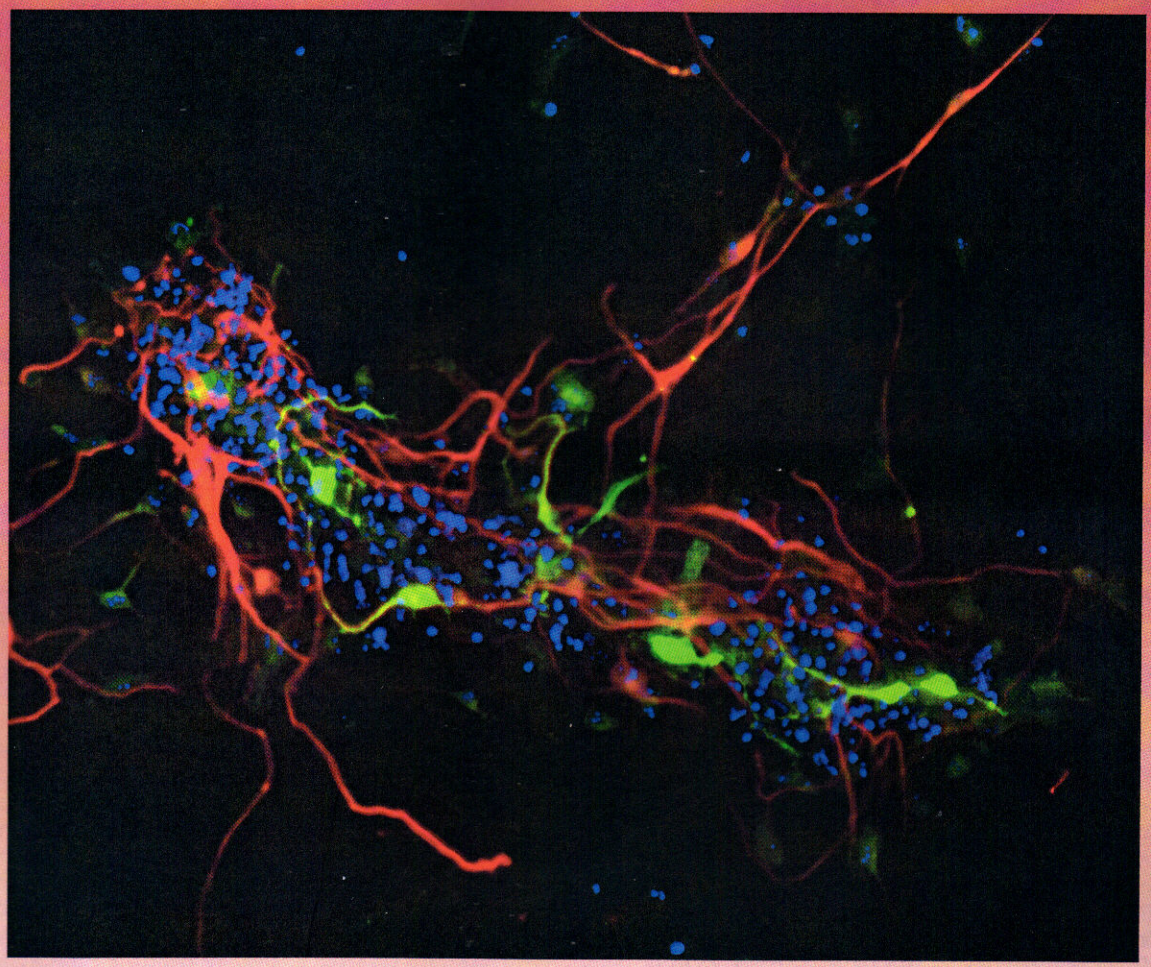
Abstracts of the 2nd Joint Meeting of Pathology And Laboratory Diagnostics



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pemphigoid. Moreover, we observed different trends in antibody titer during therapy indicating the need for a close customization of the laboratory follow-up.

IMIN9. MicroRNA as Key Regulators of Macrophage Plasticity

M. Locati[1], G. Curtale[1], M. Pesant[1], T. Renzi[1], G. Sukubo Naths[1], M. Rossato[2], F. Bazzoni[2]
[1]University of Milan, Milan, Italy; [2]University of Verona, Verona, Italy

Background: Macrophages are key elements in the induction, regulation, and resolution of inflammation, and are profoundly influenced by microenvironmental signals, which trigger different polarized activation profiles associated with a complete reorganization of their transcriptional profile. The molecular basis underlying this plasticity is still largely undefined and represents a growing field of active research for potential implications for most human diseases.
Methods: Investigating the potential role in macrophage plasticity of microRNA (miR), short non-coding RNA that regulates transduction and stability of mRNA networks, we have identified a set of miR controlling key signaling pathways and transcription factors involved in macrophage polarized activation.
Results: In classically activated macrophages (M1), we identified a set of IL-10-responsive miRs (cluster miR-125a~99b~let-7e, miR-146b, miR-187) and glucocorticoid-responsive miRs (miR-511), which operate a complex and multi-targeting regulation of the TLR pathway, with significant direct and indirect regulatory effects on the production of inflammatory cytokines and chemokines. Furthermore, we identified miR-135b as a key element in the alternative activation of macrophages (M2), via direct targeting of major transcription factors involved in this polarized activation pathway (STAT6, KLF4, c-Myc).
Conclusions: In conclusion, we report a complex network of miRs with anti-inflammatory and polarizing effects on macrophages operating via direct targeting of key signaling pathways and transcription factors controlling macrophage plasticity.

IMIN10. Polyphenols Extracted from *Vitis vinifera* as Food Supplementation: Effects on Oxidative Stress Biomarkers

S. Vasto[1], A. Barera[1], D. Nuzzo[2], M. Di Carlo[2], C. Caruso[1]
[1]University of Palermo, Palermo, Italy; [2]CNR-IBIM, Palermo, Italy

Background: In the elderly, nutrition monitoring and food consumption have the potential for dropping the rate of chronic diseases and improving quality of life. This specific information can support the development of targeted dietary intervention strategies to prevent, to some degree, age related diseases. Polyphenols are an integral component of the human diet present in most food-stuffs and beverages of plant origin; they are considered an asset to the prevention of various diseases, including cancer, neurodegeneration, diabetes and cardiovascular diseases.
Methods: Grape seed polyphenols were the main ingredient of food supplementation used in this study. Fifty healthy individuals (25 men and 25 woman) were recruited and food supplementation was administrated for 60 days. Urine and blood samples were collect at baseline and at the end of 60 days. 8-iso Prostaglandin F2α, LDLox and dihydrotestosterone were measured.
Results: The study showed the efficacy of grape seed polyphenols on biomarkers of oxidative stress.
Conclusions: Several evidences, epidemiological studies, clinical trials, experiments on animal models and mechanistic studies show a protective role of polyphenols against disease, such as cardiovascular, neurodegenerative, inflammation or cancer; however, individual variability makes a difference in efficacy and bioavailability.

IMIN11. Cytokine Polymorphism in Takotsubo Cardiomyopathy

P. Di Gangi[1], L. Scola[1], S. Giambanco[1], M. Bova[1], G. Santini[1], L. Vaccarino[1], C. R. Balistreri[1], D. Lio[1], P. Assennato[1], S. Novo[1], G. Novo[1]
[1]University of Palermo, Palermo, Italy

Background: Takotsubo (TT) cardiomyopathy is characterised by an acute left ventricular dysfunction triggered by emotional or physical stresses. Clinically, the syndrome is characterised by acute symptoms mimicking acute infarction without relevant electrocardiographic and biochemical markers of myocardial damage changes. Stressful events inducing an excess catecholamine release and myocardial β-adrenergic receptors (β-AR) seem to play a major role in TT. Accordingly, we have reported that the L41Q polymorphism of the G protein-coupled receptor kinase 5 (GRK5), which, leads to β-arrestin recruitment and mediates β-AR desensitisation might play a role in TT susceptibility. Extended sympathetic activation may influence the pro-inflammatory cytokine secretion triggering b-adrenergic receptors of the immuno system cells. In turn, IL-1, IL-6, TNF-α stimulating the synthesis and release of CRH and norepinephrine might magnify the activation of the sympathetic system. In this view, we have analyzed the role that polymorphisms of inflammatory cytokines might play in the pathogenesis of TT.
Methods: We analysed ADRB-1 (rs1801253), IL–1A (rs1800587), IL-1B (rs16944), (rs1143634), IL-6 (rs1800795), TNF-α(rs1800629), TGF-β(rs1800471), IL-10 (rs1800872), (rs1800871), (rs1800896), MAL (rs8177374) and TLR-4 polymorphisms in 25 TT patients and 100 controls using KASPar SNP genotyping method. Statistical analysis of data was performed using dominant, codominant, and recessive models.
Results: Analysis of the genotypic and allelic frequencies does not allow the detection of relevant differences in polymorphism frequencies in TT patients.
Conclusions: Because of the low number of patients, further studies are necessary to understand the role of cytokine polymorphisms in Takotsubo cardiomyopathy. Work is in progress to recruit and analyse a larger group of patients.

IMIN12. Prep1 Controls Effector and Regulatory T Cell Responses: A Novel Homeodomain Transcription Factor Linking Immunity and Metabolism

C. Procaccini[1], F. Oriente[2], S. Cabaro[3], A. Liotti[3], M. Galgani[4], P. Formisano[2], F. Beguinot[3], G. Matarese[5]
[1]Consiglio Nazionale delle Ricerche (IEOS-CNR) c/o Università di Napoli "Federico II", Napoli, Italy; [2]Università di Napoli "Federico II", Napoli, Italy; [3]Università di Napoli "Federico II", and URT del CNR Genomica del Diabete Tipo 2, Napoli, Italy; [4]IEOS-CNR c/o Università di Napoli Federico II, Napoli, Italy; [5]Università di Salerno, Baronissi Campus and IRCCS Multimedica, Baronissi, Italy

Background: Accumulating evidence has shown that metabolic disorders, such as obesity and type 2 diabetes are associated with immune system dysfunction, as they are characterized by abnormal cytokine production and activation of inflammatory pathways. Prep1 is a homeodomain transcription factor, which plays an important role in organogenesis and in the regulation of energy homeostasis and metabolism. Recent studies have demonstrated that Prep1 inhibits insulin signaling and induces insulin-resistance. Indeed, Prep1 heterozygous mice (Prep1i/+), expressing 55-57% of protein, display increased sensitivity to insulin, are protected from diabetes and downregulate hepatic lipogenesis, attenuating steatohepatitis.
Methods: Immune-phenotyping and activation of immune cells were performed by cytofluorimetric analysis, and proliferation and suppression assays were assessed by thymidine incorporation. The metabolic profile of CD4+ T cells was evaluated by extracellular flux analyzer and the intracellular molecular events by western blotting.
Results: We found a decreased production of pro-inflammatory cytokines/chemokines and enhanced anti-inflammatory cytokines secretion in serum of Prep1i/+ mice. In addition, Prep1 deficiency significantly inhibited CD4+ T proliferation, by decreasing their activation