Biomedical Studies

Teresa Pinheiro

The research activities during 2007 within the group of Biomedical Studies make use of focused ion beam techniques to image tissue and cell morphology as well as other micro-analytical techniques to assess elemental composition and molecular indicators of cell/tissue response (e.g., imaging techniques, cell detection techniques along with characterization of signalling molecules, nuclear techniques and mass spectrometry based techniques, among others).

The outcome of past and ongoing research projects in health and disease condition of human populations paved the way to the present activities. The studies on pneumology/environmental health, dermatology and haematology, combining indicators of exposure to pollution sources, the inflammatory response and metabolism, are naturally continuing as confirmed by renewed financial support of private and international entities.

A recently approved project will reactivate environmental health studies and long standing collaborations with Serviço de Pneumologia, Hospital de Santa Maria, and will make use of new technical facilities such as ICP-mass spectrometer that is being installed under the National Program for Scientific Re-equipment. The study will focus on the relationship between professional exposure to chemical agents and EBC (Exhaled Breath Condensate) characteristics, in order to develop a non-invasive human bio-indicator.

The significant funding of several projects in association with the Serviço de Cardiologia, Hospital de Santa Marta, Centro Hospitalar de Lisboa Central, stimulated the research activities to develop a clinical registry of inflammation in acute coronary syndromes and to monitor the alterations of that process during the recovery period. The driving motivation for this work is to improve medical diagnosis for the clinical atheroma. Modern imaging techniques, virtual histology intra-vascular ultrasound (VH IVUS), for the artery wall also assessing plaque composition opened new perspectives of studying the clinical atheroma. Associating the biological characteristics of the plaque with circulating indicators of plaque activity and endothelial function, may have a noteworthy outcome in VH IVUS data interpretation with direct implications in the clinical practice.

These projects will strengthen existing skills in environmental health and molecular cardiology in Portugal, and will promote advanced training for students and create new synergies by involving various research groups from different areas.

The main achievements of the research developed during 2007 are summarised in the following pages.

Researchers

T. PINHEIRO, Aux.
L.C. ALVES, Aux.

Students

P. NAPOLEÃO, Ph.D. student, FCT grant
P. ALMEIDA, M.Sc. student, FC-UL
R. CARVALHO, M.Sc. student, FC-UL

Technical Personnel

R. PINHEIRO, laboratory assistant

Collaborators

R.C. FERREIRA, M.D., Hospital Sta. Marta
M. SELAS, Hospital Sta. Marta
M.C. SANTOS, Aux. Prof., FC-UL
A.M. VIEGAS-CRESPO, Princ. Researcher, FC-UL
A. TURKMAN, Full Prof., CEAFC, FC-UL
M.C. MONTEIRO, Ass. Prof., CESPU, Porto
A. BARREIROS, Aux. Resarcher, INETI
A.B.ALMEIDA, Full Prof., FM-UL/Hospital Sta. Maria
P. FILIPE, Aux. Prof., FM-UL/Hospital Sta. Maria
R. SANTOS, M.D., Hospital Sta. Maria
R.FLEMING., M.D., Hospital Sta. Maria
J.N. SILVA, M.D., FM-UL/Hospital Sta. Maria

New Biomarkers For Human Pathologies

T. Pinheiro and L.C. Alves

A – Endothelial function and plaque activity in acute coronary syndromes

P. Napoleão, R. Cruz Ferreira, M. Selas, M.C. Monteiro, A.M. Viegas-Crespo, A. Turkman[1], V. Andreozzi, R. Carvalho

An increasing body of literature shows that the progressive development of the atherosclerotic plaque and local vascular events that encircle an acute coronary syndrome implicate pro-inflammatory mediators.

We are studying activation and apoptosis associated to endothelial cells and/or platelets by measuring molecules in circulation (signalling molecules, cytokines, adhesion molecules), their expression in platelets and leukocytes, and the microparticles released in those processes. The relationship of virtual histology intravascular ultrasound (VH IVUS)-derived measurements of atherosclerotic plaque with the above indicators of plaque activity and endothelial function are being assessed to establish correlations between plaque composition, patient morphological parameters, cardiac events and plaque progression and regression. A follow-up of acute myocardial infarction (AMI) patients has been evaluated against patients with angiographically normal coronary arteries (controls) and healthy volunteers (reference group). AMI patients are evaluated at 3 time points: at admission (day 0), two (day 2) and 40 (day 40) days after intervention.

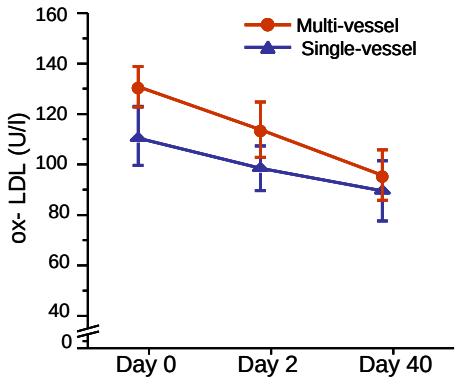

Fig. 1. Disease severity (expressed as no. of vessels involved) and concentrations of circulating ox-LDL from infarct onset to 40 days after.

We expect to obtain new indexes of plaque progression and regression and identification of at-risk patients from a systematic data evaluation of anthropometric, physiological variables, and bio-indicators. The study is supported by Liga de Amigos do Hospital de Sta. Marta and FCT (SFRHI/BD/ 18822/2004).

B – Skin as a tool in metabolic disorders and immune diseases

R. Silva, R. Fleming, P. Filipe, J.N. Silva, A. Barreiros

Skin iron as a diagnosis tool in hemochromatosis

The study used conventional and innovative laboratory tests to differentiate distortions of iron metabolism. Patients were genetically characterized and studied before starting and along the phlebotomy therapy. Nuclear microscopy and nuclear resonance techniques provided iron quantitative imaging and physiological information on skin and liver. Biochemical methods provided hepcidin contents in serum and markers of iron metabolism and organ function. The study is supported by the **projects SPDV 2004-2007 and IAEA CRP 2005-2008**.

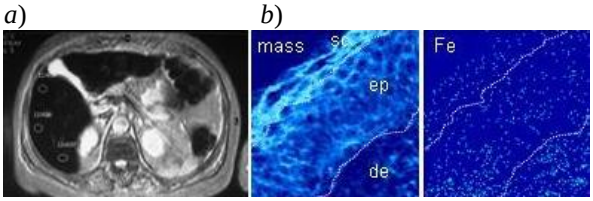

Fig. 2. Iron imaging. a) Magnetic Resonance: dark regions are hypodense liver (Fe = 210 µmol/g); b) Proton Microscopy (~100×100 μm^2): skin layers depicted from mass density image validate epidermal region of Fe deposition (10±3 µmol/g).

Skin barrier* and immune profile *in psoriasis

Psoriasis is a skin disorder characterised by an increased proliferation and disturbed differentiation of keratinocytes. The main objective of the study is to characterise the immune pattern and the markers of the inflammatory cascade, hyperproliferation and keratinisation in the psoriatic lesions of patients with moderate to severe plaque psoriasis. T-lymphocyte profile in responders and non-responders, their activation profile and how it correlates with TNF-a and keratinocyte hyperproliferation and keratinisation, the skin barrier function and the involvement of calcium and other divalent ions distribution in skin strata, are some of the aspects that are being covered in the project. This Project is supported by **SERONO, Fundación Salud 2000 (Research Prize "Investigação Clínica em Psoríase" - 2006-2008)**.

[1] Centro de Estatística Aplicada, FC-UL