 UNICA-UPF – Ana Isabel Fernández

2.8 NEURO-MAR – Eva Giralt

2.9 URLEC-IMIM – Maria Grau

2.10 CARDIO-IDIBAPS – Ana Paula Dantas

3. Conclusiones – Tod@s

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MEETING OF THE HERACLES NETWORK SCIENTIFIC COMMITTEE

Barcelona, December 15, 2011
Room: CÒRSEGA-SARDENYA
11 30h – 13 00h

AGENDA

1. **HERACLES in 2011**

2. **Update and news**
    a. Collection of Arterial Samples of the HERACLES Network (COLMAH) Study (*Colección de Muestras Arteriales de la Red HERACLES*).
    b. Awards to the best publications of the year.

3. **Prospects for the new research networking ISCIII 2013-2015**
    a. Internal evaluation system and rules for project presentation

4. **All other business**

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Monograph Meeting: **PROCELL Study**

Barcelona, December 15, 2011
Room: CÓRSEGA-SARDENYA
18 15h – 18 45h

AGENDA

1. **Resultados globales. Ander Regueiro**
2. **Control calidad. Maribel Díaz**
3. **Funcionalismo celular. Susana Novella**
4. **Movilización Ca intracelular. Gemma González**
5. **Discusión conjunta**

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Monograph meeting: **COLMAH**
(*Colección de Muestras Arteriales de HERACLES*)

Barcelona, December 15, 2011

Room: CÓRSEGA-SARDENYA

18 45h – 19 45h

AGENDA

1. **Presentación y puesta al día de la colección COLMAH**

2. **Principales novedades: Base de datos centralizada, nuevos formularios de envío de muestras vía web, nuevos tipos de muestras**

3. **Presentación del logo y el folleto informativo COLMAH**

4. **Presentación de un nuevo proyecto COLMAH (C. Hermenegildo / S. Novella)**