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# RESEARCH DAY (RD) STUDENT RESEARCH SYMPOSIUM (SOS)

PRESENTING AND PROMOTING  
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## POSTER ABSTRACTS

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# HOMOZYGOSITY MAPPING-GUIDED EXOME SEQUENCING IN LCA PATIENTS OF CONSANGUINEOUS ORIGIN REVEALS MUTATIONS IN KNOWN GENES AND A NOVEL CANDIDATE GENE.

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## Purpose

Leber congenital amaurosis (LCA) is the most severe autosomal recessive inherited retinal dystrophy (IRD) accounting for 5% of childhood blindness. To date, 70% of LCA cases can be explained by mutations in one of the 23 known LCA genes. Here we aimed to identify the underlying genetic cause of LCA in 15 Saudi-Arabian families with reported or suspected consanguinity.

## Methods

A total of 20 probands, ranging between 2-9 years old, were clinically diagnosed with LCA or early-onset IRD. The genetic workup consisted of homozygosity mapping followed by targeted next generation sequencing (NGS) or Sanger sequencing, combined or not with whole exome sequencing (WES). Co-segregation could be demonstrated for all identified mutations.

## Results

Overall, we identified 13 putative pathogenic homozygous mutations in 10 known IRD genes in 14/15 (93.3%) of the studied families, six of which are novel. Eight of these genes were known LCA genes: CRB1 (3/15, 20%), RPGRIP1 (2/15, 13.3%), SPATA7 (2/15, 13.3 %) and CABP4, CEP290, GUCY2D, MERTK, RDH12 (1/15, 6.7% for the latter five) respectively. Specifically, the recurrent RPGRIP1 mutation c.1007delA p.(Glu370Asnfs\*5) is a reported potential founder mutation in the Saudi population (Khan et al. 2014). Moreover, mutations were found in ATF6 and ALMS1 (1/15, 6.7% for each), known to be implicated in autosomal recessive achromatopsia and in Alstrofm syndrome, respectively.

## SYNTHESIS OF 1'-N-HOMOAZANUCLEOSIDES AS POTENTIAL TRANSITION STATE ANALOGUES AND ANTIVIRAL AGENTS

*Jakob Bouton, Serge Van Calenbergh*

Azanucleosides are a class of nucleoside analogues in which the furanose ring has been replaced by a functionalized pyrrolidine derivative. Most of the known azanucleosides are either C-nucleosides, or homonucleosides, in which a methylene linker is placed between the pyrrolidine and the nucleobase. A very promising class of aza-C-nucleosides are the Immucillins, which act as transition state analogue enzyme inhibitors of several nucleosidase & nucleoside phosphorylase enzymes.[1] Some of these Immucillins also exhibit potent antiviral activity; the adenosine analogue BCX-4430 is currently being developed as a potential treatment for Ebola virus disease.[2]

Inspired by the intriguing biological activities of known azanucleosides, a series of new 1'-N-homoazanucleosides was synthesized. These were constructed with a variety of nucleobases and nucleobase analogues and the synthesized compounds are currently being evaluated for antibacterial, antiprotozoal, antiviral and antitumoural activity.

### References

[1] Evans G. B., Schramm V. L., Tyler P. C., *Curr. Med. Chem.*, 2015, 22, 3097

[2] Warren, T. K. et al., *Nature*, 2014, 508, 202

## CLINICAL PATHWAY IMPROVES IMPLEMENTATION OF EVIDENCE-BASED STRATEGIES FOR THE MANAGEMENT OF ANDROGEN DEPRIVATION THERAPY-INDUCED SIDE EFFECTS IN PROSTATE CANCER PATIENTS

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### **Introduction & objectives**

To assess the effect of a clinical pathway in prostate cancer patients (PCa) to implement evidence-based strategies for the management of androgen deprivation therapy (ADT)-induced side effects.

### **Materials & methods**

A retrospective study was conducted to evaluate the effect of a clinical pathway. Patients receiving ADT before and after pathway implementation were allocated to the control and pathway group resp. Data was extracted from electronic health records of all eligible PCa patients. Chi-square and Mann-Whitney U test were used to compare groups.

### **Results**

In total, we included 126 patients in the control group and 132 in the pathway group. There were no significant differences in baseline patient characteristics (age, tumor characteristics, treatment) between cohorts. Medical assessments for ADT management were more ( $p < 0.001$ ) administered in the pathway group. Risk assessment screenings (cardiovascular, metabolic and bone screening) increased significant after pathway implementation (resp. from 16 to 61%, from 4 to 46% and from 10 to 58%). ADT preventive measures recommendations (physical activity from 11% to 62%, diet from 10% to 58%, psychological from 13% to 46% and vitamin D and calcium supplementation from 29% to 67%) increased ( $p < 0.001$ ) after pathway implementation.

### **Conclusion**

A clinical pathway can improve implementation of evidence-based strategies for ADT-induced side effects in PCa patients and therefore improve quality of care.

## GETTING FOSMIDOMYCIN INSIDE MYCOBACTERIAL CELLS: A PRODRUG APPROACH.

*Charlotte Courtens, Martijn Risseeuw, Serge Van Calenbergh*

Antimalarial and antitubercular agents with new mechanisms of action are necessary to tackle Plasmodium parasites and Mycobacteria resistant to all current therapies. Fosmidomycin has been shown to be a well-tolerated, safe and efficacious antimalarial drug in combination treatment. However, its pharmacokinetic properties are less than ideal, with only moderate bioavailability and a short plasma half-life. Moreover, because of the unique highly lipophilic cell wall of Mycobacteria, fosmidomycin cannot cross the cell wall and thus, is not active against Mycobacteria.

A lot of research has been done on the design of highly active fosmidomycin analogs. However, the problem of low bioavailability remains. Conversion into prodrugs can improve both oral bioavailability and cell penetration by passive diffusion.

To date, only acyloxymethyl- and alkoxycarbonyloxymethyl prodrugs have been reported in the literature. We synthesized and tested the inhibition potency of three amino acid (Phe, Leu, Lys) ester (OEt) based prodrugs.

For malaria, none of these was found to have higher antimalarial activity than the prodrugs previously reported in literature. For tuberculosis, the Leu OEt prodrug has promising activity. Therefore, different Leu ester (Me, iPr, Pentyl, Cyclohexyl, Benzyl) prodrugs have been prepared and are currently being tested. The amino acid series will also be expanded (Gly, Ala, Val, iLeu, Tyr) in order to optimize the prodrug moiety for mycobacterial uptake.

# CARD9 P.R70W, A TURKISH FOUNDER MUTATION ASSOCIATED WITH MUCOSAL AND INVASIVE FUNGAL INFECTIONS, DISRUPTS DOWNSTREAM NF-KB SIGNALING BY INHIBITING BCL10 RECRUITMENT

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## **Background**

Inherited CARD9 deficiency is an autosomal recessive primary immunodeficiency predisposing uniquely to chronic and invasive fungal infections in otherwise immunocompetent individuals.

## **Methods**

We studied eleven patients with CARD9 c.208C>T p.(R70W) mutations belonging to five families living currently in Belgium or France but originating from the same region in Turkey. They present a spectrum of both mucosal and systemic fungal infections. We performed haplotype analysis to investigate a possible founder origin of this mutation.

We devised an in vitro system to explore the biochemical mechanism of the R70W mutation, using a constitutively active CARD9 L213LI mutant, which allows dissection of downstream signaling events. We performed NF-kB luciferase reporter assays and co-immunoprecipitation experiments.

## **Results**

Segregation analysis of four microsatellite markers and five SNPs revealed a common haplotype of 1.03 Mb surrounding the mutation, suggesting a Turkish founder mutation.

Luciferase assays showed that the constitutive NF-kB activity of the L213LI mutant was completely eliminated in a double mutant containing both R70W and L213LI mutations. Consistent with these results, co-immunoprecipitation of CARD9 showed that the double mutant fails to pull down Bcl10 and MALT1, whereas the L213LI mutant does.

## **Conclusion**

Identification of the R70W CARD9 mutation as a founder in patients with CMC and/or invasive fungal infections originating from Turkey implies that targeted testing of this mutation would be valuable in this specific population. The R70W mutation prevents the interaction with downstream MALT1 and Bcl10, which leads to inactivation of downstream CBM complex-dependent signaling to NF-kB.

## USING SWATH-MS FOR THE ANALYSIS OF MODIFIED HISTONE PEPTIDES

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Because epigenetic histone posttranslational modifications (hPTM) regulate a plethora of fundamental biological processes, they are increasingly considered an important new "target" in e.g. toxicological screenings. Highly modified histone peptides are very difficult to study because of their high dynamic range, and the high number of isobarically modified peptides with similar retention times. The potential to quantify on MS / MS-level, therefore, makes SWATH a very suitable strategy for the analysis of these peptides. This derives from the fact that transitions can be chosen that are both unsaturated and unique. Here, we present a workflow for the SWATH data-analysis to quantify modified histone peptides.

A dilution series of commercial bovine histones was acquired using both DDA (for library building) and SWATH to find the optimal on-column loading. SWATH acquisition was done using 30 or 60 variable SWATH windows to verify the impact on specificity. Skyline was used to build an assay library from DDA data. The transitions from the assay library were selected based on (1) curated searching and filtering based on prior knowledge and (2) unique combinations of a precursor and product m/z in a SWATH window. For the validation of this workflow, a time-lapse in vitro deacetylation experiment is currently being analyzed in order to assess the performance on rising and disappearing precursor masses.

## WRIST MRI TO ESTIMATE AGE: NOT MERELY A BLACK-AND-WHITE INTERPRETATION

*De Tobel Jannick, de Haas Michiel, Thevissen Patrick, Verstraete Koenraad*

### **Study rationale**

In literature two types of MRI have been described to study the wrist for age estimation: T1-weighted spin echo (SE) and T1-weighted volumetric interpolated breath-hold examination (VIBE). Because of the chemical shift artefact, physal cartilage appears distorted on SE images. By contrast, a clear delineation of physal cartilage and fusing bony bridges can be made on VIBE images.

The aim of the study was to determine the influence of these different appearances on staging radial development for age estimation.

### **Materials and methods**

Two observers independently evaluated radial development based on the anonymised images of the males, while the images of the females were only evaluated by one observer. Both sequences were evaluated separately. Schmeling and Kellinghaus staging techniques were used and inter-observer agreement was calculated (intra-class correlation coefficient = ICC ).

### **Results**

A statistically significant shift in age distribution per stage was seen with relatively older individuals in younger stages allocated to SE images, compared to VIBE images.

Reproducibility was lower for VIBE, because 19/64 cases got allocated stage 4 by one observer, while the other observer allocated stage 5.

### **Conclusion**

MR sequence specific reference data are necessary to estimate age based on wrist MRI.



## ZEBRAFISH MODELING OF THE B4GALT7-DEFICIENT TYPE OF EHLERS-DANLOS SYNDROME

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Biallelic mutations in B4GALT7, encoding an enzyme for the biosynthesis of the linker region in proteoglycans, are the cause of a rare autosomal recessive variant of Ehlers-Danlos syndrome (EDS). This disorder is mainly characterized by short stature, hypotonia and skeletal abnormalities. Our current knowledge about this disabling disease is limited, in part due to the lack of a relevant in vivo model. Therefore, we developed and characterized a knockdown (KD) zebrafish model for  $\beta$ 4GalT7-deficient EDS by using morpholino injections targeted against *b4galt7*. Morphant embryos showed morphological abnormalities compared to wild-type and negative control embryos. The total amount of sulfated GAGs was severely reduced in morphant embryos and whole-mount immunohistochemistry showed that heparan and chondroitin sulfate proteoglycans were severely diminished in the heads of *b4galt7* KD embryos. In addition, alcian blue and alizarin red staining demonstrated that cartilage and bone structures in the heads of morphant embryos are absent or strongly misshapen. Furthermore, morphant embryos suffered from a lack of muscle tone and immunohistochemical staining revealed a disturbed filamentous actin pattern in *b4galt7* KD embryos' head and tail. To conclude, a *b4galt7* morphant zebrafish model has been developed, which partly phenocopies the human phenotype of patients suffering from  $\beta$ 4GalT7-deficient EDS. This model enables the in vivo investigation of the pathogenesis of this condition.

## EXPLORING BINDING CHARACTERISTICS AND RELATED COMPETITION OF DIFFERENT URAEMIC TOXINS

*Olivier Deltombe, Henriette de Loor, Griet Glorieux, Annemieke Dhondt, Wim Van Biesen, Björn Meijers, Sunny Eloot*

We evaluated the binding characteristics of hippuric acid (HA), indole-3-acetic acid (IAA), indoxyl sulphate (IS), and p-cresylsulphate (pCS) by deriving a binding curve in: (i) serum from healthy controls (healthy serum), (ii) blank serum from haemodialysis patients (blank HD serum; i.e. cleared from uraemic toxins), and (iii) non-treated serum from HD patients (HD serum). Additionally, the mutual binding competition of these protein-bound uraemic toxins (PBUTs) was studied in blank HD serum. Equilibrium dialysis was used to separate the free and bound fractions of each PBUT. Free and total PBUT concentrations were quantified by ultra-high performance liquid chromatography with mass spectrometer detection. The percentage protein binding (%PB) of each PBUT was calculated from the measured free and total PBUT concentrations. For all compounds, the binding capacity of healthy serum was higher than blank HD serum, which was comparable to non-treated HD serum, except for HA. The competition experiments revealed that at high uraemic concentrations, mutual competition was observed for IS and pCS. The %PB of HA and IAA was lower (trend) only for the addition to blank HD serum containing the strongly bound IS or pCS. We conclude that there is an intrinsic impact on %PB in uraemia as compared to healthy controls by post-translational modifications of albumin. In addition, competitive binding is only relevant for the strongly bound PBUTs IS and pCS at high uraemic concentrations.

## mRNA TO INDUCE SUSTAINED EXPRESSION OF NEUROTROPHIC FACTORS IN THE RETINA

*Joke Devoldere, Karen Peynshaert, Stefaan C. De Smedt and Katrien Remaut*

### **Introduction**

The progressive loss of retinal cells represents the main cause of vision loss and irreversible blindness. This work aims to evaluate the potential of chemically modified mRNA as a generic gene therapy strategy to stimulate neuronal survival and ultimately save vision.

### **Methods**

To examine whether non-viral delivery of mRNA to the retina is feasible, we first compared the transfection efficiency of three different commercial carriers for the delivery of non-modified green fluorescent protein (GFP) mRNA in vitro on MIO-M1 Müller cells. The in vitro data were further confirmed by means of an ex vivo bovine retinal explant. Expression and uptake of a cy5-labeled GFP mRNA was assessed 24 hours post-transduction of the bovine retinal explant.

### **Results**

The percentage of GFP positive MIO-M1 cells upon 24h incubation with TransIT packaged mRNA reaches up to 70% and GFP expression remains for at least two weeks after single administration in vitro. In treated retinas, we observed a strong cy5-signal in the ganglion cell layer, confirming uptake of the particles in the retina.

### **Conclusion**

Our findings suggest that mRNA-loaded lipid based carriers have potential to transfect MIO-M1 Müller cells in vitro. In addition, clear uptake of our particles was visible in a bovine retinal explant 24 hours after transduction. Although more extensive optimization of the delivery will be required, this could be the first successful delivery of mRNA to the retina.

## CALCIUM OSCILLATIONS ANALYSIS DESCRIBES HUMAN OOCYTE ACTIVATION DEFICIENCIES IN SPERM INVOLVED IN RECURRENT FERTILIZATION FAILURES

*Ferrer-Buitrago M, Lu Y, Lierman S, Van den Abbeel E, Van der Jeught M, Deforce D, Leybaert L, De Sutter P, Heindryckx B*

Fertilization failure (FF) occurs in 3% of assisted reproduction technology (ART) cycles. It is known that oocyte activation deficiencies are the main cause of FF after ART. However discerning whether there is an oocyte or a sperm origin still challenging. After monitored ovarian stimulation, the majority of the oocytes are retrieved at the second meiotic metaphase (MII). Phospholipase C zeta (PLC $\zeta$ ), the sperm-borne factor introduced upon fertilization, initiates the oocyte activation through an inositol triphosphate (IP3) signaling cascade that stimulates cytoplasmic calcium (Ca $^{2+}$ ) changes named oscillations. The initiation of the oocyte activation is not a species-specific event. Tests such as, the mouse oocyte activation test (MOAT) and the mouse oocyte calcium analysis (MOCA) are used to discern whether FF could be related to sperm or oocyte factors. According to the result, the application of assisted oocyte activation (AOA) could be counsel for following ICSI cycles. Human-PLC $\zeta$  shows greater potency than mouse-PLC $\zeta$  to activate mouse oocytes. Thus, human sperm capable to activate mouse oocytes fails to induce human oocyte activation. The present study aimed to describe the Ca $^{2+}$  profile induced by human sperm involved in recurrent FF using both, mouse and human oocytes. Human oocyte calcium analysis (HOCA) is a more sensitive test to detect sperm-related activation deficiencies. HOCA is a valuable test to predict whether AOA would be beneficial in a following treatment.

## PULMONARY SURFACTANT COATED NANOGELS: ROLE OF SURFACTANT PROTEIN B AS siRNA DELIVERY ENHANCER.

*Roberta Guagliardo, Lynn De Backer, Pieterjan Merckx, Stefaan De Smedt, Koen Raemdonck.*

Small interfering RNAs (siRNAs) represent a relevant tool to silence gene expression involved in a wide range of pathologies, including cancer and inflammatory diseases. Important barriers for siRNA as therapeutic molecules are their rapid degradation and clearance upon in vivo administration as well as the poor cellular delivery efficiency. Different nanocarrier platforms are being studied with the aim to overcome these limitations.

Previous studies highlighted the key role of pulmonary surfactant (PS) on the delivery efficiency of cationic biodegradable nanogels. Here, we aim to shed light on the key component of PS, responsible for the enhanced siRNA delivery.

## GRADING OF MITRAL REGURGITATION SEVERITY WITH THE API METHOD IN MITRAL VALVE PROLAPS

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## THE INVOLVEMENT OF SUBCORTICAL GREY MATTER IN GRAMMATICAL PROCESSING: A SYSTEMATIC REVIEW

*E. Lanckmans, K. Desmalines, P. van Mierlo, W. Duyck, P. Santens & M. De Letter*

Since the emergence of new neuroimaging techniques, involvement of the subcortex in language processing has been demonstrated more accurately. However, the precise language function of the subcortical grey matter structures still remains disputed. The goal of this review is to map the current knowledge on the involvement of subcortical grey matter structures specifically in grammatical processing. We considered experimental studies demonstrating subcortical grey matter involvement in healthy adults, studies in patients with a neurodegenerative disorder involving subcortical grey matter, and in patients with subcortical grey matter lesions. The results of 60 studies indicate that the basal ganglia, thalamus and cerebellum are all involved in at least one modality of grammatical processing. This review suggests caudate nucleus involvement in grammatical modalities requiring more cognitive resources, putaminal involvement in more basic grammatical processing and cerebellar involvement in grammatical tasks requiring manipulation.

**CONTROLLED INTRACELLULAR DELIVERY OF FLUORESCENT LABELS IN LIVE-CELL BY LASER-INDUCED PHOTOPORATION WITH GRAPHENE QUANTUM DOTS**

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## IDO AS AN EARLY MARKER OF IMMUNE TOLERANCE IN MELANOMA

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### **Background**

Indoleamine 2,3-dioxygenase (IDO) has been demonstrated to be a normal endogenous mechanism of acquired peripheral immune tolerance in vivo acting by tryptophan degradation. IDO expression has been reported to be associated with negative prognostic factors and worse outcome in several cancers.

### **Materials and Methods**

Departing from the IDO status of 116 sentinel nodes of melanoma patients we studied IDO expression and the effect on TILs at the level of the corresponding primary tumour (n=85), the IDO expression and shifts in immune profile in corresponding PBMC samples (n=72) and the IDO expression in corresponding metastatic tissue (n=16).

### **Results**

Peritumoral and not intratumoral IDO expression is strongly correlated with the IDO expression at the sentinel node level ( $p < 0.001$ ). Moreover peritumoral IDO expression decreases TILs at the primary ( $p < 0.01$ ) and increases Foxp3 expression ( $p = 0.03$ ). IDO expression in metastatic tissue seems to be consistent with the expression of IDO in the primary and the sentinel. IDO expression in the sentinel was associated with IDO expression in PBMCs of these patients ( $p = 0.016$ ). This was associated with increased kynurenin/tryptophan ratio in the blood, suggesting IDO mediated tryptophan degradation. Increased MFI for IDO in PBMCs was associated with increased PD-L1+ CD8+ T cells ( $p = 0.009$ ), in its turn strongly correlated with CTLA4+ Treg ( $p = 0.005$ ).

### **Conclusion**

Endothelial IDO expression is highly consistent in the primary, the sentinel and metastatic tissues of melanoma patients, indicating that immune suppression in melanoma is determined very early in the disease course. These results provide evidence that IDO expression in melanoma is a marker of the patients' antitumor immune response with an independent prognostic value.

## A NOVEL EX VIVO MODEL TO EVALUATE THE ROLE OF MÜLLER CELLS IN RETINAL DRUG DELIVERY

*Joke Devoldere, Karen Peynshaert, Stefaan C. De Smedt and Katrien Remaut*

### **Purpose**

To develop a bovine ex vivo retinal model that, in contrast to existing models, keeps the vitreoretinal barrier intact. This model would allow us to evaluate the influence of particle physicochemistry on their ability to cross the vitreoretinal interface after intravitreal injection.

### **Methods**

Bovine eyes are obtained from the abattoir. The retina - with vitreous attached - is detached from the RPE and placed on a Transwell-filter, after which supplemented Neurobasal medium is added below the filter. Mitotracker Deep Red (stains Müller cells) and FM 1-43 lipid dye is added to the medium and intravitreally injected prior to incubation overnight. Images are taken at multiple z-levels using a Nikon 60x NIR Apo water dipping objective with a Nikon C1si confocal microscope.

### **Results**

The Mitotracker staining of the explant confirms that the ganglion cell layer is virtually completely occupied by Müller cell endfeet. Moreover, the vitreoretinal interface of bovine eyes greatly resembles human physiology. Following intravitreal injection of polystyrene particles, some colocalize with Müller cells, suggesting these cells could form a transport route across the retina.

### **Conclusions**

We developed a model that maximally mimics human ocular physiology. We suggest that this model can serve as a set-up to aid in the evaluation and design of ocular non-viral gene delivery vectors with the retina as their target.

**EXPLORING THE POTENTIAL OF VNB PHOTOPORATION FOR  
MRNA/PDNA DELIVERY AND CRISPR/CAS9 GENE EDITING**

*Raes L, Xiong R, Verfaillie C, De Smedt S, Raemdonck K, Braeckmans K.*

**EVALUATING THE POTENTIAL OF NANOMATERIALS FOR IP  
ADMINISTRATION OF CHEMOTHERAPEUTICS AND NUCLEIC  
ACIDS**

*Molood Shariati, Stefaan De Smedt, Katrien Remaut*

## CRYOPRESERVATION OF PLATELETS AFFECTS THROMBUS FORMATION DESPITE FASTER ONSET OF COAGULATION

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### **Background and aim**

Cryopreservation of platelets offers a solution for the limited shelf-life and increasing demand for platelet concentrates. The effect of cryopreservation on platelet function was studied by comparison of cryopreserved platelets from three independent production sites and by paired comparison of cryopreserved versus not frozen platelets.

### **Methods**

Platelet concentrates were cryopreserved at  $-80^{\circ}\text{C}$  in 6% (v/v) dimethylsulfoxide. Thawing procedures differed between production sites by resuspension medium (saline or ABO matched plasma) and volume. Platelet function analysis was performed by light transmission aggregometry, flow cytometry and microfluidic flow chambers with anticoagulated reconstituted blood onto collagen or von willebrand factor (VWF). Coagulation in the presence of (cryopreserved) platelets was examined by rotational thromboelastography (ROTEM), thrombin generation assay (TGA) and microfluidic flow chambers with recalcified reconstituted blood onto collagen.

### **Results**

Cryopreservation caused slower thrombus formation rates onto collagen in flow chambers. This could not be explained by the significant decreases in GPIIb expression because ristocetin agglutination was only partially decreased and binding to VWF under flow was unaffected. Defective activation responses are underlying the defect because aggregation to thrombin, ADP and epinephrine was abolished and the fibrinogen receptor could no longer be activated by collagen. Notably, initiation of coagulation was faster in the presence of cryopreserved platelets measured by ROTEM, TGA and under flow. Yet, coagulation in itself was slower and the coagulum less firm.

### **Conclusion**

Cryopreservation affects platelet activation and thrombus growth despite faster coagulation onset. Differences between production sites suggests there is room for standardization between production facilities.

## CONCENTRATIONS OF REPRESENTATIVE UREMIC TOXINS IN A HEALTHY VERSUS NON-DIALYSIS CHRONIC KIDNEY DISEASE PAEDIATRIC POPULATION

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Chronic kidney disease (CKD) in childhood is poorly explained by routine markers and is in adults better depicted by other uraemic toxins. This study describes concentrations of representative uraemic toxins in non-dialysis CKD versus healthy children.

In 50 healthy and 57 children with CKD stage 1-5 (median eGFR 48 [24;71] mL/min/1.73m<sup>2</sup>; none on dialysis), serum concentrations were measured of symmetric and asymmetric dimethyl-arginine (SDMA respectively ADMA),  $\beta$ 2-microglobuline ( $\beta$ 2M), complement factor D (CfD), p-cresylglucuronide (pCG), hippuric acid (HA), indole-acetic acid (IAA), indoxyl sulfate (IxS), p-cresyl sulfate (pCS) and 3-carboxy-4-methyl-5-propyl-furanpropionic acid (CMPF).

SDMA, CfD,  $\beta$ 2M, IxS, pCS, IAA, CMPF, and HA concentrations were higher in the overall CKD group compared to controls, ranging from 1.7 SD for IAA and HA to 11.1 SD for SDMA. SDMA, CfD,  $\beta$ 2M, IxS and CMPF accumulated already in CKD 1-2 with concentrations of respectively 4.8, 2.8, 4.5, 1.9, and 1.6 SD higher. In contrast, pCS, pCG, and IAA concentrations were only higher than controls from CKD 3-4 onwards, while this was just in CKD 5 for ADMA and HA (z-score 2.6 and 20.2 respectively).

This is the first study to establish reference values for a wide range of uraemic toxins in non-dialysis CKD and healthy children. We observed accumulation of multiple uraemic toxins, each with a particular retention profile according to the different CKD stages.

## SYSTEMATIC REVIEW AND META-ANALYSIS OF THE AUDITORY P3 COMPONENT IN PARKINSON'S DISEASE

*Kim De Keyser, Jara Stalpaert, Patrick Santens, Durk Talsma, Dick Botteldooren, Annelies Bockstael, Miet De Letter*

Event-related potentials (ERPs) are widely addressed in the neurophysiological examination of patients with Parkinson's disease (PD). Generally, latency and amplitude values of the P3 component are determined based on an auditory oddball paradigm. The aim of this systematic review was to summarize the results of independent studies which have investigated the effect of PD on the auditory P3b and/or P3a component. A systematic database search was performed within 4 databases until January 2017. Out of 5018 records, 36 studies were identified that addressed the objective and met the eligibility criteria. Meta-analysis was performed to combine the data of the included studies. The results of the P3b component indicate that a significantly prolonged latency and decreased amplitude could be demonstrated in non-demented patients with PD in the on-state of their medication cycle, compared with healthy controls. In contrast, no differences in P3b latency and an increased P3b amplitude were found when patients were tested without dopaminergic medication. When separate analyses were performed regarding the nature of the ERP task, heterogeneity of the P3b meta-analysis decreased remarkably. The results of the P3a component were described qualitatively since not all data were available to perform a reliable meta-analysis. In conclusion, a prolonged P3b latency and decreased P3b amplitude can be found in non-demented patients with PD when the medication state of the patient is considered.

# COMBINED HIGH DOSE RADIATION AND TYROSINE KINASE INHIBITORS IN METASTATIC RENAL CELL CARCINOMA: A PHASE I DOSE ESCALATION TRIAL

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## **Introduction & objectives**

Tyrosine kinase inhibitors (TKIs) targeting vascular endothelial growth factor are currently standard of care for patients with metastatic renal cell carcinoma (RCC) in first and second line. Nevertheless, durable responses are rare and most patients eventually develop progressive disease. New therapeutic approaches are needed to improve durable disease control. We studied a combination of high-dose radiotherapy and TKIs because of the immunomodulatory properties of both therapies. The primary endpoint was to determine the maximum tolerated radiotherapy doses. Secondary endpoints were local control and tumour response in non-irradiated lesions as per RECIST 1.1 or as per MD Anderson (MDA) criteria for bone lesions next to progression-free survival (PFS).

## **Materials & methods**

Treatment-naïve patients with clear cell metastatic RCC, who had undergone cytoreductive treatment of their RCC at least 6 weeks prior to inclusion, were treated with a first line TKI, pazopanib, during a 1-week run-in period. Stereotactic body radiotherapy (SBRT) was delivered to the largest metastatic lesion concurrently with pazopanib administration at day 8. SBRT doses were escalated in 3 dose levels (24 Gy, 30 Gy and 36 Gy all in 3 fractions) using a time-to-event continuous reassessment method design. Pazopanib was continued post-radiotherapy as maintenance therapy until disease progression.

## **Results**

Thirteen patients were enrolled, with a median follow-up of 19 months. Their median age was 66 years, with 54% male and 46% female patients. No dose-limiting toxicities were noted at dose levels 1 or 2. Of 7 patients at dose level 3, 1 patient experienced a dose-limiting toxicity consisting of grade 4 hypoglycemia. Grade 3 to 4 pazopanib-related adverse events (AEs) occurred in 38% of patients. Local control was achieved in all irradiated lesions, we noted a complete local response in 1 irradiated lesion (8%), partial response in 6 irradiated lesions (46%), and stable disease in 6 irradiated lesions (46%) as best response. Mean duration of local control was 23 months (95% confidence interval 16 - 31). Assessment of responses outside the radiation field revealed that 5 of 13 patients (38 %) developed a partial response, 7 patients (54 %) had stable disease and 1 patient (8%) had progressive disease as best response. Median PFS was 6.7 months (95% confidence interval 3 - 10).

## **Conclusion**

SBRT in combination with pazopanib treatment is well-tolerated with long-term local control and favourable response rates outside the radiation field. Larger trials are needed to study the impact of the combination on overall survival and PFS.



## WNT INHIBITION DURING HESC CULTURE PROVIDES AN ALTERNATIVE PLURIPOTENT STATE STARTING POINT FOR DIRECTED DIFFERENTIATION.

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Human embryonic stem cells (hESCs) hold great promise for therapeutic applications. However, standard culture conditions maintain hESC in a primed state of pluripotency, which harbors disadvantageous heterogeneity and spontaneous differentiation propensity. An alternative state has been described recently in mouse epiblast stem cells using the Wnt inhibitor JP-Inh, which seems to restrict the primed pluripotent state to one with less heterogeneity and less spontaneous differentiation. We set out to investigate whether JP-Inh supplemented conditions can improve hESC characteristics and their functional potential.

Two in-house derived hESC lines were cultured in standard primed conditions. In addition, hESC were exposed to two extra culture conditions: JP-Inh supplemented medium and our in-house naïve medium. Comparative transcriptomic analysis was performed on primed, JP-INH and naïve conditions using NGS. Cells from all conditions were also differentiated towards the neuronal lineage.

Specific neuronal gene expression profiles were analyzed using qPCR and protein marker presence was assessed through immunocytochemistry. Primed hESC show significantly higher expression of differentiation associated genes compared to JP-INH hESC. Markers from all three germ lineages were found to be elevated in primed hESC. Both primed and JP-INH-treated hESCs proved capable to differentiate into neuronal cells, whereas naïve hESC showed problematic radial neuronal growth.

## NOVEL NON-CODING HOMOZYGOUS MUTATION "GHENT +49A>G" IN THE IRON-RESPONSIVE ELEMENT OF L-FERRITIN CAUSES HEREDITARY HYPERFERRITINAEMIA-CATARACT SYNDROME

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Cataracts in combination with elevated serum ferritin levels are characteristic of hereditary hyperferritinaemia-cataract syndrome (HHCS), a disorder caused by heterozygous mutations in the iron responsive element (IRE) of the L-ferritin gene (FTL). Here, we report a case of homozygosity in a consanguineous family affected with HHCS. The proband was diagnosed with severe bilateral cataracts and elevated serum ferritin. Investigation of the proband's parents, sister and brother revealed varying degrees of bilateral cataracts combined with elevated levels of circulating ferritin. Mutational analysis of the FTL gene in the proband revealed the homozygous "Ghent +49A>G" mutation, located in the FTL-IRE. In the parents and two siblings, the mutation is present in heterozygous state. The severity of the phenotype shows a correlation with the copy number of the mutation, a phenomenon not always seen in the HHCS families with homozygous FTL mutations. The impact of the mutation on the IRE structure was assessed using the Sfold program, indicating that the mutation is likely to induce broad rearrangements of base pairing in the IRE, resulting in the loss of specific secondary structures involved in the direct contact with iron regulatory proteins (IRPs), responsible for the post-transcriptional regulation of L-ferritin expression. Electrophoretic mobility shift assays (EMSA) are planned to evaluate the impact of the mutation on the binding affinity between the IRE and IRPs.

## IL-1 $\beta$ ACTAKINES: NEW ADJUVANTS IN VACCINATION

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The pro-inflammatory cytokine interleukin-1 $\beta$  activates T cell subsets and dendritic cells, contributing to the induction of a protective cellular immune response towards cancer cells and different pathogens. This suggests great therapeutic potential as adjuvant, but translation of these findings to the clinic has been hampered by the toxicity associated with administration of IL-1 $\beta$ . Recently, at the Cytokine Receptor Laboratory, we developed the AcTakine concept ("Activation by Targeting Cytokines"), where a mutated cytokine with low residual activity is coupled to a VHH single domain antibody, making it possible to restore the cytokine activity on cells expressing the VHH target. In this way, the undesirable toxic side effects of cytokines with interesting therapeutic properties can be circumvented, whilst keeping their beneficial effects intact on selected target cells only. The aim of this project is to develop IL-1 $\beta$  AcTakines as adjuvants in cancer vaccination, by targeting mutated IL-1 $\beta$  to cytotoxic T lymphocytes and cross-presenting DCs using VHHs recognizing CD8 $\alpha$  and CLEC9A. We showed that daily subcutaneous or intraperitoneal administration of 40  $\mu$ g of the IL-1 $\beta$  AcTakine (for five consecutive days) did not elicit toxicity. Preliminary data suggests that the CD8 $\alpha$ -targeted IL-1 $\beta$  AcTakine induces anti-tumour action in C57BL/6J mice carrying a B16 melanoma. Next, we aim to test the IL-1 $\beta$  AcTakines as adjuvants in a tumor vaccination study using the B16-OVA melanoma model.

## ULTRA STRUCTURE OF THE INTERCALATED DISC IN MURINE CARDIOMYOCARD REVEALED BY VOLUME ELECTRON MICROSCOPY

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Cardiac muscle cells are extensively interconnected at their ends through their intercalated discs (IDs). This is a complex region composed of different kinds of intercellular junctions (desmosomes, gap junctions (GJs) and hybrid junctions) essential for maintaining correct contraction of the heart. The aim of our research is visualize the ultrastructure of the ID and the different junctions in a three-dimensional (3D) model. Ventricular cardiomyocytes are used of both healthy mice and mice suffering with cardiomyopathy ( $\alpha$ T-catenin knockout mouse model).

Recently, the first 3D models of the in vivo organization of the ID were unveiled. Two similar, complementary techniques, e.g. Serial Blockface Scanning Electron Microscopy (SBF-SEM) and Focused Ion Beam SEM (FIB-SEM), are used to create high resolution serial images of en bloc tissue samples. With SBF-SEM, several complete IDs can be reconstructed, but the junctions are not clearly visible. Using heavy weight tannic acid for contrasting membrane complexes and subsequent analyses with the FIB-SEM, it was possible to distinguish between GJs, desmosomes and hybrid junctions. Preliminary results shows remodeling of the junctions in the diseased mice compared to control mice.

The high resolution of this novel bio-imaging tool allow us to reconstruct connectivity between cells and visualize membrane organizations invisible by previously used methods.

## MESSENGER RNA-BASED NANOPARTICLES FOR THERAPEUTIC CANCER VACCINATION

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mRNA as an active pharmaceutical ingredient in cancer immunotherapy has been validated using an ex vivo approach, where isolated dendritic cells (DCs) are activated and loaded with tumor-encoding mRNA, after which the cells are re-injected into the patient as a cellular vaccine. Nowadays, there is a growing interest in finding ways to deliver mRNA directly to DCs in vivo. We have validated lipid nanoparticles for the systemic delivery of mRNA vaccines. We here performed a comparison study between the lipid delivery of three different cargos; (1) unmodified mRNA, in which the mRNA has a "self-adjuvant" effect, resulting in a type I IFN-driven T cell stimulation, (2) nucleoside-modified mRNA which incorporate 5'-methylcytidine and pseudouridine in the transcript, these modifications provide the mRNA construct a better stability and reduces the mRNA's immune recognition, resulting in higher translational capacity but lower immunogenicity and (3) nucleoside-modified mRNA which is simultaneously delivered with the clinically-approved adjuvant monophosphoryl lipid A (MPLA) by embedding it in the lipid bilayer. We hypothesized that by combining modified mRNA with a well-known immune adjuvant within one single particle, high antigen expression in vivo can be obtained while the type I IFN response can be substituted by a more controllable and safer adjuvant effect. This strategy will likely open new combinatorial options for mRNA nanoparticle-mediated cancer immunotherapy.

## ELECTROSPRAY IONIZATION MASS SPECTROMETRY FOR THE HYDROLYSIS COMPLEXES OF CISPLATIN: IMPLICATIONS FOR THE HYDROLYSIS PROCESS OF PLATINUM COMPLEXES

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Non-enzyme dependent hydrolysis of the drug cisplatin is important for its mode of action and toxicity. However, up until today, the hydrolysis process of cisplatin is still not completely understood. In the present study, the hydrolysis of cisplatin in an aqueous solution was systematically investigated using electrospray ionization mass spectrometry coupled to liquid chromatography. A variety of previously unreported hydrolysis complexes corresponding to mono-, di-, and tri-meric species were detected and identified. The characteristics of the Pt-containing complexes were investigated using collision induced dissociation (CID). The hydrolysis complexes demonstrate distinctive and correlative CID characteristics, which provides tools for an informative identification. The most frequently observed dissociation mechanism was sequential loss of  $\text{NH}_3$ ,  $\text{H}_2\text{O}$ , and  $\text{HCl}$ . The formation mechanisms of the observed complexes were explored and experimentally examined. The strongly bound dimeric species, which existed in solution, are assumed to be formed from the clustering of the parent compound and its mono- or di-hydrated complexes. The role of the electrospray process in the formation of some of the observed ions was also evaluated and the ESI related cold clusters were identified. The previously reported hydrolysis equilibria were tested and subsequently refined via an hydrolysis study resulting in a renewed mechanistic equilibrium system of cisplatin as proposed from our results.

## LOSS OF TOLL-LIKE RECEPTOR 5 POLARISATION OF INTESTINAL EPITHELIUM IN RESPONSE TO TGF $\beta$

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Crohn's disease is caused by a sustained immune response to the gut microbiota. In healthy intestinal epithelial cells (IEC), the expression of Toll-like receptor 5 (TLR5) is confined to the basolateral membrane. We hypothesized that transforming growth factor  $\beta$  (TGF $\beta$ ), which induces epithelial-to-mesenchymal transition (EMT) in CD, may result in the depolarization of TLR5 in IEC. We compared E-cadherin in inflamed vs. healthy ileum and in stenotic vs. non-stenotic biopsies from the same patients. T84 differentiated monolayers were grown in a dual-compartment culture system and treated with luminal (L) or basolateral (BL) flagellin in order to verify the polarization. Next, differentiated monolayers were treated with TGF $\beta$  for 96h to mimic EMT. Lastly, they were stimulated L or BL with 10ng/ml flagellin.

Inflamed and stenotic biopsies exhibited less E-cadherin compared to healthy and non-stenotic biopsies. IL8 secretion after L treatment of a monolayer of T84 IEC with flagellin was not induced, whereas BL treatment resulted in a significant dose responsive IL8 secretion. L stimulation with flagellin after TGF $\beta$  treatment resulted in an increased BL IL8 production following L stimulation with flagellin as compared to placebo-treated cells. The TEER measured across the monolayers of IECs remained stable throughout the experiments, suggesting that there was no loss of barrier function.

E-cadherin, a marker for EMT is less expressed in inflamed and stenotic biopsies in vivo.

# THE EFFECTS OF DIFFERENT IRRADIATION DOSES ON MICROVESSELS IN A DORSAL SKINFOLD WINDOW CHAMBER MODEL IN MICE: AN INTRAVITAL MICROSCOPY STUDY.

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## **Background and aim**

Recently, the development of nanomedicine has introduced new methods to fight cancer. Nanoparticles can deliver drugs within the tumour, showing some benefits compared to conventional chemotherapy. The use of these nanoparticles for specific tumour targeting is based on the enhanced permeability and retention effect. Our aim was to investigate the effects of radiotherapy on microvascular permeability, in order to gain more insight in the influence of concomitant radiotherapy on nanoparticle delivery.

## **Methods**

Twenty-one mice were randomly distributed in four groups. One control group and three groups receiving a single dose of radiotherapy. Group A, B and C received 2, 8 and 15 Gy respectively. A dorsal skinfold window chamber was implanted to allow visualization of the microvessels in the irradiated zone. Intravital fluorescence microscopy was performed to study microvascular permeability.

## **Results**

Analysis of microvascular diameter, red blood cell velocity and volumetric blood flow showed no significant changes or differences between the four groups over the course of the experiment. All three irradiated groups showed an increased permeability with the lowest radiation dose resulting in the biggest increase.

## **Conclusions**

Radiotherapy seems to increase microvascular permeability, which is probably the result of endothelial disruption. However, the inverted dose response association is in contradiction with other literature and requires more investigation



## THE SEARCH FOR PREDICTORS OF RESPONSE FOR VAGUS NERVE STIMULATION

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### **Introduction**

Vagus nerve stimulation (VNS) is an effective alternative treatment option for refractory epilepsy patients. Because the mechanism of action (MOA) is not fully understood, today, VNS-therapy is initiated empirically. Elucidating these mechanisms is fundamental in developing biomarkers for VNS. This combined review and pilot study discusses potential MOA's for VNS with potential predictors of response arising from them. The pilot study investigated ictal heart rate (HR)-changes. HR and heart rate variability (HRV) are good markers of the autonomic status. Epilepsy patients have both ictal and interictal autonomic dysfunction. It is hypothesized that epileptic discharges occurring in autonomic nervous system (ANS)-regulating brain centres lead to cardiovascular changes. VNS may have effects on these ANS centres through anatomical afferent pathways of the vagus nerve. This study aimed to investigate potential associations between ictal autonomic manifestations and seizure control with VNS in a pediatric population.

### **Methods**

Pre-ictal and ictal HR-changes of 28 seizures from 8 patients obtained prior to VNS treatment were retrospectively assessed and together with clinical characteristics compared to VNS-responsiveness at 1 year.

### **Results**

Bradycardia was significantly associated with VNS-responsiveness at 1 year ( $p=0.05$ ).

### **Discussion**

These results support the hypothesis that pre-implantation HR changes occurring around seizure onset are able to predict VNS-response.

# ORAL GLUCOSE TOLERANCE TESTING BEFORE AND ONE YEAR AFTER INITIATION OF GENDER-AFFIRMING HORMONES IN TRANSGENDER PERSONS

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*\*Both first authors contributed equally*

## **Introduction**

Several studies showed the effect of sex hormones on the development of insulin resistance (IR). Knowing IR can lead to diabetes mellitus type 2, the aim of this study is to see if there is a relationship between IR and gender-affirming hormone therapy in transgender persons.

## **Methods**

90 transgender persons, 35 trans men and 55 trans women, were included in this study at the Ghent University Hospital in Belgium from the 15th of February 2010 until the 2nd of September 2014. In order to evaluate glucose metabolism in the study population, an oral glucose tolerance test (OGTT) was performed in all participants, at baseline (M0) and one year after the introduction of hormonal therapy (M12). Based on results of serum glucose levels, the area under the curve (AUC) was determined.

## **Results**

There was no significant difference in the AUC of serum glucose levels or serum insulin levels during OGTT in trans men. The AUC of serum glucose levels decreased significantly from 16286 mg\*min/dl  $\pm$  2861 mg\*min/dl at baseline to 14070 mg\*min/dl [12855 mg\*min/dl -16830 mg\*min/dl] after one year in trans women (P = 0.024). There was no significant difference in the AUC of serum insulin levels during OGTT in trans women.

## **Conclusion**

We can conclude that in trans women, one year of gender-affirming hormone treatment had a beneficial influence in IR. In trans men, there was no significant difference in IR one year after gender-affirming hormone treatment.

## REAL-TIME NAVIGATION: THE BEGINNING OF A NEW ERA IN GUIDED IMPLANT SURGERY

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## MOBILE FEMTOSECOND LASER-ASSISTED CATARACT SURGERY: EFFECTIVENESS & SAFETY?

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This study examined the intraoperative events and outcomes of laser assisted cataract surgery (LACS) cases using the mobile Femto LDV Z8 (Ziemer Ophthalmic Group) from May '15 through September '15.

Strict patient screening was used, with LACS offered only to patients who demonstrated good dilation and clear corneal media and who had no other contraindications for LACS (eg, severe glaucoma, orbital malformations). Severe myopia or hyperopia, Fuchs dystrophy, or cornea guttata were not contraindications.

A total of 99 eyes were included in the study (LACS group, n=51; control group, n=48). Patient demographics and baseline characteristics were similar between groups. There was only one area of statistically significant difference, with a greater number of younger patients in the LACS group.

EPT is significantly lower in the LACS group than the control group. Patients in the LACS group typically have clear corneas and close to 20/20 acuity at day 1 postoperative, whereas those in the control group have more corneal edema. The total duration of surgery is  $21.69 \pm 6.03$  min in the LACS group and  $20.31 \pm 5.69$  min in the control group. There is no significant difference in total duration of surgery. Surgeons perform better with experience after 15 LACS cases, in comparison with the first 15 cases. Statistically significant improvement is seen in capsulotomy time, in overall treatment time, and in avoiding suction loss, between the first 15 LACS cases and the next 15.

## THE INFLUENCE OF THE STORAGE METHOD ON CELL DENSITY AND CLINICAL OUTCOME AFTER LAMELLAR AND PENETRATING KERATOPLASTY

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Het doel van deze scriptie is het nagaan of er al dan niet een statistisch significant verschil bestaat in de evolutie van de klinische outcome (visus en al dan niet rejectie) en van de endotheelceldensiteiten van greffes op basis van het verschil in bewaringsmethode (de koude tegenover de warme bewaringsmethode) bij lamellaire (DSAEK) en penetrerende (PKP) corneatransplantaties.

De methode van deze scriptie beslaat een retrospectieve cohortstudie. De operaties zijn uitgevoerd in 2 centra door dezelfde chirurg. Er is gebruik gemaakt van een database met data van de donor en de acceptor/patiënt. Voor DSAEK zijn 230 ogen opgevolgd en voor PKP zijn 92 ogen opgevolgd.

Voor de resultaten zijn enerzijds de evolutie van de endotheelceldensiteit (ECD) en anderzijds de klinische outcome beschouwd. Voor de ECD is een statistisch significant verschil gevonden bij DSAEK in het voordeel van de koude methode. Voor de visus is er een statistisch significant verschil gevonden bij DSAEK in het voordeel van de koude methode. Voor al dan niet rejectie is een statistisch significant verschil gevonden bij DSAEK in het voordeel van de koude methode. Bij PKP is telkens geen verschil waargenomen.

De conclusie van deze studie omvat dat er een statistisch significant verschil is gevonden in het voordeel van de koude bewaarmethode bij DSAEK. Bij PKP kon echter geen verschil worden vastgesteld, waarbij een kleinere steekproefgrootte een mogelijke rol in zou kunnen spelen.

## THE ROLE OF THE RIGHT HEMISPHERE IN THE RECOVERY OF STROKE-RELATED APHASIA: A SYSTEMATIC REVIEW

*Elissa-Marie Cocquyt, Lisa De Ley, Patrick Santens, John Van Borsel, Miet De Letter*

Stroke in the language dominant hemisphere is the most frequent cause of aphasia. In the course of post-stroke aphasia different mechanisms can contribute to the recovery of language: recovery from ischaemia, compensatory rerouting of language modalities and neuroplasticity occur at different time scales after the initial injury. These mechanisms may occur spontaneously or may be induced or influenced by various therapeutic interventions. This report contains a systematic review of the literature concerning the debated role of the right hemisphere in the recovery from stroke-related aphasia. The existing literature was approached using the PICOS-principle and well-established inclusion and exclusion criteria. Although many gaps remain in the knowledge on the role of the right hemisphere, there is some evidence of a facilitation of spontaneous language recovery in the acute and subacute phase. In the subacute and chronic phase, the right hemisphere homologous language areas, along with memory and attention-related areas, facilitate treatment related improvement. In contrast, in therapy-free periods in the chronic stage, the right hemisphere no longer contributes to language recovery or may even be inhibitory. Injury-, language and therapy-related variables impact on the role of the right hemisphere in aphasia recovery.

## "DIVING RESPONSE" AN ARGUMENT FOR THE AQUATIC APE THEORY IN HUMAN EVOLUTION?

*De Bock S., de Jager S., Bouten J., Dumortier J., Bourgois G., Derom E., Boone J., Herregods L., Bourgois J. G.*

## BIOPRINTING OF SINGLE CELLS AND MICRO-TISSUES

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Three-dimensional bioprinting is a cell-friendly rapid prototyping method that allows a lot of freedom in terms of spatial organization, heterogeneous populations of cell types and bioinks. It offers great potential in the field of tissue engineering (TE), especially for the bottom-up (modular) tissue engineering strategy. Modular TE uses building blocks, micro-tissues, to build up complex macro-tissues. Micro-tissues can be cell sheets, cell-laden hydrogels or spheroids. In this research, single cells and spheroids are encapsulated in modified gelatin (GelMod) and bioprinted with a time-pressure nozzle based system. Spheroids are formed by seeding HepG2 cells or GFP-transformed SKOV cells onto agarose microchips where they will self-assemble into micro-aggregates. Two photo-initiators will be compared: the well-known Irgacure 2959 and the less known but considered to be more cell-friendly VA-086. The bioprinted scaffolds are used for mechanical analysis, sol/gel assessments, viability assays and scaffold integrity assays.



## APNEA TRAINED ATHLETES: RATHER MARINE MAMMALS THAN HUMANS?

*de Jager S, De Bock S, Dumortier J, Bouten J, Bourgois G, Boone J, Herregods L, Bourgois JG*

## THE USE OF SITUATIONAL PROBABILITY IN BADMINTON

*Thijs Demeyere, Frederik Deconinck*

### **Introduction**

Badminton is a very fast racquet sport and therefore very well suited to study anticipation. Anticipation consists of two information sources. Firstly, there is the well-known visual information like body kinematics of the opponent and his racquet during a hitting action. Secondly, the less studied area of situational probability also seems to play a major role in the (early) anticipation process.

### **Methods**

During a quasi-realistic badminton rally, subject's vision was occluded at various instances before hitting action and/or movement of the opponent. Despite the occlusion, the subject was instructed to make a prediction about the oncoming stroke by moving to one of the six zones and executing a racket movement.

### **Preliminary Results**

Expert players appear to score better than chance (50% correct) independent of the time of occlusion. Also, expert players generally show higher total scores compared to lower level players. There are no better scores if the occlusion is closer to the racket shuttle contact of the opponent. Intermediate and expert level subjects show a better score in the prediction of the side compared to the length of the stroke.

### **Conclusion**

Experts show scores that cannot just be due to chance, so this suggests the use of SPI in the early anticipation process. If the RT is limited, which especially appears to happen in expert play, the subject tends to make a better prediction.

## FACTORS ASSOCIATED WITH THE DEVELOPMENT OF SKIN EROSION DUE TO INCONTINENCE (IAD)

*Lisan Deolet, Nele Van Damme, Prof. Dr. Dimitri Beeckman*

IAD is een veel voorkomend ernstig probleem bij patiënten met incontinentie. De aandoening is moeilijk en tijdrovend om te behandelen. Daarbovenop reduceert IAD de kwaliteit van leven. Verder werd reeds aangetoond dat IAD een risicofactor is voor het ontwikkelen van decubitus en secundaire infecties. Deze aandoening heeft ook een economische impact maar kan mits tijdige preventie vermeden worden. Om deze preventieve maatregelen gericht te kunnen toepassen en kosteneffectief te werken, is het nodig de risicofactoren voor deze aandoening te kennen. Deze studie tracht deze risicofactoren te identificeren, zodat er kwalitatieve en kosteneffectieve zorg verleent kan worden.

Om de risicofactoren van IAD te identificeren, werd een matched-case-control studie uitgevoerd in vijf intensieve zorgen afdelingen van Vlaamse ziekenhuizen. Alle patiënten opgenomen op een intensieve zorgen afdeling, meerderjarig en fecaal incontinent die tevens een geïnformeerd toestemming ondertekenden, werden meegenomen in de studie. De Vergelijkende variabele was fecale incontinentie en patiënten met IAD categorie 2 werden vergeleken ten opzichte van patiënten met IAD categorie 0. Er werd data gecollecteerd over 19 vermoedelijke risicofactoren van IAD door getrainde observatoren.

Data-collectie werd nog niet afgerond. De voorlopige sample bestaat uit 28 participanten, waarvan slechts 25% met IAD categorie 2. Daarnaast is de gemiddelde leeftijd 61 jaar (SD 16,93) en is 60% van de participanten mannelijk.

## GALECTIN-3: MORE THAN JUST AN INNOCENT BYSTANDER?

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### **Background**

Galectin-3 is a member of a closely related lectin family, which is detected in several vertebrate epithelial and myeloid cell types. This beta-galactoside-binding soluble protein plays an important role in multiple biological processes. Depending on its location, type of injury or site of damage, the effects by galectin-3 can be various and sometimes contrasting.

### **Summary**

In this review, we discuss the general characteristics and functions of galectin-3. More specifically, we focus on the role of galectin-3 in the onset and development of diabetic and non-diabetic nephropathies. Finally, the therapeutic potential of anti-galectin-3 inhibitors is discussed.

### **Key Messages**

Due to its multifunctional character, galectin-3 plays a pivotal role in interstitial fibrosis and progression of chronic kidney disease. Inhibition of galectin-3 may be a promising therapeutic strategy to prevent end-stage renal disease.

## THE INFLUENCE OF DIFFERENT RECOVERY INTENSITIES AND DURATIONS ON THE ANAEROBIC WORK CAPACITY

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### **Introduction**

The power-duration relationship is defined as a hyperbolic function which asymptote is termed the Critical Power (CP). The anaerobic work capacity ( $W'$ ) is the finite amount of work that can be performed above CP. Although the importance of  $W'$  in sport is known, its physiological basis remains controversial. Therefore, we wanted to assess the underpinning influences of  $W'$  (time to exhaustion and blood lactate) and the influence of the intensity of the work bout, intensity and duration of the recovery.

### **Methods**

10 non experienced cyclist completed all 17 trials: 1) incremental test to exhaustion 2) four constant-load tests at different work rates (WR) for estimation of CP and  $W'$  and 3) 12 experimental trials with 2 work bouts and a recovery in between with different durations and intensities.

### **Results and conclusions**

The time to exhaustion and blood lactate are significantly ( $P < 0,05$ ) influenced by the intensity of the work bout, intensity and duration of the recovery. A longer and less intensive recovery leads to a better recovery of  $W'$ .

## ANAL PROBLEMS DURING PREGNANCY AND POSTPARTUM: A PROSPECTIVE COHORT STUDY

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### **Introduction**

Many pregnant women have anal symptoms during pregnancy and postpartum. The most common proctological problems reported are haemorrhoids, anal fissures and anal incontinence.

### **Aims**

The aim of this study is to determine the prevalence of anal problems and constipation during the different study periods and to identify the risk factors.

### **Methods**

This is a prospective cohort study. Women between their 19th and 25th week of pregnancy are included. Ninety-four women were followed with a symptom questionnaire in the second and third trimester, in the immediate postpartum (within 3 days) and three months postpartum. A specific proctological diagnosis was presumed on the basis of combined symptoms (rectal bleeding, anal pain and swelling). Constipation was defined by the Rome III criteria.

### **Results**

68% of the women developed anal symptoms during the whole study period. Anal symptoms occurred in 50% of the women during pregnancy, in 56,2% in the immediate postpartum and in 62,9% during the three months postpartum. The most prevalent symptom was anal pain. Constipation was reported by 60,7% of the patients. Most prevalent diagnoses were: hemorrhoidal thrombosis, haemorrhoidal prolapse and anal fissure. Constipation and a history of anal problems are significant risk factors.

### **Conclusions**

2/3 of pregnant women deal with anal symptoms during pregnancy or postpartum. This emphasises the clinical importance. Prevention of constipation in pregnant women is recommended.

## ANAL PROBLEMS DURING PREGNANCY AND POSTPARTUM: A PROSPECTIVE COHORT STUDY

*Yaliva Dorreman, YD, Kymentie Ferdinande, KF, Kristien Roelens, KR, Steven Weyers, SW, Wim Ceelen, WC, Hans Van Vlierberghe, HVV, Danny De Looze, DDL*

### **Introduction**

Many pregnant women have anal symptoms during pregnancy and postpartum. The most common proctological problems reported are haemorrhoids, anal fissures and anal incontinence.

### **Aims**

The aim of this study is to determine the prevalence of anal problems and constipation during different study periods. We also want to identify the risk factors for the development of anal symptoms.

### **Methods**

This is a prospective cohort study. Women between their 19th and 25th week of pregnancy are included. Ninety-four women were followed with a symptom questionnaire in the second and third trimester, in the immediate postpartum (within 3 days) and three months postpartum. A specific proctological diagnosis was presumed on the basis of combined symptoms. Constipation was defined by the Rome III criteria.

### **Results**

68% of the women developed anal symptoms during the whole study period. Anal symptoms occurred in 50% of the women during pregnancy, in 56,2% in the immediate postpartum and in 62,9% during the three months postpartum. The most prevalent symptom was anal pain. Constipation was reported by 60,7% of the patients. Most prevalent diagnoses were: hemorrhoidal thrombosis, hemorrhoidal prolapse and anal fissure. Constipation and a history of anal problems are significant risk factors.

### **Conclusion**

2/3 of pregnant women deal with anal symptoms during pregnancy or postpartum. This emphasises the clinical importance. Prevention of constipation in pregnant women is recommended.

## IMPACT OF PROXIMAL HUMERAL FRACTURES ON THE 3D- GLENOHUMERAL RELATIONSHIP

*Alexander Gallant, Thomas Van Isterdael, Lieven De Wilde, Alexander Van Tongel*



## PREDICTING THE SRPE: IN SEARCH OF NEW POSSIBILITIES

*Geurkink, Y., Lievens, M., Vandewiele, G., Boone, J.*

### **Purpose**

Controlling and monitoring the internal training load (ITL) is important in order to provide the appropriate training stimulus. The ITL is influenced by the external training load (ETL) and the players' individual characteristics (IC). The session Rate of Perceived Exertion (sRPE), a simple tool representing the player's perception of physiological and psychological training load, can be used as a measure of ITL. This research aimed to predict the sRPE and identify the main influencing factors.

### **Methods**

sRPE-scores from 28 professional soccer players were coupled to the ETL, heart rate and individual characteristics. The ETL included factors such as distance in different speed zones. IC contained factors as deviations from mean group sRPE and performance determinants. Heart rate data was included as a different measure of ITL.

### **Results**

39.1% of the cases were correctly classified. When classifying deviations within 1 point from the observed score as correct, 87.7% of the cases were correctly classified. Mean absolute deviation was found to be 0.79 and mean squared distance to be 0.99.

### **Conclusion**

The sRPE can be predicted quite accurately, using only a relatively small dataset. Variables can be dropped from the predictive model, which implies that applications of the model may also be used by non-professional teams.

### **Practical implications**

Applications of this predictive model may be used for planning, monitoring and evaluating training sessions.

## INCONTINENCE-ASSOCIATED DERMATITIS: POINT- PREVALENCE AND RISK FACTORS

*Kanervo H., Ahtiala M., Van den Bussche K., Lundgrén-Laine H. & Beeckman D.*

### **Background**

Incontinence-associated dermatitis (IAD) is a type of moisture wound that is specifically caused by incontinence. Prevalence numbers range from 5.6% to 50%, partly due to incorrect assessments. Also, risk factors of IAD are still underresearched. If risk factors - and subsequently patients at risk - are identified, adequate preventive measures can be applied.

### **Objectives**

To (1) measure the point-prevalence of IAD and to (2) identify its risk factors.

### **Methods**

A cross-sectional study was conducted in 25 wards in Turku University Hospital (TYKS) in Finland. A convenience sample of adult (18+) patients with urinary and/or faecal incontinence was included. Patients with a urinary catheter and/or faecal management system were excluded. Twelve tissue viability nurses received training about the study, wound photography and IAD observation. A patient data form was used to collect patient information, lab results and to assess the skin.

### **Results**

Eleven participants were included. A prevalence rate of 27% was found for patients with IAD. The small sample size made it impossible to find any significant associations between IAD and possible risk factors. In this hospital, urinary catheters and faecal management systems are applied when a patient is incontinent.

### **Conclusion**

The point-prevalence of IAD in TYKS was 27%. However, only 11 patients were included in the study and the sample size was too small to find any significant results regarding risk factors. More research is needed to identify IAD risk factors and to investigate the effectiveness of applying urinary catheters and faecal management systems to prevent IAD.

**THE VALUE OF THE PSYCHOLOGICAL QUESTIONNAIRE  
PCDEQ2V2 IN A MULTIDIMENSIONAL GYMNASTICS TEST  
BATTERY**

*Felien Laureys, PhD Andy Hill, Prof. Dr. Dave Collins, Prof. Dr. Matthieu Lenoir*

## LONG-TERM OUTCOME OF IMPLANTS INSERTED USING FLAPLESS OR CONVENTIONAL SURGERY

*Emitis Naeini; Dr. Melissa Dierens; Dr. Wolfgang Jacquet; Dr. Mandana Atashkadeh; Prof. Dr. Hugo De Bruyn*

### **Aim**

Evaluate clinical outcome of solitary implants inserted using flap or flapless surgery after 10-12 years of function.

### **Material & Methods**

49 patients with 53 single implants, inserted with one-stage flap / flapless surgery and delayed loading, were recalled after 10-12 years of function. Implant survival, radiographic bone-level changes (from bone-implant contact - implant-abutment junction), peri-implant health using plaque and bleeding indices and oral health related quality of life using OHIP-14 were registered. Changes between flap and flapless were statistically tested using Mann-Whitney U-Test and within groups using Wilcoxon Signed Ranks Test (SPSS version 24.0).

### **Results**

36/49 patients participated (15F and 21M, average age 64.5years). Implant survival was 100% after 10.9 years (range 9.9-12.5). Bone-loss in flap was 0.56mm (SD 0.89; range -0.9-2.02); in flapless - 0.85mm (SD 0.98; range -2.84-0.53), indicative of bone gain towards implant-abutment interface ( $p=0.003$ ). There was, no difference between flap and flapless with respect to bone-level ( $p=0.126$ ) due to a difference at baseline. Furthermore, for flap and flapless respectively, results were comparable regarding patients' quality of life; (3.44 and 2.95), probing pocket depth; (3.32 and 3.19), and bleeding index (0.15 and 0.22).

## ANALYSIS OF REPAIR SEQUENCES IN PEOPLE WITH PRIMARY PROGRESSIVE APHASIA

*Reynaert L., De Letter M., Muntigl P.*

The objective of the preliminary study is to describe repair strategies in the initial phase of primary progressive aphasia.

Video fragments of eleven patients with PPA have been transcribed and analysed according to the principals of conversation analysis. Subsequently different repair trajectories (self-/other-initiated self-/other-repair) have been described in detail by using fragments of the transcriptions to state possible differences between the PPA-types.

Self-initiated self-repairs with synonyms were only observed in the nonfluent variant. Only logopenic patients used self-initiated other-repairs as repair strategy for word-finding difficulties. In comparable situations in the nonfluent and semantic variant there was no repair initiation by the patient, but other-initiated other-repair by the therapist. In semantic dementia other-initiated self-repairs proved to be difficult by lack of content related word comprehension or logorrhea.

The results from this preliminary study showed indications for differences in repair between the types of PPA. Further research is required to offer clinically relevant advice for the future diagnostics and therapy of this patient population.

## THE IMPACT OF A HEMATOPOIETIC STEM CELL TRANSPLANTATION ON DENTAL DEVELOPMENT

*Laure Ruyssinck, Kaat Toulouse, Rita Cauwels, Victoria Bordon, Catharina Dhooge*

Pediatric patients (pts) treated with a hematopoietic stem cell transplantation (HSCT) often suffer from late side effects. This study investigated following effects on dental development: dental agenesis (A), microdontia (M) and root-crown ratio (RCR). Additionally, pts/parents were asked about their knowledge and interest in dental screening at the follow-up clinic.

42 pts treated at GUH who were <12y at time of HSCT were examined clinically and radiographically. 12 pts underwent conditioning regimen with total body irradiation, 21 pts with busulfan and 9 pts with other chemotherapeutic agents. 16 pts were <3y, 9 pts were 3-6y and 17 pts were >6y at HSCT. Significantly more M is found in patients treated with busulfan (68,4%;  $p=0,023$ ) compared to other chemotherapeutic agents. Patients treated <3y show significantly more M (76,9%;  $p<0,001$ ) as well as A (92,3%;  $p<0,001$ ) compared to patients treated at an older age. Prevalence of A and M in our study group is respectively 51,3% and 46,2% which are both significantly more than in a standard population. 76,3%pts had an aberrant RCR of at least one element. Age at HSCT possibly has a more severe effect on A and M compared to conditioning regimen. 86% of the pts/parents find it important to receive information and follow-up.

HSCT has a negative impact on dental development, depending on age at HSCT and conditioning regimen. Dental follow-up of these patients is essential and should be incorporated in the post-treatment program.

## MUMPS VACCINE FAILURE: RESEARCH INTO THE IMMUNOLOGICAL AND EVOLUTIONARY PRESSURE ON MUMPS VIRUS PROTEINS

*Van Cleemput J, Vandermarliere E, Vermeire T, Martens L*

Recent years have seen a resurgence in mumps infections, often in vaccinated young populations. This study focusses on the mutations which may occur in the viral proteins as a result of both immunological and evolutionary pressure and which could be at the base of the reduced effectiveness of the used vaccine. Using a methodology that is mainly routed in bioinformatics, we try to determine the difference in mutation speed between internal and external viral proteins. Homology models were built and used in Scop3D analyses. DynaMine analyses were performed and linked to Scop3D data.

## EPIDEMIOLOGIE, OORZAKEN, EVOLUTIE EN PROGNOSE VAN HYPOXISCHE HEPATITIS BIJ 1177 KRITIEK ZIEKE PATIËNTEN

*Van Coile L, Van den broecke A, Decruyenaere A, Van Vlierberghe H, Colpaert K, Decruyenaere J*

### **Inleiding**

Hypoxische hepatitis (HH) wordt gekenmerkt door centrilobulaire levercelnecrose met een snelle, abrupte stijging van aspartaat-aminotransferase (ASAT) t.g.v. hemodynamisch falen. Het is vaak voorkomend op Intensieve Zorg en heeft een hoge mortaliteit.

### **Methode**

De cohorte bevat alle volwassen patiënten met een 1ste episode van HH (ASAT > 5x ULN) op de dienst IZ van het UZ Gent tussen 1 januari 2007 en 21 september 2015 (n=1177). Deze patiënten worden o.b.v. de oorzaak verdeeld in 8 groepen. Bevindingen worden weergegeven met mosaïc, longitudinale en soccer plots.

### **Resultaten**

De incidentie van HH bedraagt 4,2%. De meest voorkomende oorzaken zijn cardiale oorzaak (40,2%) en septische shock (SS) (28,3%). De mortaliteit is 42,8% waarvan longembolen (LE) en SS de hoogste mortaliteit (resp. 56,2% en 52,9%) en snelste sterfte vertonen (overleving resp. 5,4 en 12,3 dagen). I.t.t. andere studies worden patiënten met een beperkte ASAT-stijging (5xULN < ASAT < 10xULN) toch geïncludeerd. Deze subgroep toont een hoge mortaliteit (26,2%). 136 patiënten ontwikkelen HH na majeure ingreep met algemene anesthesie, zonder enige hemodynamische problemen tijdens de ingreep. De labowaarden tonen een typisch patroon, waaronder de abrupte ASAT-stijging.

### **Conclusie**

Deze studie beschrijft de grootste monocentrische cohorte in literatuur. De incidentie van 4,2% toont dat het een vaak voorkomende oorzaak is van leverfalen in kritiek zieke patiënten. Ook de mortaliteit is met meer dan 40% zeer hoog.



**INFLUENCE OF ANTHROPOMETRIC, PHYSICAL PERFORMANCE  
AND MOTOR COORDINATION CHARACTERISTICS ON DROPOUT  
OF TALENT IDENTIFIED VOLLEYBALL PLAYERS**

*Pieter Van Dam, Mireille Mostaert, Matthieu Lenoir*

# ONTWIKKELING VAN EEN MULTIVARIAAT PREDICTIEMODEL IN EEN STUDIECOHORTE VAN 1177 KRITIEK ZIEKE PATËNTEN MET HYPOXISCHE HEPATITIS.

*Van den broecke A, Van Coile L, Decruyenaere A, Van Vlierberghe H, Colpaert K, Decruyenaere J*

## **Inleiding**

Hypoxische hepatitis (HH) is een vaak voorkomende oorzaak van acuut leverfalen met hoge mortaliteit op Intensieve Zorg (IZ). Het doel van deze studie is de validatie van 2 bestaande predictiemodellen en de ontwikkeling van een eigen multivariaat predictiemodel van de mortaliteit.

## **Methode**

De cohorte bestaat uit alle volwassen patiënten met een eerste episode van HH (asparaat aminotransferase (ASAT)-stijging  $>5x$  ULN) op de dienst IZ van het UZ Gent tussen 1 januari 2007 en 21 september 2015 ( $n=1177$ ). Het UZ Gent model werd opgesteld met multivariate logistische regressie en achterwaartse eliminatie. Predictieve accuraatheid werd nagegaan met de ROC-curve, calibratiecurve en de Hosmer-Lemeshow test.

## **Resultaten**

Na exclusie wegens ontbrekende waarden, correlatie en achterwaartse eliminatie werden 7 significante variabelen in het UZ Gent model weerhouden: oorzaak, ventilatie, leeftijd, INR, ASAT, trombocyten en pH. Het UZ Gent model vertoont een goede discriminatie (AUC 0,79) in tegenstelling tot de modellen van Raurich en Fuhrmann (resp. AUC 0,59 en 0,67). Het UZ Gent model vertoont tevens een goede overeenkomst tussen de geobserveerde en de voorspelde mortaliteit.

## **Conclusie**

Het betreft de grootste monocentrische cohorte van patiënten met HH. 7 risicofactoren voor mortaliteit geassocieerd aan HH werden geïdentificeerd. Dit UZ Gent model heeft een goede discriminatie en calibratie. De 2 bestaande modellen vertonen slechts een zwakke discriminatie in onze cohorte.

## A LONGITUDINAL STUDY OF REPAIR STRATEGIES IN PRIMARY PROGRESSIVE APHASIA USING CONVERSATION ANALYSIS

*Van der Straeten, C., Muntigl, P., De Letter, M.*

### **Background**

A systematic review on spontaneous speech, conversation and interaction in primary progressive aphasia (PPA) was conducted until October 2015. While it was possible to distinguish PPA subtypes based on spontaneous speech characteristics, differentiation between subtypes for conversation and interaction was impossible due to scarcity of publications on the subject. These findings were used as basis for a preliminary longitudinal study, the aim of which was to provide a description of the evolution in repair strategies used by patients with PPA during the first two years of disease progression.

### **Method**

Video recordings of natural occurring patient-therapist conversations were systematically transcribed for two participants: MJG (progressive nonfluent aphasia, PNFA) and RG (logopenic progressive aphasia, LPA). These transcriptions were analysed both quantitatively and qualitatively using a conversation analytic method.

### **Results**

Differences in repair strategies between MJG and RG were found in the relative importance of the repair trajectories and the context in which they were used throughout the disease progression.

### **Conclusion**

These findings demonstrate the evolution in the use of repair strategies throughout the progression of PPA. Though not generalisable, there are clear indications for differences between the PPA subtypes. Further research within this subject is required for a clearer and more universally applicable view on repair sequences in PPA patients.

**DO STUDENTS WITH DIFFERENT ACTUAL COMPETENCE LEVELS  
RESPOND DIFFERENTLY TO CHOICE AND COMPETENCE  
ENHANCING FEEDBACK?**

*Van Duyse F., De Meester A., De Muynck G., Stennes B., Haerens L.*

**DISCRIMINATIVE VALUE OF ATHLETIC COMPETITION  
PERFORMANCES VERSUS TEST BATTERY SCORES**

*Paulien van Luijk, Mireille Mostaert, Matthieu Lenoir*

## CANCER IMMUNOTHERAPY: WHAT DRIVES CARS?

*Van Schandevyl S, Prof. Dr. Kerre T.*

Cytotoxische T-cellen zijn essentieel voor tumorcontrole, maar kankercellen kunnen door aanpassingen ontkomen aan het immuunsysteem. Immunotherapie poogt deze ontsnappingsmechanismen te omzeilen. Chimere antigeenreceptoren (CARs) wapenen T-cellen van de patiënt met tumorspecifieke antigeenherkenning en bijkomende eigenschappen. Tweede en derde generatie CAR T-cellen integreren costimulatoire domeinen voor verhoogde werkzaamheid. Vierde generatie CAR T-cellen (TRUCKs) leveren cytokines en andere stoffen aan om de vijandige tumormicro-omgeving te bedwingen. Om ernstige bijwerkingen tegen te gaan, zijn veiligheidsschakelaars en bijkomende voorzorgen noodzakelijk. Bemoedigende klinische resultaten in anders terminale patiënten met B-cel maligniteiten tonen aan dat CAR T-cellen aan het evolueren zijn van een veelbelovend concept tot een levensreddende therapie.

## EVALUATION OF SKIN CAMOUFLAGE TECHNIQUES FOR VITILIGO

*Elise Vandersichel, Reinhart Speeckaert, Elfie Deprez, Aurélie Vanhauter, Valerie Cannaert, Mia van Renterghem, Marleen Cozyns, Emma Coussens, Sumit Gupta, Defreyne Justine, Carole Van Haverbeke, Nele Maes, Grine Lynda, Nanja van Geel*

**RESECTION RADICALITY OF BASAL CELL CARCINOMA (BCC): A  
PILOT STUDY.**

*Vanhaecke A, De Schepper S, Creytens D, Ongenae K.*



## REVISION OF REVERSED SHOULDER ARTHROPLASTY: IS REOPERATION POSSIBLE?

*Stijn Casier, Bart Middernacht, Alexander Van Tongel, Lieven De Wilde*

### **Introduction**

The number of reversed shoulder arthroplasty (RSA) procedures increases, and so does the revision rate. In case of severe bone insufficiency, instability or infection of the primary RSA, revision to another RSA is preferable but not always possible. Hemiarthroplasty (HA), spacers and resection arthroplasty (RA) have been described in this indication.

### **Materials and Methods**

Between 2004 and 2016, 20 shoulders in 19 patients were treated in the Ghent University Hospital for failed revision of RSA. Nine received a Megahead prosthesis, a spacer was implanted in 6, and 5 underwent resection arthroplasty.

### **Results**

Indications for implantation of a Megahead prosthesis were loosening RSA (5), infection (4), dislocation (1) and nerve irritation (1). Improvement of ROM was observed. Anterosuperior migration of the prosthesis was noted in 2 patients. Another 2 patients were ultimately revised to RSA. Seven permanent spacers were implanted for infection, of which 2 remain in place till today. The other 5 were revised to RSA. Of the 5 patients treated with RA, 3 were revised further on to RSA, resulting in pain relief and function regain.

### **Discussion**

Our study shows that a Megahead prosthesis has better functional results than RA in failing RSA, but is inferior to another RSA. In HA and RA the functional results are poor, and pain relief is uncertain. Results of spacers are variable and can be satisfactory. Due to increasing surgical experience and improving technique, 9 patients could ultimately be reconverted to another RSA with favourable results.