1ère Journée de l'Ecole Doctorale en Médecine Clinique et Expérimentale

Samedi 15 mars 2008

Académie Royale de Médecine de Belgique

FRS-FNRS
Ecole doctorale thématique en
Médecine Clinique et Expérimentale
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Académie Royale de Médecine de Belgique
Palais des Académies
Rue Ducale, 1
1000 Bruxelles

Programme

08 h 45	**Accueil** des participants, café-croissants, mise en place des posters à partir de 8h45
09 h 40 Salle Baudouin	**Introduction** par le Professeur Janos FRÜHLING, Secrétaire perpétuel de l'Académie Royale de Médecine de Belgique
09 h 50	**Conférence inaugurale** (modérateur: Professeur Gustave MOONEN) Prof. Elie COGAN (Université Libre de Bruxelles, Porte Parole de l'Ecole Doctorale) "Intégrité dans la recherche biomédicale : de l'éthique personnelle à la responsabilité collective"
10h20 - 12h20	**Communications orales** I (modérateurs : Prof. Alexandre LEGRAND et Pierre GIANELLO)
12h 20– 13h40	**LUNCH et Discussion des posters** (Salle des Marbres) en présence des directeurs des laboratoires et de la commission scientifique de l'Ecole Doctorale
13h40-16h:	**Communications orales** II (modérateurs : Prof. Bruno FLAMION et Gustave MOONEN)
16h	**Clôture**

P08 **T cell response to Trichophyton in a skin biopsy from a patient with GVHD-like disease**

Méric de Bellefon L[1], Theunis A[3], De Maubeuge J[3], Michel O[4], Goldman M[1], Roufosse F[1,5], Coulie PG[2] (ULB)

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A young male who developed a systemic immune-mediated disorder reminiscent of chronic graft-versus-host disease, characterized by lymphocytic inflammation of lungs, small bowel and skin, after professional exposure to vinyl chloride, has been studied extensively to investigate the role of maternal microchimerism in the induction of disease. His disease is partially controlled by chronic immunosuppressive therapy associating low-dose corticosteroids and azathioprine. Numerous attempts to demonstrate patient-derived T cell reactivity against maternal antigens have proven unsuccessful.
A skin lesion was biopsied to derive and analyze infiltrating T lymphocytes. After a few days of culture with IL2 and human serum, robust CD4 T cell proliferation and slow fungal growth were observed. The fungus was identified as a dermatophyte – most probably Trichophyton rubrum –, which in all likelihood is coming from the patient's skin. T cell cloning was performed using OKT3-CD28 stimulation; and ten CD4 T cell clones were isolated. Cytokine secretion assays were performed in presence of autologous B-EBV cells pulsed with Trichophyton culture supernatant. Two of these CD4 T cell clones secreted cytokines (IL5, IL4, IL10, TNFα, IFNγ) in these conditions. HLA restriction was also investigated using different B-EBV cell lines, indicating a peptide presentation through HLA DR*11. We will try to identify the antigenic peptide within a cDNA library prepared from Trichophyton.
This is the first time that human Trichophyton-specific CD4 T cell clones are obtained and be characterized in detail. We hypothesize that Trichophyton, a frequent cutaneous pathogen, plays a role in the chronic inflammatory disease of this patient.

P19 **Fluoride effects on bone formation, mineralization and mechanical properties are influenced by genetics**

M. Mousny[1], S. Omelon[2], L. Wise[2], E.T. Everett[3], M. Dumitriu[2], D.P. Holmyard[2], X. Banse[1], J.P. Devogelaer[6], M.D.Grynpas[2,5] (UCL)

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Introduction: Only few animal studies explore an underlying genetic basis for extrinsic factors effect on bone metabolism. The purpose of this study was to assess the effect of increasing fluoride doses on bone properties in inbred mouse strains in order to study the influence of genetic background.
Materials and Methods: Three inbred mouse strains with different susceptibilities to developing dental fluorosis (A/J a "susceptible" strain, SWR/J an "intermediate" strain, 129P3/J a "resistant" strain) were studied. Bone fluoride concentrations were determined. Bone mineral density (BMD) was evaluated through DEXA. Mechanical properties of cortical and trabecular bone were determined. Bone microarchitecture was quantified with microcomputed tomography and strut analysis. Bone formation was evaluated by static histomorphometry. Bone mineralization was quantified with Back Scattered Electron Imaging (BSE) and powder X-ray diffraction. Microhardness measurements were taken from cortical and trabecular bone.
Results: Fluoride bone concentration increased in all 3 strains. Fluoride treatment had little effect on BMD. Mechanical testing showed significant alterations in "bone quality" in A/J, moderate alterations in SWR/J and no effect in 129P3/J. Fluoride treatment had no significant effect on bone microarchitecture. Each strain demonstrated a significant increase in osteoid formation. The bone mineralization profiles showed a non-significant increase towards higher mineralization with increasing F- dose. Powder X-ray diffraction showed significantly smaller crystals for 129P3/J, and increased crystal width with increasing F- dose for all strains. There was no effect on bone microhardness.
Conclusion: Genetic factors may contribute to the variation in bone response to fluoride exposure. The increased crystal cross-section with increasing F- dose correlates with most of the decreased mechanical properties. An increase in bone F- might affect the mineral-organic interfacial bonding and/or bone matrix proteins. The smaller bone crystallites of the resistant strain may indicate a stronger organic/inorganic interface, reducing crystallite growth rate and increasing interfacial mechanical strength.

P13 **Three-dimensional CT-based craniofacial cephalometric analysis: concept, software, and experimental validations**

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The aim of a three-dimensional (3D) cephalometric analysis is to provide a truly 3D diagnostic tool and planning for computer-assisted maxillofacial surgery. We transformed and adapted to the third dimension the classical two-dimensional cephalometric topological Delaire's analysis. Our 3D-CT craniofacial cephalometric analysis, ACRO 3D, is based on a 3D reference frame constructed upon 22 craniofacial landmarks identified directly on 3D-CTsurface rendering. 13 reference planes are automatically calculated and visualized with ACRO 3D software. 3D diagnosis of craniofacial dysmorphosis is based on comparing 3D anatomical craniofacial structures (e.g.maxilla, mandible) to the reference planes and frame.
In order to experimentally validate our 3D CT-based cephalometric analysis, we compared inter- and intra-observer reproducibility of measurements achieved on profile radiography versus 3D-CT surface rendering (2 observers, twice, 9 distances between 7 landmarks, 26 dry skulls). We also compared the accuracy of measurements achieved on 3D-CT surface rendering (obtained with ACRO 3D software) to this of direct measurements on dry skulls by means of 3D measuring instrument (2 observers, twice, 12 landmarks/skull, 17 distances/skull, 26 skulls). Inter- and intra-observer reproducibility proved to be significantly better for 3D-CT method ($p<0.0001$). There were no significant difference between measurements achieved respectively on 3D-CT surface rendering by ACRO 3D software, and 3D measuring instrument.
To be able to spread out potential clinical applications of our 3D-CT cephalometric analysis methodology we finally developed and validated a low dose 3D-CT protocol (35 mAs).
Further post-doctoral research will consist on clinical validation of the 3D-CT based craniofacial cephalometric analysis.

O 15:40 **TNF-α and IL-1β induction of NF-κB and its downstream genes has a pro-apoptotic role in pancreatic beta cells**

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Background and Aims: IL-1β and TNF-α contribute to pancreatic beta cells death in type 1 diabetes. Both cytokines activate the transcription factor NF-κB, but recent observations suggest that NF-κB blocking prevents IL-1β+IFN-α- but not TNF-α+IFN-γ-induced beta cell apoptosis. We presently compared cell death and the pattern of NF-κB activation and global gene expression induced by IL-1β and TNF-α in beta cells.
Material and Methods: Cell viability was measured after exposure to either IL-1β or TNF-α alone or in combination with IFN-γ and blocking of NF-κB activation or protein synthesis. INS-1E cells exposed to IL-1β or TNF-α in time course experiments were used for IKK activation assay, immunocytochemistry for p65 NF-κB, real-time RT-PCR and microarray analysis.
Results: Blocking NF-κB activation protected beta cells against IL-1β+IFNγ- or TNFα+IFNγ-induced apoptosis. Blocking de novo protein synthesis did not increase TNF-α- or IL-1β-induced beta cell death, in agreement with similar cytokine-induced expression of the anti-apoptotic genes A20, IAP-2 and XIAP. Microarray analysis of INS-1E cells treated with IL-1β or TNF-α showed similar patterns of gene expression. IL-1β, however, induced a higher expression of NF-κB target genes putatively involved in beta cell dysfunction and death and a stronger activation of the IKK complex leading to an earlier translocation of NF-κB to the nucleus.
Conclusions: NF-κB activation in beta cells has a pro-apoptotic role following exposure not only to IL-1β but also to TNF-α. The more marked IL-1β-induced beta cell death is at least in part explained by higher intensity of NF-κB activation, leading to increased transcription of key target genes.

P01 **Duhoux** PRDM16, a multi-partner gene with oncogenic properties in myeloid proliferations	**P02** **Hanin** In vivo exposure to octreotide in neuroendocrine tumor-bearing rats: a micro-PET study	**P03** **Lysy** Differentiation of Human Skin Fibroblasts into Mesodermal and Hepatocyte-Like Lineages	**P04** **Sana** In vitro study of the immunogenic properties of human isolated liver cells	**P05** **Van Rompaey** TLR4 desensitization downregulates alloimmune response	**P06** **Meric de Bellefon** T cell response to Trichophyton in a skin biopsy from a patient with GVHD-like disease	**P07** **Kapessidou** INTERLEUKIN-22 deficiency accelerates the rejection of full major histocompatibility complex-disparate heart allografts	**P08** **Ricour** The Leader protein of Theiler's virus interferes with the host innate immune system	**P33** **Lenaerts** The effects of clonidine on the diuretic response in cirrhotic patients with ascites and activation of sympathetic nervous system: a randomized double-blind placebo controlled study.
Adult-Derived Human Liver Mesenchymal-Like Stem/Progenitor Cells increase hepatic metabolic function after in vitro differentiation **Khuun Ngoc** **P09**	Estrogen-induced regulation of ERα level in MCF-7 breast cancer cells. Distinct potency of type I and II prototypes **Voillard** **P10**	What is the role for regulatory T-cells after nonmyeloablative conditioning ? **Baron** **P11**	Acute effects of passive smoking on peripheral vascular function. **Argacha** **P12**	Three-dimensional CT-based craniofacial cephalometric analysis: concept, software, and experimental validations **Olszewski** **P13**	Implication de l'IL-17 dans le rejet d'allogreffes **Vokaer** **P14**	Sensitivity of intestinal fibroblasts to TNF-Related Apoptosis-Inducing Ligand mediated apoptosis in Crohn's disease. **Reenaers** **P15**	Differential modulation of HLA molecules following human cytomegalovirus infection of fibroblasts and epithelial cells. **Twite** **P16**	
P17 **Gruson** Urotensin II and Urocortin induced hypertrophy of adult rat cardiomyocytes is associated with phosphorylation of the Protein Kinase B - Glycogen Synthase Kinase 3b pathway and stabilization of b-catenin	**P18** **Lanthier** After short-term exposure of mice to a high fat diet leading to a hepatic insulin resistance, f4/80 positive macrophages are preferentially found in the vicinity of lipid-loaded hepatocytes	**P19** **Mousny** Fluoride effects on bone formation, mineralization and mechanical properties are influenced by genetics	**P20** **Pastijn** Inhibition of ERK increases paw withdrawal latency and threshold in a rodent postoperative pain model	**P21** **Breuskin** Role of Sox10 in the development of the inner ear	**P22** **Dang Vu** Processing of Sounds during Sleep Spindles in humans: an EEG/fMRI study of Auditory Stimulation in non-REM sleep	**P23** **Poirrier** Pharmacological models of sensorineural hearing loss in the mouse and the guinea pig: a comparative study. Is there a deaf mouse aboard?	**P24** **de San** Phenotypic characterization of human alveolar type II pneumocytes	
Effects of exogenous gonadotropin administration on follicular growth and ovulation in ob/ob and db/db mice **Pintiaux** **P25**	Altered expression of angiogenesis and lymphanglogenesis markers in the uninvolved skin of plaque-type psoriasis. **Henno** **P26**	Pulmonary vascular reactivity in relatives of patients with idiopathic pulmonary arterial hypertension – an echocardiographic study **Pavelescu** **P27**	Regulation of voltage-dependent calcium channels by APP **Santos Ferrao** **P28**	Metabolic evidence for remote inhibition in epilepsies with continuous spike-waves during sleep **De Tiège** **P29**	Walking in stroke patients : how does the mechanical work determine the energy cost of walking? **Stoquart** **P30**	Electron paramagnetic resonance (EPR) as a tool to evaluate human ovarian tissue reoxygenation after xenografting **Van Eyck** **P31**	Study of the angiogenic cytokines, inflammatory chemokines and their receptors in normal and pathologic placentation **Chantraine** **P32**	