"Visus" the valve diseases. Transcatheter technologies take advantages from the open heart technique using catheter based instruments for elderly and high risk patients. Transcatheter mitral valve commisurotomy was the first surgical therapy converted to transcatheter one in the 1980. Today with a new art of transcatheter technology, with more clinical efficacy and safety is this "The Procedure of Choice" with a faster recovery and less peri-operative pain. But although it seems the TAVI procedure is more effective at elderly high risk or non-operable patients. The German TAVR registry shows that at low risk population, the observed mortality & morbidity is higher than that population by the EUROSCORE. The key and the crucial point at the introduction of a new clinical technology is the optimal "TRANSLATION" to the daily human practice. The new interventional technology has to be supported – after previous excellent results of animal and all clinical phase studies - by "Clinical Evidence!!!". In this technology imaging is the crucial factor in the selection with and in the screening process, to guide patients to the right size and art of device selection, as well as in playing a fundamental role during procedures to guide the implant safely and effectively. In the future the best imagination with a real touch will be probably holographic by an almost "REAL " 3D or 4D anatomical peri-operative representation.

PTEN as a therapeutic target in motor neuron diseases (ALS/SMA)

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Abstract

The tumor suppressor protein Phosphatase and Tensin Homolog deleted on Chromosome 10 (PTEN) is a member of the protein tyrosine phosphatase family that can negatively regulate the serine/threonine kinase Akt to exert its tumour suppressor function. In addition to its normal functions such as neuronal migration and neuronal size control, PTEN protein is involved in pathological processes surrounding neuronal injury such as those associated with brain ischemia, neurological and mental disorders. It has been shown that modulation of the PTEN/mTOR pathway promotes axon regeneration in the adult CNS. We have previously shown that down-regulating the expression of PTEN protects against ischaemic neuronal death in vitro and in vivo (Ning et al. 2014). Recently, we showed that PTEN knockdown via siRNA increases motor neuron survival in Amyotrophic lateral sclerosis (ALS) (Kirby et al. 2011) in vitro and spinal muscular atrophy (SMA) in vivo (Ning et al. 2010, Little et al., unpublished). Our preliminary data show that the PTEN inhibitor, bpV, promotes cell survival in NSC34 G93A motor neuronal cell line. We have also showed that PTEN silencing increases cell survival in iPS-derived motor neurons from human fibroblasts (D-J Yang et al., 2014). Taken together, PTEN inhibition results in neuroprotective effects on motor neuron survival in vitro and in vivo. The outcome of our studies provide evidence that PTEN is potential therapeutic target for neuroprotection in ALS or SMA patients and other neurodegenerative disorders.

Poster Presentations

SRM-based quantification of malignant biliary stenosis biomarkers in human bile

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Abstract

The differential diagnosis of biliary stenosis is a critical problem for gastroenterologists. An early identification of malignant lesions would enable the rapid resort to surgical resection which currently represents the only potentially curative option. Unfortunately, the diagnostic value of all available methods (e.g. imaging technics, standard serum biomarkers) is limited by relatively poor accuracy and negative predictive value. Recently, our group and others highlighted new potential cancer biomarkers in bile by using comparative proteomic analysis. Nevertheless, to date, only a few candidates have been verified for their diagnostic performances in discriminating between malignant and non-malignant stenoses. In addition, no data have yet been collected on the simultaneous measurement of these proteins with the intent of evaluating the diagnostic interest of a panel of biomarkers. To overcome the limitation of classical verification tools and give a new impetus to the translation of bile biomarkers into clinical diagnostics, mass spectrometry-based quantification could represent a rapid and cost-effective opportunity thanks to its capacity for multiplexed, high-throughput analysis, combined with its analytical specificity and reliable quantification. Here we developed the first Selected Reaction Monitoring (SRM) assay for the multiplexed measurement of cancer biomarkers in human bile. For this purpose, 8 potential biomarker candidates previously highlighted by proteomic analysis were selected. Equal volumes of bile collected from patients presenting with malignant and non-malignant biliary stenosis were stacked on the top of a SDS-PAGE gel. Proteins were then digested in-gel with trypsin and proteotypic peptides of each candidate biomarker were quantified by nanoLC-SRM on a 5500-QTrap mass spectrometer (ABSciex) using heavy synthetic peptides as standards (PEPotecTM, Thermofisher). SRM data were finally analysed using Skyline software and manual validation. The developed assay proved to be valuable and reliable to quantify all the selected candidates. Moreover, the results confirmed the simultaneous overexpression of some of the proteins in bile samples from malignant stenoses. Overall, our data demonstrate the ability of SRM to quantify cancer biomarkers in human bile and emphasize the interest of using multiplexed SRM assays to assess the diagnostic potential of a panel of bile biomarkers in differentiating biliary stenoses. Work supported by the PRIME-XS consortium.

Hemopexin, a potential biomarker for the diagnosis of chronic predisposition to acute kidney injury

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Abstract

In the last years, the new concept of predisposition to acquire acute kidney injury (AKI) is emerging. This concept was observed in our group when experimental animals exposed to an absolutely subnephrotoxic acute treatment with certain drugs (e.g. gentamicin and cisplatin) developed AKI when they were treated with a second insult with another drug, while control animals exposed to the same second drug experimented no toxicity. On these grounds, we decide to study if chronic exposure to nephrotoxicants might induce this predisposition to AKI and investigate how to detect this condition by the search of predisposition biomarkers. To this end, rats (Sprague-Dawley) were treated with a subtoxic dosage of the experimental nephrotoxin uranyl nitrate (UN) in the drinking water for 22 weeks, or plain water (as control). After 21 weeks both groups were treated with subtoxic regime of getamicin during 7 days. Renal function was monitored by means of serum creatinine, serum urea, proteinuria, N-acetyl-beta-D-glucosamini-dase and lactate dehydrogenase excretion measurement. After and before