BELGIAN SOCIETY OF

PHYSIOLOGY AND PHARMACOLOGY

NATIONAL COMMITTEE OF PHYSIOLOGY AND PHARMACOLOGY

Spring Meeting

Friday, April 24th 2015

PROGRAMME

&

ABSTRACTBOOK

Venue

Palace of the Academies
Royal Academy of Medicine of Belgium
"Zaal Rubens"
Rue Ducale / Hertogsstraat 1
1000 Brussels

Local host

Prof. Dr. Pasale LYBAERT
Laboratoire de Physiologie et Pharmacology (LAPP)
Faculté de Médecine – CP 604
Université Libre de Bruxelles
Route de Lennick 808
B-1070 BRUXELLES

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Royal Flemish Academy of Belgium for Science and the Arts

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Palace of the Academies
"Royal Academy of Medicine of Belgium
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Main Lecture

10.00-11.00 "Understanding human sperm physiology to provide rational – non IVF - therapy"

Prof. Dr. Christopher BARRATT – Tayside Academic Health Sciences Center – Ninewells Hospital & Medical School – Dundee (United Kingdom)

Oral Communications

11.00-11.15 F. HORICKS, G. VAN DEN STEEN, S. HOUBEN, Y. ENGLERT, I. DEMEESTERE (ULBruxelles)
GNRH analogues effects on follicular growth and their potential ovarian protection against alkylating agent in mice.

11.15-11.30 R. HOUBEN, C. LELEU, A. FRAIPONT, D. SERTEYN, D.M. VOTION (ULiège, EQUI-TEST, Grez-en-Bouere, France)
Muscle mitochondrial respiratory capacity in standardbred racehorses.

11.30-11.45 JP. DAVID, J.I. STAS, N. SCHMITT, E. BOCKSTEINS (Univ Copenhagen, UAntwerpen)

KCNE5 subunits modulate both Kv2.1 homotetramers and Kv2.1/Kv6.4 heterotetramers.

11.45-12.00 K. PHILIPPAERT, S. KERSELAERS, R. VENNEKENS (KULeuven)
Identification of TRPM5 modulating compounds by high throughput thallium based fluorescent screening.

12.00-13.30 **Lunch – Guided Poster Session**

Posters

(height 120 cm – width 100 cm)

1. F. SEGHERS, S . JANAS, S. TERRYN, O. SCHAKMAN, J. VRIENS, B. NILIUS, J. LOFFING, P. GAILLY, O. DEVUYST (UCLouvain, KULeuven Univ Zurich)
   Renal expression of TRPV4 and its role in osmoregulation.

2. M. KECSKES, G. JACOBS, R. VENNEKENS (KULeuven)
   Role of TRPM4 ion channel in calcium induced arrhythmias.

3. E. BOCKSTEINS, D.J. SNYDERS, M. HOLMGREN (UAntwerpen, NIH)
   Movements of the S4 segments of the Kv2.1 and Kv6.4 subunits in Kv2.1/Kv6.4 heterotetramers.

4. N. EMERIAU, P. GAILLY, N. TAJEDDINE (UCL)
   ErbB receptors control the store-operated entry of Ca^{2+}.

5. D. HOORELBEKE, E. DECROCK, M. DE BOCK, C. VANDEVOORDE, B. DESCAMPS, H. THIERENS, C. VANHOVE, L. LEYBAERT (UGent)
   Propagation of radiation-induced brain microvascular endothelial DNA damage: a tight interplay between connexin channels, paracrine ATP signaling and the calcium/ROS signaling axis.

6. S. KOULCHITSKY, C. DELAIRESSE, E. BULLINGER, V. SEUTIN (ULiège, Lab Systems Theory & Automatic Control, Magdeburg-Germany)

Correlation between local field potential frequencies in the ventral tegmental area and qualitative aspects of locomotor behavior.

7. I. HADAD, D. EGRISE, C. DE GRAFF, J-Y. SPRINGAEL, F. LIEBERT, F. MIOT, J. FOGUENNE, R. NAEIJE, X. DE DEKEN, K. MC ENTEE (ULBruxelles, CHU ULiège)
   Genomic effects of SDF-1α on rat neonatal cardiomyocytes: comparison between commercial SDF-1α and supernatant of SDF-1α overexpressing mesenchymal stem cells.

8. B. MARTIN, A.E. DECLÈVES, V. COLOMBARO, I. JADOT, C. DEPOMMIER, G. FEDERICI, I. HABSH, J. NORTIER, N. CARON (UNamur, ULBruxelles)
   Effects of iNOS inhibition in high-fat diet-induced obesity.

9. S. SEBAA, I. DARDOUR, Z. BOUCHERIT-OTMANI, P. COURTOIS (ULBruxelles, Univ. Belkaïd Algeria, Haute Ecole Fr. Ferrer Bruxelles)
   Effect of tyrosol and farnesol on Candida albicans biofilms.

10. R. CRUTZEN, M. VIRREIRA, N. MARKADIEU, V. SHLYONSKY, W.J. MALAISSE, R. BEAUWENS, A. BOOM, P. GOLSTEIN (ULBruxelles)
    Anoctamin 1 (Ano1) is required for glucose–induced membrane potential oscillations and insulin secretion by murine β-cells.

11. A. HANTHAZI, S. GOMART, P. JESPERS, J.Y. SPRINGAEL, R. NAEIJE, L. DEWACHTER, K. MC ENTEE (IRBHM, ULBruxelles)
    Chemerin potentiates pulmonary artery reactivity to endothelin-1.

12. L. DEWACHTER, C. DEWACHTER, A. BELHAJ, S. LALANDE, B. RONDELET, M. REMMELINK, J.L. VACHIÉRY, R. NAEIJE (ULBruxelles, UCLouvain, Erasmus Hospital Brussels)
    Insulin-like growth factor-1 contributes to pulmonary artery smooth muscle cell proliferation in idiopathic pulmonary arterial hypertension.

13. A. HENNES, K. DE CLERCQ, K. HELD, T. VOETS, T. D'HOOGHE, J. VRIENS (KULeuven)
    Mechanosensitive piezol as a key player to start endometrial decidualization?

Oral Communications

13.30-14.00 J. HANSON (ULg)
Identification of GPCR ligands with a real time cAMP biosensor.

14.00-14.15 E. BOGAERTS, F. HEINDRYCKX, L. DEVISSCHER, A. PARIDAENS, Y-P VANDEWYNCKEL, A. VAN DEN BUSSCHE, X. VERHELST, L. LIBBRECHT, L.A. VAN GRUNSVEN, A. GEERTS, H. VAN VLIERBERGHE (UGent)
Time-dependent effect of hypoxia on tumor progression and liver progenitor cell markers in primary liver tumors.

14.15-14.30 S. LEPANNETIER, N. ZANOU, X. YERNA, P. GAILLY (UCL):
Sphingosine-1-phosphate-activated TRPC1 channel controls chemotaxis of glioblastoma cells.

14.30-14.45 P. ROWART, P. ERPICUM, J.O. DEFRAIGNE, J.M. KRZESINSKI, FR. JOURET (ULiège)
Renal ischemia/reperfusion decreases the expression of type 4 dipeptidyl-peptidase at both mRNA and protein levels.

15.45-15.00 F. JOURET, P. DE TULLIO, J-O DEFRAIGNE, J-M KRZESINSKI (ULiège)
Activation of the calcium-sensing receptor before renal ischemia/ reperfusion exacerbates kidney injury.

Coffee – Tea

ABSTRACTS

Legend
O = Oral communication numbered and scheduled time
O = Poster numbered

O-01 (11.00-11.15)

GNRH ANALOGUES EFFECTS ON FOLLICULAR GROWTH AND THEIR POTENTIAL OVARIAN PROTECTION AGAINST ALKYLATING AGENT IN MICE

F. Horicks[1], G. Van Den Steen[1], S. Houben[1], Y. Englert[1,2], I. Demeestere[1,2]

[1]Research Laboratory on Human Reproduction, Université Libre de Bruxelles, Brussels 1070, Belgium, [2]Gynecology and Obstetrics Department, Erasme Hospital, Brussels 1070, Belgium

Among the different options to preserve fertility of young cancer patients treated with chemotherapy, the possibility of minimizing chemotherapy-induced gonadal damage by implementing *Gonadotrophin-Releasing Hormone* analogues (GnRHa) has been studied in animals and women. However, their efficacy is still controversial and their mechanisms of action are unknown. Moreover, the question about a direct action on the ovary or an indirect action through gonadotropins secretion needs to be investigated. The objectives were to evaluate the cyclophosphamide (Cy)-induced ovarian damages, verify the GnRHa inhibitory effect on follicular development, and their potential gonadoprotective effect during chemotherapy treatment in mice. Female mice (C57BL/6jxCBA/ca, 5-8 weeks-old) received a Cy-injection (ip, 100, 200, and 500 mg/kg; 6/group) and were sacrificed at different time points between 1h and 21days (d) later or mated with male. Mice were injected with GnRHa (sc or im; 2, 20, 200 and 500µg/kg, 4mg/kg; 4/group) for 15 or 21d with Cy on the 15th day (3/group). Following parameters have been evaluated: fertility, oestrus cycle, ovarian reserve, folliculogenesis, FSH level and follicular viability (TUNEL, caspase-3 and Ki67 staining). Statistical analysis was done by using one-way ANOVA test. Cy induced a dose-dependent impairment of fertility and health. Follicular depletion was observed at each follicular stage but mainly in the primordial follicles. With 200mg/kg, 51.91% (p=0.01) of resting follicles were depleted compared to control. Apoptosis peaked before 18h but was not observed in resting follicles. The oestrus cycles were disturbed during both GnRH agonist and antagonist administration whatever the dose or injection site but the distribution between growing and quiescent follicles within the ovaries and FSH levels remained similar to the untreated mice. The ovarian reserve was not preserved by GnRHa administration during chemotherapy treatment. These results showed that Cy induces a dose-dependent follicular depletion affecting both resting and growing follicles through different mechanisms. GnRHa don’t inhibit the pituitary-gonadal axis in mice as effectively as in human, calling into question the reliability of this mice model to investigate the protection mechanisms of the GnRHa on the ovarian function during chemotherapy.

O-02 (11.15-15.30)

MUSCLE MITOCHONDRIAL RESPIRATORY CAPACITY IN STANDARDBRED RACEHORSES

R. Houben[1], C. Leleu[2], A. Fraipont[1], D. Serteyn[1,3], D.M. Votion[1]

[1]Equine Clinic, Fundamental and Applied Research for Animals & Health (FARAH), Faculty of Veterinary Medicine, Bat B41&B42, University of Liege, Sart Tilman, 4000 Liège Belgium, [2]EQUI-TEST, Grez-en-Bouère, France, [3]Center for Oxygen Research and Development (CORD), Institute of Chemistry Bat B6a, Liège University, Sart Tilman, 4000 Liège, Belgium.

This prospective cohort study examines the potential of high resolution respirometry (HRR) applied to permeabilized muscle fibers for fitness evaluation in French Standardbred racehorses. At the start of a racing season, the fitness of ten trained Standardbreds was evaluated by means of a standardized exercise test with determination of the velocity (*i.e.* trotting speed) at which blood lactate concentration reaches 4 mmol/L (VLa4). Using univariate logistic regression, certain oxidative phosphorylation and electron transport system capacities were predictive of exertional rhabdomyolysis occurrence whereas no correlations were found for HRR parameters *vs* VLa4 and racing performance over the following racing season.

O-03 (11.30-11.45)

KCNE5 SUBUNITS MODULATE BOTH KV2.1 HOMOTETRAMERS AND KV2.1/KV6.4 HETEROTETRAMERS

JP. David[1], J.I. Stas[2], N. Schmitt[1], E. Bocksteins[2]

[1]University of Copenhagen, Copenhagen, 2200, Denmark and [2]University of Antwerp, Antwerp, 2610, Belgium.

The voltage-gated K^+ (Kv) channel subfamily Kv2 contains two members that display similar properties. The diversity is increased by assembly with members of the so-called silent Kv (KvS) subfamilies (Kv5-Kv6 and Kv8-Kv9). KvS subunits do not form functional homotetramers on their own but assemble into functional Kv2/KvS heterotetramers that display modified biophysical properties compared to Kv2.1 homotetramers. Further diversity arises from interactions with auxiliary β-subunits. While Kv2.1 subunits interact with both modulatory KvS α-subunits and auxiliary β-subunits, it has not yet been investigated whether these two types of modulating subunits can associate within and modify a single channel complex simultaneously. Here, we demonstrate that the transmembrane β-subunit KCNE5 associates with Kv2.1/Kv6.4 channels in “triple subunit” Kv2.1/Kv6.4/KCNE5 channel complexes that possess unique properties compared to the channel complexes containing only the modulatory α-subunits or auxiliary β-subunits. Kv2.1/Kv6.4/KCNE5 channel complexes displayed accelerated activation kinetics, slowed deactivation and a steeper voltage-dependence of the Kv6.4-induced closed-state inactivation process due to an accelerated recovery rate of the closed-state inactivation compared to Kv2.1/Kv6.4 heterotetramers. In contrast, KCNE5 did not modulate the biophysical properties upon co-association with Kv2.1 subunits alone but did reduce the Kv2.1 current density ~2-fold. Formation of Kv2.1/Kv6.4/KCNE5 and Kv2.1/KCNE5 complexes was confirmed by immunocytochemical and Fluorescence Resonance Energy Transfer (FRET) experiments performed in HEK293 cells. These results demonstrate that a triple complex consisting of Kv2.1, Kv6.4 and KCNE5 subunits can be formed in a heterologous cell system. *In vivo*, formation of such a tripartite Kv2.1/Kv6.4/KCNE5 channel complex might contribute to tissue-specific fine-tuning of excitability.

O-04 (11.45-12.00)

IDENTIFICATION OF TRPM5 MODULATING COMPOUNDS BY HIGH THROUGH-PUT THALLIUM BASED FLUORESCENT SCREENING

K. Philippaert, S. Kerselaers, R. Vennekens

KULeuven, Lab. of Ion Channel Research, Dep. Cel. and Mol. Medicine. Leuven, 3000, Belgium.

TRPM5 is a monovalent cation permeable ion channel in the plasma membrane and is activated by a raise of intracellular calcium. The channel is expressed in pancreatic β-cells and type II taste receptor cells. Modulation of TRPM5 is of great economical interest, it helps optimizing a desired flavour in industrial prepared foods. Furthermore pharmacological potentiation of TRPM5 leads to an increase in the glucose-induced insulin release, quickly establishing normoglycemia after food intake. Currently known pharmacology for TRPM5 lacks selectivity and mainly consists of non-selective blocking compounds. We established a high-throughput screening method based on TRPM5 mediated thallium flux capable of identifying both TRPM5 potentiators and TRPM5 inhibitors. We could confirm previously described pharmacological properties of certain compounds. A library with compounds with a high chemical diversity consisting of possible bioactive compound s.a. drug components and natural products was screened. From this the most interesting TRPM5 modulators were identified and their activity was studied in more detail. Patch clamp studies on TRPM5 overexpressing HEK cells were used to confirm the activity of the compound. Finally we analysed the changes in calcium oscillations of pancreatic islets upon perfusion with these novel identified TRPM5 modulators. The novelty lies in the identification of TRPM5 as molecular target of these compounds. These compounds can be used as a novel lead for the development of insulinotropic drugs and taste enhancers.

O-05 (13.30-14.00)

IDENTIFICATION OF GPCR LIGANDS WITH A REAL TIME cAMP BIOSENSOR

J. Gilissen, P. Geubelle, N. Dupuis, B. Pirotte, J. Hanson

University of Liège, GIGA Research center, CHU-Sart-Tilman 4000 Liège, Belgium.

G Protein-Coupled Receptors (GPCR) represent the largest family of membrane receptors. They are currently targeted by 30% of marketed drugs. Nevertheless, most of GPCRs remain orphan or under-characterized and have never been investigated for a potential therapeutic use. The elusive understanding of their physiology is often the consequence of a lack of selective small molecule pharmacological tool that precludes further validation as drug target. The signaling pathways coupled to GPCR have been widely studied. It implies coupling to heterotrimeric G proteins that are composed of subunits α, β and γ and form 4 main families Gi, Gs, Gq and G12/13. Upon activation, the heterotrimeric complex dissociates into Gα and Gβγ that trigger downstream signaling events. For instance, Gαi and Gαs respectively inhibits and activates adenylate cyclase that synthesizes cyclic AMP (cAMP). However, each receptor is unique and may display non-canonical behavior. Before any screening campaign, it is important to proceed to a straighforward characterization of the signaling pathways of the receptor under scrutiny. This might be challenging in the absence of a ligand. In addition, many GPCR ligands are now described as being able to discriminate between signal pathways by displaying functional selectivity. Therefore, there is also a clear interest for screening with more specific assays directed toward defined signaling pathways rather than unbiased assays. For some of our projects on Gi and Gs coupled receptors, we chose to focus on measurement of intracellular cAMP. We developed an assay for real time sensitive determination on cAMP levels with the Glosensor technology (Promega). We validated the assay by measuring basal activity and identified ligands for GPCR by screening chemical libraries.

O-06 (14.00-14.15)

TIME-DEPENDENT EFFECT OF HYPOXIA ON TUMOR PROGRESSION AND LIVER PROGENITOR CELL MARKERS IN PRIMARY LIVER TUMORS

E. Bogaerts[1], F. Heindryckx[2], L. Devisscher[1], A. Paridaens[1], Y-P Vandewynckel[1], A. Van den Bussche[1], X. Verhelst[1], L. Libbrecht[3], L.A. van Grunsven[4], A. Geerts[1], H. Van Vlierberghe[1]

[1]Gastro-enterology and hepatology, Ghent University, Ghent, Belgium, [2]Department of Medical Biochemistry and Microbiology, Uppsala University, Uppsala, Sweden, [3]Department of Pathology, University Hospital Ghent, Ghent, Belgium, [4]Liver Cell Biology Lab, Vrije universiteit Brussel, Brussels,Belgium

Expression of liver progenitor cell (LPC) characteristics has been proposed as a negative prognostic marker in primary liver tumors. Hypoxia has been linked to activation of the Notch pathway which is responsible for activation and proliferation of LPCs and hypoxia-induced LPC activation has been shown in hepatocellular carcinoma. Our aim was to elucidate the time-dependent effects of hypoxia on the LPC niche in hepatocellular carcinoma which could aid in determining a safe time frame for use of hypoxia inducing therapies.We used dimethyloxaloylglycine to mimic a hypoxic reaction in mice by stabilizing hypoxia-inducible factor 1 alpha at three distinct time points in diethylnitrosamine induced hepatocarcinogenesis. LPC, metastasis and Notch pathway markers were determined by quantitative PCR and (immune)histochemistry (heamatoxillin-eosin, reticulin, Sirius red and cytokeratin 19 staining). Activating the hypoxia inducible pathway early in hepatocarcinogenesis resulted in an increased incidence of both cholangioma and hepatocellular lesions, associated with high expression of LPC, metastatic and Notch pathway markers. Adversely, activating the hypoxic response during tumor development resulted in decreased incidence of hepatocellular lesions and increased cholangioma incidence, with an unaltered gene expression profile of LPC-, Notch pathway- and metastatic markers. A hypoxic insult at advanced stages of hepatocarcinogenesis severely increased the expression of LPC characteristics, however without increased expression of actors of the Notch pathway and metastatic markers and minor changes in incidence of hepatocellular and cholangioma lesions.Our results indicate that increased hypoxia at the onset of tumor development has detrimental effects on tumor progression; patients with HCC developed in a background of fibrosis/cirrhosis might therefore represent a more difficult treatment group. In contrast, hypoxia during tumor development appears to favor tumor outcome, highlighting the importance of early detection. Finally, hypoxia in advanced stages resulted in increased expression of LPC characteristics indicating poor outcome.

O-07 (14.15-14.30)

SPHINGOSINE-1-PHOSPHATE-ACTIVATED TRPC1 CHANNEL CONTROLS CHEMOTAXIS OF GLIOBLASTOMA CELLS

S. Lepannetier, N. Zanou, X. Yerna, P. Gailly

Université catholique de Louvain, B-1200, Brussels, Belgium

We previously showed that TRPC1 channel plays an important role in muscle cell migration and differentiation. Here, we investigated the gating mechanism of TRPC1 channel and its role in U251 glioblastoma cells migration in response to chemoattraction by PDGF growth factor. PDGF stimulation induces the production of sphingosine-1-P (S1P), a bioactive lipid linked to numerous cellular functions including growth, differentiation and migration. We observed that stimulation of U251 cells with PDGF induced an influx of Ca^{2+} from the extracellular medium that was partially inhibited after pretreatment of the cells with SKI-II, a specific inhibitor of sphingosine kinase producing S1P. S1P by itself also induced an entry of Ca^{2+}. Both were lost in siRNA-TRPC1 treated cells. Migration of U251 cells in response to PDGF was studied in modified Boyden chambers. Chemotaxis was dramatically inhibited in cells treated with SKI-II, and the inhibition was almost completely rescued by addition of synthetic S1P. Chemotaxis was also completely lost in siRNA-TRPC1 treated cells and the rescue of migration of cells treated with SKI-II by S1P was dependent on the expression of TRPC1. Immunocytochemistry revealed that, in response to PDGF, TRPC1 translocated from inside the cell to the front of migration (lamellipodes). This effect was inhibited by pre-treatment with LY294002, a PI3-kinase inhibitor. Our results thus identify S1P as a potential activator of TRPC1, a channel involved in cell orientation during chemotaxis by PDGF.

O-08 (14.30-14.45)

RENAL ISCHEMIA/REPERFUSION DECREASES THE EXPRESSION OF TYPE 4 DIPEPTIDYL-PEPTIDASE AT BOTH mRNA AND PROTEIN LEVELS

P. Rowart, P. Erpicum, J.O. Defraigne, J.M. Krzesinski, Fr. Jouret

Groupe Interdisciplinaire de Génoprotéomique Appliquée (GIGA), Cardiovascular Sciences, University of Liège, Liège (B-4000), Belgium

Type 4 dipeptidyl-peptidase 4 (DPP-4) is a serine protease expressed at the surface of most epithelia, including renal proximal tubules (PT). Since DPP-4 participates to inflammation, recruitment of immune cells and apoptosis, we investigated its expression and distribution in case of renal ischemia/reperfusion (I/R). Transient I/R is a common cause of acute tubular necrosis (ATN) in operative settings, including cardio-thoracic surgery and kidney transplantation. Renal ischemia was induced in Wistars rats by unilaterally clamping the left kidney for 60 minutes. The right kidney was simultaneously excised and used as comparator. The first group of animals (n=6) had no reperfusion: the kidney was removed straight after ischemia. In the other groups, renal reperfusion occurred for 6 (n=6), 24 (n=6) or 48 (n=6) hours. Kidneys were snap-frozen and lysed for mRNA and protein extraction. In parallel, the expression and distribution of DPP-4 was studied by immunohistochemistry on 10 biopsies of human kidneys with non-toxic ATN. In rat kidneys, mRNA abundance of DPP-4 was significantly decreased following I/R in all groups: no reperfusion (2.1-fold), 6h (8.1-fold), 24h (12.5-fold) and 48h (12.9-fold). Immunoblotting analyses showed a 2-fold reduction of DPP-4 expression *post* reperfusion. In human kidneys with ATN, the abundance of DPP-4 appeared reduced in comparison to healthy controls. Still, we did not observe evidence of DPP-4 internalization into PT cells. In conclusion, renal I/R is associated with reduced expression of DPP-4 in rat and human kidneys, which may be caused by PT tubulorrhexis and/or DPP-4 shedding into the urine.

O-09 (14.45-15.00)

ACTIVATION OF THE CALCIUM-SENSING RECEPTOR BEFORE RENAL ISCHEMIA/REPERFUSION EXACERBATES KIDNEY INJURY

Fr. Jouret[1], P. de Tullio[2], J-O Defraigne[1], J-M Krzesinski[1]

[1]Groupe Interdisciplinaire de Génoprotéomique Appliquée (GIGA), Cardiovascular Sciences and [2]Center for Interdisciplinary Research on Medicines (CIRM), University of Liège, Liège (B-4000), Belgium

Activation of the calcium-sensing receptor (CaSR) by ischemia/reperfusion (I/R) favours apoptosis in cardiomyocytes, hepatocytes and neurons. Its role in renal I/R is unknown. We investigated the impact of pharmacological preactivation of the CaSR on kidney structure and function in a murine model of bilateral renal 30-min ischemia and 48-hour reperfusion, and in a 6-year cohort of kidney transplant recipients (KTR). C57BL/6J mice were administered daily with CaSR agonist, R-568, or with vehicle for 48 hours. Evaluation of serum urea and creatinine levels, renal histology and urine metabolome by nuclear magnetic resonance showed that R-568 was not nephrotoxic *per se*. Following I/R, serum urea and creatinine levels increased higher in R-568-treated animals than in controls. Jablonski's score was significantly greater in R-568-treated kidneys, which showed a higher rate of cell proliferation and apoptosis in comparison to controls. Next, we retrospectively identified 36 patients (10.7% of our cohort) who were treated by CaSR agonist, cinacalcet, at the time of kidney transplantation (KTx). After matching these to 61 KTR upon type of donor, cold ischemic time, residual diuresis, and donor age, we observed that delayed graft function, i.e. need for dialysis in the first week after KTx, occurred in 42 and 23% of cinacalcet-treated and control groups, respectively ($p \leq 0.05$). These data suggest that pharmacological preactivation of the CaSR before renal I/R exacerbates kidney injury.

P-01

RENAL EXPRESSION OF TRPV4 AND ITS ROLE IN OSMOREGULATION

F. Seghers[1], S . Janas[1], S. Terryn[1], O. Schakman[1], J. Vriens[2], B. Nilius[2], J. Loffing[3], P. Gailly[1], O. Devuyst[1]

[1]Université catholique de Louvain, B-1200, Brussels, Belgium, [2]Katholieke Universiteit Leuven, B-3000, Leuven, Belgium, [3]Universität Zürich, 8006 Zürich, Switzerland

TRPV4 is a polymodal cation channel of the transient receptor potential (TRP) family. It is expressed in the organum vasculosum laminae terminalis, where it could play a role in osmotic sensing. TRPV4 has also been evidenced in the mouse and rat nephron, where its role remains unclear. To further analyze the role of TRPV4 in osmoregulation, we investigated its renal distribution pattern and the functional consequences of its disruption in mouse. Using qPCR on microdissected segments, immunohistochemistry and a mouse model reporting *Trpv4* expression, we found that TRPV4 is abundantly expressed in the proximal tubules (PT, apical and basolateral), late distal convoluted tubules (DCT) and throughout the connecting tubules (CN) and collecting ducts (CD, basolateral), including principal and intercalated cells. By contrast, TRPV4 was undetectable in glomeruli and thick ascending limb (TAL), and weakly abundant in early DCT. Metabolic studies on 12 weeks old *Trpv4*$^{-/-}$ and wild-type (*Trpv4*$^{+/+}$) mice revealed that disruption of *Trpv4* did not influence renal function and urinary concentration at baseline. The KO mice did not exhibit anomalies in activity, rearing, food and water intake. Moreover, both WT and KO mice showed a similar renal NaCl and water excretion in response to furosemide injection, acute water loading, overnight water deprivation, and 2-week dietary NaCl restriction. However, in the *Trpv4*$^{-/-}$ mice, acute administration of hypertonic saline solution resulted in a significantly delayed water intake. A lower rate of vasopressin release and synthesis was also observed after 24 h water deprivation. This study does not highlight a major role of TRPV4 in the kidney. Our data indicate that TRPV4 plays an important role in the central regulation of osmolality.

P-02

ROLE OF TRPM4 ION CHANNEL IN CALCIUM INDUCED ARRHYTHMIAS

M. Kecskes, G. Jacobs, R. Vennekens

Laboratory of Ion Channel Research, Department of Cellular and Molecular Medicine, KU Leuven, Belgium

Cardiac arrhythmia is a leading cause of death and disabilities worldwide. Arrhythmia is a broad term for any kind of disturbances on heart rhythm, while in our work we are interested in a certain type of arrhythmia where the initial event in arrhythmogenesis is the overload of the sarcoplasmic reticulum (SR) with calcium. This overload may result in an aberrant release of calcium from the SR and trigger a transient inward current and membrane depolarization. If this delayed afterdepolarisation (DAD) reaches the action potential threshold an ectopic beat will occur, and the normal heart rhythm and pump function will be disturbed. The current hypothesis is that the transient inward current underlying DAD's is generated by the sodium calcium exchanger. TRPM4 is a calcium activated non-selective cation channel present in the mouse and human ventricles. In our experiments we have found that calcium overload induced arrhythmias are reduced in mouse isolated *Trpm4*$^{-/-}$ left ventricular papillary muscles. Furthermore isolated *Trpm4*$^{-/-}$ myocytes showed significantly less transient inward current and spontaneous Ca^{2+} release events during *in vitro* calcium overload conditions compared to WT cells. Finally the sarcoplasmic reticulum calcium content after the calcium overload protocol was smaller in case of *Trpm4*$^{-/-}$ myocytes compared to WT. Analyzing the activity of NCX under the overload conditions we have found an increased NCX activity in the *Trpm4*$^{-/-}$ cells explaining the better calcium extrusion and less SR load. Based on our observations we hypothesize that the calcium activated inward sodium current via TRPM4 negatively modifies NCX activity, thus the higher sodium level results in a less effective calcium extrusion in WT myocytes. Taken together these results point to a novel role of TRPM4 in the patho-mechanism of Ca^{2+} dependent arrhythmias.

P-03

MOVEMENTS OF THE S4 SEGMENTS OF THE Kv2.1 AND Kv6.4 SUBUNITS IN Kv2.1/Kv6.4 HETEROTETRAMERS.

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The voltage-gated K^+ (Kv) channel subunit Kv6.4 does not form functional channels when expressed alone but tetramerizes with Kv2.1 subunits into functional Kv2.1/Kv6.4 heterotetramers. Within these heterotetrameric Kv2.1/Kv6.4 channels complexes, Kv6.4 causes an approximately 40 mV hyperpolarizing shift in the voltage-dependence of inactivation as compared to Kv2.1 homotetramers without affecting the voltage-dependence of activation significantly. By comparing gating current (I_Q) recordings that represent the molecular movements of the subunit voltage sensing domains (VSDs), we recently showed that a second component in the charge (Q) versus voltage (V) distribution appeared in heterotetrameric Kv2.1/Kv6.4 channels. This second component develops at more negative potentials than Kv2.1 homotetramers suggesting that the voltage sensor of Kv6.4 subunits move in a more negative voltage range than the remaining Kv2.1's voltage sensors. Using cysteine accessibility studies, we demonstrate that the voltage-dependence of the rates of MTSET modification at V335C in Kv6.4 correspond with the second component of the QV distribution of Kv2.1/Kv6.4 heterotetramers. Similarly, the voltage-dependence of modification rates at V296C in Kv2.1 follow the QV distribution of Kv2.1 homotetramers. These results indicate that in functional Kv2.1/Kv6.4 heterotetramers the voltage sensors from the Kv6.4 subunits move at more negative potentials than the voltage sensors belonging to Kv2.1 subunits.

P-04

ErbB RECEPTORS CONTROL STORE-OPERATED ENTRY OF Ca^{2+}

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SOCE (Store-Operated Calcium Entry) is the main mechanism by which external Ca^{2+} enters into non-excitable cells after endoplasmic reticulum emptying. It is implicated in several processes such as proliferation and migration. Alterations in SOCE could initiate or support the development of hallmarks of cancer. At least two proteins are involved in SOCE : the stromal interaction molecule 1 (STIM1), and Orai1. The role of TRP channels in SOCE, especially TRPC1, is more controversial. We previously showed that TRPC1 depletion inhibited SOCE in non-small cell lung carcinoma (NSCLC) cell lines. In those cells, inhibition of SOCE resulted in an impairement in the full activation of epidermal growth factor receptor (EGFR), a receptor tyrosine kinase (RTK) that constitutes, with other RTKs such as ErbB2, a major target in the treatment of advanced cancers. In this study, we investigated the role of EGFR and ErbB2 in the modulation of SOCE. *In silico*, we identified that the amino-acid sequence of STIM1 contained several tyrosine residues possibly phosphorylated by EGFR and ErbB2. Moreover, we observed that lapatinib, a dual inhibitor of EGFR and ErbB2, dramatically decreased SOCE in A549 (NSCLC) and SKBr3 (a breast cancer cell line overexpressing ErbB2). We thus hypothesized that SOCE modulation by RTKs activation could be achieved by posttranslational modifications of STIM1. Several reports showed that serine phosphorylation of STIM1 at ERK1/2 target sites is required to allow its translocation and subsequent SOCE activation. However, STIM1 phosphorylation on tyrosine residues could be also important for SOCE

P-05

PROPAGATION OF RADIATION-INDUCED BRAIN MICROVASCULAR ENDOTHELIAL DNA DAMAGE: A TIGHT INTERPLAY BETWEEN CONNEXIN CHANNELS, PARACRINE ATP SIGNALING AND THE CALCIUM/ROS SIGNALING AXIS.

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Healthy endothelial cells(ECs) are prone to radiation-induced damage. X-ray exposure of cells not only results in damage in the irradiated cells but this damage can be propagated to non-exposed bystander cells, a phenomenon called the radiation induced bystander effect(RIBE). RIBE can be studied by means of different end points such as DNA damage, cell death and transformation. DNA Double strand breaks(DSBs)are considered to be the most dangerous lesions and the precursors of other endpoints. We optimized a set-up in which a well-delineated zone of adherent brain microvascular ECs are exposed to X-rays (1 and 20 Gy). As such, we were able to investigate radiation-induced effects in both the irradiated and adjacent non-irradiated bystander zone separately. The percentage of γ-H2AX-positive cells, i.e. marker for DSBs, was quantified in both areas and revealed the presence of γ-H2AX-positive cells in the bystander zone with a maximum response 3 h after irradiation. Hence, this time point was chosen to further investigate possible signaling pathways. Reactive Oxygen Species (ROS) have been proposed as forefront mediators of RIBE but the mechanism of long-distance effects of these messengers remain unclear. We here found that ROS as well as calcium ions (Ca^{2+}), extracellular ATP and transmembrane connexin(Cx) channels are key players in this phenomenon. We propose that intercellular Ca^{2+} signaling via Cx gap junction channels (direct cell-cell coupling) and hemichannels (paracrine ATP release pathway) acts as a feed-forward propagation mechanism of ROS production underlying the RIBE in brain microvascular ECs. We can conclude that a tight interplay between ROS, Ca^{2+}, ATP and Cx channels is important in bystander signaling following exposure to X-rays. Further unraveling these mechanisms can contribute to the development of protective strategies against radiation-induced EC damage.

P-06

CORRELATION BETWEEN LOCAL FIELD POTENTIAL FREQUENCIES IN THE VENTRAL TEGMENTAL AREA AND QUALITATIVE ASPECTS OF LOCOMOTOR BEHAVIOR

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At the end of the last century, one of the influential figures in the field of affective neuroscience, Philip Teitelbaum, proposed a conceptual framework for goal-directed behaviors. This framework proposes that a complex behavioral pattern can be reduced to the sequence of simple stereotyped acts controlled by different behavioral subsystems. Experimentally this predicts that local brain lesions and/or psychostimulant drugs should dysregulate higher neural circuits and uncover normally obscured lower layers of brain machinery. We used dopaminergic psychostimulants to modify the behavior of rats pre-implanted with 8-microelectrode-arrays within the ventral tegmental area (VTA). This brain region is strongly involved in the regulation of goal-directed behavior, motivation, reward and salience. Electrophysiological recordings were performed using a telemetric system allowing to record brain potentials from freely behaving animals. Rats were observed and recorded during baseline and after the intraperitoneal injections of saline, or one of four solutions containing dopamine agents: (i) cocaine (10 mg/kg, i.p.), (ii) amphetamine (4 mg/kg, i.p.), (iii) high-dose of the dopamine D2 receptor agonist quinpirole (0.5 mg/kg, i.p), and (iv) combination of low-dose of quinpirole (0.5 mg/kg, i.p) with cocaine (10 mg/kg, i.p). All dopamine agents or combinations increased locomotor activity. After the injections of amphetamine, high-dose quinpirole, and a combination of low-dose quinpirole with cocaine, the rats demonstrated various signs of stereotyped behavior. In the case of quinpirole-containing injections the rats demonstrated higher level of locomotor path~~s~~ repetitions (locomotor stereotypy). In the case of amphetamine, ~~the~~ animals tended more to repeat the particular movements (focused stereotypy), but not the paths. In all the recording sessions, including baseline, power spectrum analysis of the LPFs revealed a prominent peak in the theta frequency range (~7-9 Hz) during locomotor activity. However, the values of the LFP theta peak were significantly different depending on the experimental conditions. Drugs increasing dopamine levjels – cocaine and amphetamine – shifted the peak of LFP theta power toward a higher frequency, as compared to the baseline and saline. In contrast, after the injections of the solutions containing D2 agonist quinpirole – high-dose quinpirole or a combination of low-dose quinpirole with cocaine – the peak was shifted toward a lower frequency (by ~15%, $p<0.001$). Taken together, the results demonstrate that a moderate shift in frequency of LFPs in the VTA is associated with a strong behavioral alteration. In addition, the nature of electophysiological changes within the VTA depends on the pattern of dopamine receptor stimulation. We hypothesize that a changed oscillation main frequency within the VTA may change–the ability of this brain area to communicate with its output structures.

P-07

GENOMIC EFFECTS OF SDF-1α ON RAT NEONATAL CARDIOMYOCYTES: COMPARISON BETWEEN COMMERCIAL SDF-1α AND SUPERNATANT OF SDF-1A OVEREXPRESSING MESENCHYMAL STEM CELLS

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Given the keen interest in using SDF-1α, alone or in combination with a stem cell therapy, as a therapeutic stem cell homing factor for treatment of myocardial infarction, it is essential to investigate direct effects of these interventions on cardiomyocytes. The objective of this work was to identify new signaling pathways modulated by SDF-1α in cardiomyocytes, the latter acting alone or as part of a hybrid therapy. Passage 4 mesenchymal stem cells (MSC) isolated from bone marrow of adult rats were transduced with the lentiviral particles SDF-1α-IRES-GFP-pWXLd or GFP-pWXLd. Neonatal rat cardiomyocytes were culture-expanded then stimulated 1 hour with commercial SDF-1α (5μM) diluted in cardiac culture medium versus cardiac culture medium alone and with conditioned medium of MSC overexpressing SDF-1α versus supernatant of MSC transduced with GFP-pWXLd. Gene expression profile was analyzed by micro-array and confirmed by RTQ-PCR and/or ELISA. Micro-array analysis revealed that SDF-1α regulated 1.21% of all transcripts in rat cardiomyocytes. Two pathways implicated in lipid metabolism (the adipocytokines and PPAR signaling pathways) were downregulated in the 2 conditions (commercial SDF-1α and supernatant of MSC overexpressing SDF-1α). We confirmed by RTQ-PCR that SDF-1α upregulated JAK2 and AKT, factors implicated in the anti-apoptotic and pro-survival pathways. We also showed that commercial SDF-1α downregulated the fatty acid binding protein, angiopoietin-related protein 4 precursor and adiponectin gene expression, factors implicated in fatty acid metabolism. Interestingly, supernatant of MSC transduced with the GFP-pWXLd lentivirus upregulated gene expression of fatty acid binding protein and angiopoietin-related protein 4 precursor while this response was inhibited by SDF-1α overexpression. We concluded that in rat neonatal cardio-myocytes, SDF-1α modulates negatively the expression of factors implicated in lipid metabolism. Moreover, modulation of cardiomyocytes gene expression by conditioned medium of MSC overexpressing SDF-1α cannot be deducted from the response to commercial SDF-1α.

P-08

EFFECTS OF iNOS INHIBITION IN HIGH-FAT DIET-INDUCED OBESITY

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Obesity is a worldwide problem caused by caloric excess promoting deleterious cellular responses in organs. Endothelial dysfunction, impaired vasodilation and insulin resistance are considered as key features of obesity. Interactions between metabolic and hemodynamic factors activate intracellular signalling pathways, leading to the production of oxidative stress, pro-inflammatory cytokines and fibrotic factors. Among vasoactive factors, nitric oxide (NO) has been determined as playing a critical role in the pathogenesis of metabolic diseases. The aim of this study is to investigate the involvement of inducible nitric oxide synthase (iNOS) in the development of progressive renal dysfunction leading to obesity-induced kidney disease as well as in liver and adipose tissue. To do so, C57Bl/6 male mice were randomized to a low fat diet (LFD) or a high fat diet (HFD) and treated with pharmacological agent, L-NIL (iNOS inhibitor; 0.1 % in drinking water).We have demonstrated that iNOS inhibition prevented several changes in mice fed with HFD: increase of body weight, urine glucose level, plasma triglyceride and insulin levels, proteinuria and tissue hypertrophy. However, the significant increase in albuminuria and mesangial matrix expansion were not ameliorated with L-NIL. To evaluate the beneficial effect of L-NIL in the development of insulin resistance, liver and peri-renal white adipose tissue were also investigated. Histological analysis revealed an increasing size of adipocytes and an accumulation of lipid vacuoles into hepatocytes of mice fed with HFD along with increased liver triglyceride level which were significantly decreased with L-NIL treatment. However, inflammation, as attested by macrophage infiltration and enhanced MCP-1 level, was only prevented by L-NIL in the adipose tissue but not in the liver. These results suggest that inhibition of iNOS leads to beneficial effects in kidney, liver and adipose tissue in mice fed with HFD. However, further investigations are needed to better determine the role of iNOS in the targeted organs.

P-09

EFFECT OF TYROSOL AND FARNESOL ON *CANDIDA ALBICANS* BIOFILMS

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Candida albicans (*C. a.*) is the major yeast responsible of oral candidiasis including stomatitis associated with dentures. Adaptation of *C. a.* to its environment (growth, filamentation, …) is mediated by *quorum sensing* mechanisms implying yeast secretion of tyrosol and farnesol which modify phenotypic expression in return on a dose-dependent manner. This investigation aims at evaluating the role of these *quorum sensing* molecules as modulators of biofilms formation. The investigations were conducted on the reference strain *C. a.* ATCC 10231 and on wild strains isolated from dentures. *C. a.* biofilms were formed in 96-well plates in the presence of tyrosol (from 3 µM to 20 mM) or farnesol (from 1 µM to 3 mM). Planktonic growth was evaluated by turbidimetry at 600 nm and biofilms were quantified by Cristal Violet staining. *C. a.* ATCC 10231 planktonic phase was not influenced by both molecules while biofilm formation has been shown modulated. On one hand, tyrosol prevented the formation of *C. a.* biofilms at 20 mM: the attached biomass represented then 15.9 ± 1.4 % (mean ± SEM) of that observed for the control. On the other hand, farnesol presented a biphasic effect: anti-biofilm at 3 mM concentration (the attached biomass was 18,4 ± 4,0 % of the control) and pro-biofilm at 3 µM (the attached biomass was then 193,0 ± 28,5 % of the control; ANOVA test, $p < 0,01$). Similar effects are inconstantly observed in 3 wild strains. After a 45-min incubation of *C. a.* ATCC 10231 in water, supernatant contained *quorum sensing* agents which reduced biofilm formation down to 69.3 ± 2.5 % of the control ($N = 3$, t test, $p < 0.0001$) while the same supernatant had no effect on planktonic growth (t test, $p = 0.5964$). These data suggest that *quorum sensing* molecules modulate *in vitro* yeast biofilm formation.

P-10

ANOCTAMIN 1 (ANO1) IS REQUIRED FOR GLUCOSE–INDUCED MEMBRANE POTENTIAL OSCILLATIONS AND INSULIN SECRETION BY MURINE β-CELLS.

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It is well known that Cl^- and HCO_3^- play an important role in glucose-stimulated insulin secretion. We find that the channel mediating glucose-induced Cl^- efflux from β-cells corresponds to the Ca^{2+}-activated Cl^- channel anoctamin 1 (Ano1) also called TMEM16A. We show that Ano1 is expressed in murine islets. Its gating switches on/off the oscillating electrical activity, critical for glucose-stimulated insulin secretion (GSIS). The Ano1 blockers 2-(5-ethyl-4-hydroxy-6-methylpyrimidin-2-ylthio)-N-(4-(4-methoxy-phenyl)thiazol-2-yl)acetamide (T-AO1) and tannic acid (TA) reduce action potential (AP) rate and repolarize residual AP peak on islets and dispersed murine β-cells. In the latter case, the reduction of AP rate is larger than 87 %. With T-AO1, the average membrane potential is repolarized by at least 13 mV. These inhibitors effects on membrane potential are associated with inhibition of GSIS (8.3 mM glucose, 100 % with T-AO1 and 94 % with TA; 16.7 mM glucose, 100 % with T-AO1 and 67 % with TA). Single-channel Cl^- currents from rat β-cells are activated by 1 µM Ca^{2+}. Current-voltage relationship is linear and exhibits an unique unitary slope-conductance of 8.37 pS, matching the Ano1 described conductance. T-AO1 and TA respectively inhibit by 100 and 86 % the open probability while they had no effect on Ba^{2+} currents. Lowering intracellular anion concentration (low Cl^- and HCO_3^- media with bumetanide and acetazolamide) provokes a 65% reduction in AP amplitude and a 15 mV AP peak repolarization. Taken together, these data demonstrate that Ano1 is required to sustain glucose-induced β-cell membrane potential oscillations and insulin secretion.

P-11

CHEMERIN POTENTIATES PULMONARY ARTERY REACTIVITY TO ENDOTHELIN-1

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The adipokine chemerin has been recently reported to increase aortic contractile response to endothelin-1, which is a potent pulmonary vasoconstrictor. In the present study, we hypothesized that chemerin could potentiate pulmonary artery contractile response to endothelin-1. Vascular reactivity to chemerin (10^{-16}-10^{-7}mol/L) and to phenylephrine (10^{-10}-10^{-5} mol/L), serotonin (10^{-8}-10^{-3}mol/L) and endothelin-1 (3.10^{-10}-1.10^{-7}mol/L) after 1-hour pre-treatment with chemerin (10^{-8}mol/L) was evaluated in endothelium-intact and -denuded pulmonary artery (PA) and thoracic aorta (TA) from male 18-week old Wistar rats. Arteries were also sampled for pathobiological evaluation. Relative gene expression of chemerin, chemR23 and GPR1 were similar in PA and TA, while CCRL2 mRNA content was higher in PA. Chemerin alone did not alter pulmonary or aortic vascular tone. Pre-treatment with chemerin did not modify phenylephrine- and serotonin-induced vasoconstriction in both PA and TA. However, chemerin pre-treatment potentiated endothelin-1-induced vasoconstriction in both endothelium-intact and -denuded TA and PA ($p<0.01$). Chemerin increased the sensitivity to endothelin-1 in endothelium-intact (EC50: vehicle = $1.4.10^{-8}$M, chemerin = $8.5.10^{-9}$M) and -denuded PA (EC50: vehicle = $7.6.10^{-9}$M, chemerin = $4.6.10^{-9}$M). The maximal contraction (Emax) was 162% and 168% in vehicle treated endothelium-intact and -denuded vessels respectively, while it was 171% and 194% in chemerin pre-treated vessels. It is concluded that chemerin potentiates pulmonary artery vaso-constriction induced by endothelin-1.

P-12

INSULIN-LIKE GROWTH FACTOR-1 CONTRIBUTES TO PULMONARY ARTERY SMOOTH MUSCLE CELL PROLIFERATION IN IDIOPATHIC PULMONARY ARTERIAL HYPERTENSION

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Pulmonary arterial hypertension (PAH) is a fatal disease characterized by a progressive increase in pulmonary vascular resistance, mainly due to obstructive remodelling of distal pulmonary arteries and excessive pulmonary artery smooth muscle cell (PA-SMC) proliferation. Insulin-like growth factor-1 (IGF-1), a well-known mitogen for vascular SMCs, has been linked to vascular remodelling and atherosclerosis in diabetes. Low circulating IGF-1 level has been associated with increased susceptibility to develop cardiovascular diseases. We, therefore, hypothesized that IGF-1 signalling could play a role in the pathogenesis of PAH, more precisely in PA-SMC hyperplasia. Expressions of IGF-1 and IGF-1 receptor were evaluated in total lung homogenates and in primary cultured PA-SMCs obtained from six patients with idiopathic PAH and ten controls. PA-SMCs treated with IGF-1 (10 and 100 ng/mL) were assessed for cell proliferation (by MTT assay) and apoptosis (by the evaluation of Bax-to-Bcl2 ratio). Seric IGF-1 level was evaluated in sera from patients with idiopathic PAH (n=25) and control subjects (n=26). IGF-1 expression was 5-fold increased in total lung homogenates from PAH patients compared to controls, while pulmonary IGF-1 receptor expression did not change. In PA-SMCs from PAH patients, the expressions of IGF-1 and IGF-1 receptor were increased. Treatment with IGF-1 dose-dependently induced the proliferation and decreased the pro-apoptotic Bax-to-Bcl-2 ratio in PA-SMCs. These effects were stronger in PAH compared to control PA-SMCs. After adjustment for age and body mass index, seric IGF-1 level was higher in PAH patients compared to controls. In PAH, the IGF-1 signalling is exacerbated in the lungs, probably contributing to PA-SMC hyperplasia, while circulating IGF-1 is reduced.

P-13

MECHANOSENSITIVE PIEZO1 AS A KEY PLAYER TO START ENDOMETRIAL DECIDUALIZATION?

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Embryo implantation is a complex process that involves an intimate interaction between an implantation-competent blastocyst and a receptive uterus. Not surprisingly, poor endometrial receptivity during an IVF cycle has been highlighted as a contributing factor for implantation failure and is suggested to be responsible for up to two-thirds of unsuccessful embryo transfers. Several studies have been conducted to investigate the molecular mechanisms, but to date a complete understanding of this process remains elusive. The indispensable physical embryo-uterine interaction suggests a possible role for mechanosensors. Recently, members of the piezo-family were identified in endothelial cells (piezo1) and in Merkel cells (piezo2) as pore-forming proteins involved in sensing mechanical stimuli. Using qRT-PCR we were able to detect high expression levels of piezo1 in endometrial biopsies throughout the menstrual cycle. Interestingly, RNA expression levels of piezo1 in human endometrial epithelial cells (HEEC) exceeded those of other known mechanosensitive ion channels. Functional expression of mechanosensitive ion channel(s) was shown using Ca^{2+} microfluorimetry and whole-cell patch clamping experiments in primary HEEC. In addition, a functional relationship between a mechanical stimulus and uterine decidualization was demonstrated using a menstruating mouse model in the presence or absence of a blocker of mechanosensitive ion channels, GsmTX-4. Taken together, these preliminary data suggest evidence for a potential role of piezo1 during the decidualization and implantation process.