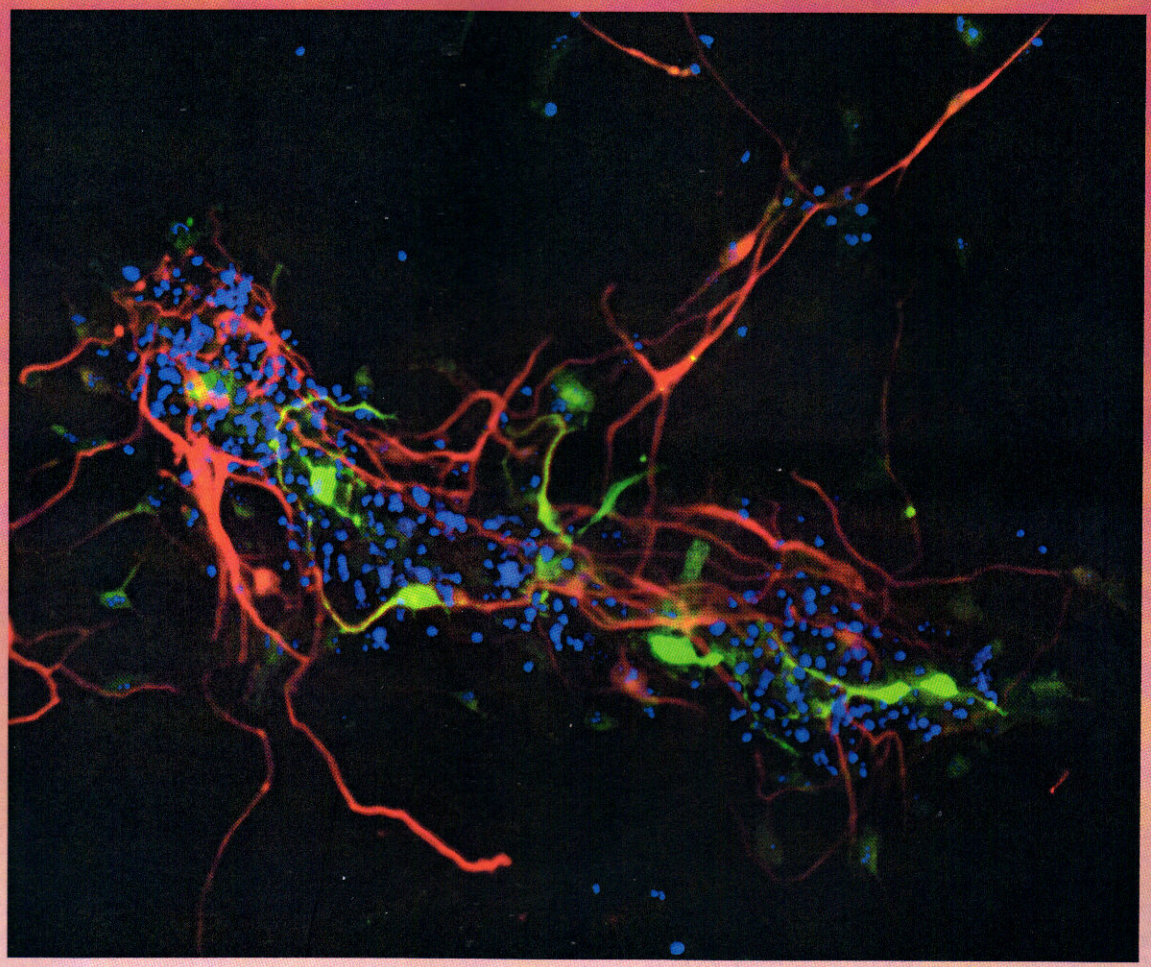
Abstracts of the 2nd Joint Meeting of Pathology And Laboratory Diagnostics



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associated with AD. Our previous works suggested that all these genes might be linked to different herpes viral mechanisms. Here we present genetic data on different molecules regulating antiviral response.
Methods: SNPs in the promoter region of *IL28B*, *MED23* and *IRF7* were analyzed by RFLP and Real Time PCR in DNA from AD and control (CTR) subjects. ELISAs for two different EBV IgG were also performed. The presence of EBV and HHV-6 DNA was analyzed by RT-PCR.
Results: No difference in genotype distribution of *IL28B* SNP among AD and CTR was observed but allele frequencies show that T allele was more frequent in AD patients even after stratification by *APOEe4* positivity. *MED23* GG genotype appeared to influence the progression of the disease, being more frequent in the elderly that developed AD; this association was stronger in *APOEe4* non carrier patients. *MED23* GG genotype also correlated with the positivity to HHV-6 DNA. Finally, EBV IgG were elevated in AD carrying *IRF7* GG genotype.
Conclusions: Our findings suggest that a differential genetic background in these genes is associated with an increased risk of AD and correlate with the progression of the disease. In addition, these genes influence HHV6 positivity and EBV IgG plasma levels in AD.

AGE8. Is the Serum N Terminal Pro-Brain Natriuretic Peptide the Best Candidate Biomarker for Long-term Prognosis in Patients with Prosthesis-patient Mismatch after Mitral Valve Replacement?

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Background: Natriuretic peptides (NPs) are released from the heart in response to pressure and volume overload. Among these, B-NP and N-terminal-proBNP (NT-proBNP) have become important diagnostic tools for the management of heart failure. However, B-NP and NT-proBNP levels reflect complications of systolic and diastolic function as well as alteration of right ventricular and valvular function. In addition, their serum levels have a prognostic value in multiple clinical settings. Based on these observations, we sought to evaluate the relationship between prosthesis patient mismatch (PPM) and serum NT-pro-BNP levels after mitral valve replacement (MVR). PPM following MVR has been less investigated and it seems to mediate deleterious effects on long-term survival, even if contrasting opinions and data exist in the literature.
Methods: A total of 100 patients that have undergone this surgical treatment will be enrolled, and opportune clinical data and peripheral blood samples will be collected. Blood samples are utilized to analyze clinical conditions and serum NT-proBNP levels. Evaluation of hemodynamic performances before or under dobutamine infusion is also being assessed.
Results: The preliminary data on the serum NT-proBNP levels obtained seem to be interesting and promising, as well as their correlations with hemodynamic performances.
Conclusions: The demonstration of negative effects on tricuspid valve and pulmonary hypertension and consequently on survival induced by PPM after MVR through the serum quantification of NT-proBNP levels might lead to consider it as an optimal biomarker to evaluate patients' long-term prognosis and optimize surgical recommendations (i.e. tricuspid valve repair during mitral valve surgery in patients with moderate-severe mismatch).

AGE9. Insulin/IGF-1 Signaling: More than a Metabolic Pathway

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Background: Dietary intervention and genetic alterations in gene encoding proteins involved in nutrient-sensing pathways can modulate lifespan, influencing longevity. It depends on under/over-expression of regulatory molecules that lead to different expression of homeostatic genes. Insulin/IGF-1 pathway was associated with longevity and lifespan modulation in model organisms. In humans, a key molecule in this pathway is *FOXO3A* that acts as a TF on homeostatic genes in response to decreased signaling increasing life span. Interestingly, other genes that increase lifespan interact with *FOXO3A* such as *SIRT1*, which modulates the oxidative stress response.
Methods: We used meta-analytical and candidate-gene approaches to investigate the association of SNPs encoding proteins involved in Insulin/IGF-1 pathway with ageing and longevity.
Results: Our study confirmed previous results related to the association between *FOXO3A*, *IGF-1R*, *KLOTHO* and longevity. No association was reported between *IGF-1* and *SIRT1* although all *IGF-1* SNPs could affect its serum levels, known to modulate ageing and longevity. Moreover, we showed a new association between *SHIP2* SNPs and longevity.
Conclusions: Our results showed that specific SNPs of *IGF-1R*, *FOXO3A*, *SHIP2* and *KLOTHO* influence ageing and longevity in different ethnic populations and that *FOXO3A* could be the most relevant gene in lifespan extension, particularly in males. Moreover, it could be speculated that a reduction of insulin signaling may decrease the activation of *NF-kB* slowing down inflammatory gene transcription. Thus, the intervention on ageing and longevity should be based both on nutrient-sensing and inflammatory pathways. The first simple step could be represented by the adherence to the Mediterranean diet with low glycaemic index and low animal proteins.

AGE10. Age- and Glycaemia-related miR-126 Levels in Plasma and Endothelial Cells

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Background: To gain insight into the combined effect of age and glycaemic conditions on miR-126 expression.
Methods: miR-126 circulating levels were determined in 136 healthy subjects (CTR) aged from 20 to 90 years and in 193 type 2 diabetes mellitus (T2DM) patients aged 40-80 years. Intra/extracellular miR-126 level was measured in human endothelial cells (HUVECs) undergoing senescence under normoglycaemic and hyperglycaemic conditions.
Results: Measurement of plasma miR-126 in CTR disclosed significantly higher value in the oldest subjects compared with the younger ones (<45 vs. >75 years; miR-126 relative expression in a.u: 0.27 ± 0.29 vs. 0.48 ± 0.39, p=0.047). Lower values were observed in T2DM patients compared with age-matched CTR, after adjustment for confounding variables (0.23±0.21 vs. 0.34±0.31, F test=2.964, p=0.033), especially in those with poor glycaemic control. When CTR and diabetic patients were compared based on different age groups, the difference remained significant only in the oldest groups (age >75 years, CTR vs. T2DM: 0.22 ± 0.23 vs. 0.48 ± 0.39, p<0.005). The age-related increase in plasma miR-126 was paralleled by a 5/6-fold increase in intra/extracellular miR-126 levels in *in vitro*-cultured HUVECs undergoing senescence. Significant down-regulation of SPRED-1 protein, one validated miR-126 target, was observed in senescent HUVECs. Moreover, miR-126 expression was down-regulated in intermediate HUVECs grown in high-glucose medium.
Conclusions: Overall, these data suggest that ageing/senescence-associated miR-126 up-regulation is likely a senescence-associated compensatory mechanism that is blunted when endothelial cells are exposed to high glucose levels, a phenomenon that probably occurs *in vivo* in T2DM patients, especially in the oldest patients with poor glycaemic control.