

P-41-010**Pathway dynamics in progeroid****DNA-repair-deficient mice: a multi-tissue analysis**

R. van der Marel, I. van Galen, R. Ozinga, W. Vermeij
The Netherlands Society for Biochemistry and Molecular Biology, Utrecht, Netherlands

The rise in the elderly population in industrialized countries is increasing cases of age-related diseases, with the number of people over 60 expected to double by 2050. Understanding aging mechanisms is crucial for managing these diseases, and growing evidence suggests that DNA damage plays a key role in aging. The *Ercc1Δ/-* mouse model, which exhibits accelerated aging due to a DNA repair defect, serves as a valuable system to study this interplay. This study investigates the systemic effects of DNA repair deficiency across multiple tissues in *Ercc1Δ/-* mice by integrating RNA-seq data to identify common cellular and molecular changes. Through Gene Set Enrichment Analysis (GSEA) and Overrepresentation Analysis (ORA), we analyze transcriptomic data to gain insights into gene expression changes. Our findings reveal a significant systemic dysregulation of immune system pathways, suggesting that persistent DNA damage signaling leads to chronic immune activation. Additionally, we identify other pathways previously linked to aging, further validating the model. This study presents a pipeline for identifying shared and systemic responses to DNA repair deficiency, contributing to our understanding of DNA damage as a major driver of aging and age-related diseases.

P-41-011

Fibroblast growth factor-12 regulates vascular smooth muscle cell stiffness and mechanosignaling, driving aortic aneurysm development in Marfan syndrome mice

K. L. Kim, W. Suh

College of Pharmacy, Chung-Ang University, Seoul, South Korea

Emerging evidence suggests that dysregulated mechanosignaling in vascular smooth muscle cells (VSMCs) and increased VSMC stiffness play a critical role in the aortopathy of Marfan syndrome (MFS). However, the key mediators driving these alterations in mechanosignaling and cellular stiffness during thoracic aortic aneurysm (TAA) formation in MFS remain largely undefined. Here, this study shows that fibroblast growth factor 12 (FGF12) is highly expressed in VSMCs within the aneurysmal walls of MFS (*Fbn1*^{C1039G/+}) mice and MFS patients. In human aortic SMCs, FGF12 is upregulated by transforming growth factor-β and cyclic mechanical stretch. FGF induces aberrant mechanosignaling, as evidenced by increase in RhoA-GTP level, actin polymerization, and focal adhesion assembly, leading to significant elevation in VSMC stiffness, via Angiotensin II (AngII)/AngII type 1 receptor (AT1R) signaling pathway. In an AngII/β-aminopropionitrile-induced aneurysm model, *Fgf12*^{+/-} mice exhibit significant reduction of TAA formation and arterial stiffness, along with a marked attenuation of AT1R hyperactivation and aberrant mechanosignaling in the arterial walls compared to wild-type mice. Furthermore, *Fgf12*^{+/-}*Fbn1*^{C1039G/+} mice display substantial decrease in both TAA formation and arterial stiffness compared to *Fbn1*^{C1039G/+} mice. These findings establish FGF12 as a novel factor mediating aberrant mechanosignaling and elevated stiffness of VSMCs, contributing to TAA pathogenesis in MFS.

P-41-012

Could high serum CRP levels serve as a biomarker for children and adolescents diagnosed with generalized anxiety disorder?

K. Ünal^{*I,II,III,IV}, Y. Taş Torun^{*II}, Z. K. Kurt^{*III}, C. Özbaş^{*IV}
^IGazi University, Medical Biochemistry, Ankara, Türkiye, ^{II}Gazi University, Child and Adolescent Mental Health and Diseases, Ankara, Türkiye, ^{III}Ankara Etlik City Hospital, Child Adolescent Psychiatric Clinic, Ankara, Türkiye, ^{IV}Gazi University, Faculty of Medicine, Department of Public Health, Ankara, Türkiye

Generalised anxiety disorder (GAD) is a common anxiety disorder characterized by persistent and uncontrollable worry and anxiety. Recently, the role of neuroinflammation in the pathogenesis of psychiatric disorders has been increasingly discussed. Our study aims to detect levels of serum C-reactive protein (CRP), neopterin, TWEAK, IFN-γ, TNF-α, and IL-6 in patients with GAD and thereby contribute to existing evidence about inflammation and GAD. The study included 25 treatment-naïve GAD patients aged 8-18 and 30 healthy controls. The criteria for diagnosis were established by the Schedule for Mood Disorders and Schizophrenia for Children (K-SADS-PL-DSM-5) and the Revised Child Anxiety and Depression Scale (RCADS). The study participants' serum CRP, neopterin, TWEAK, IFN-γ, TNF-α, and IL-6 levels were analyzed. The results were compared between the children and adolescents diagnosed with GAD and controls. Serum CRP levels of GAD patients 1.7 [1.2–2.94 mg/L] were significantly higher than healthy controls 1.3 [1.2–1.7 mg/L] ($p = 0.034$). There was no difference, which was statistically significant, between groups in terms of other biomarker levels ($p > 0.05$). Based on the ROC curve analysis, the AUC was determined as 0.665 (95% CI: 0.511–0.820) for CRP ($p: 0.036$). Positive correlations were found between RCADS-CV total anxiety score ($r = 0.729$, $p = 0.001$) and RCADS-CV GAD score ($r = 0.642$, $p < 0.001$) with the illness duration. Our results showed that the levels of CRP, an indicator of inflammation, were higher in children and adolescents diagnosed with GAD. The results are consistent with a role of inflammation in anxiety disorders. CRP may have increased due to neuroinflammation, which is thought to play a role in GAD pathophysiology. On the other hand, the increase in CRP levels may have triggered GAD pathophysiology. CRP contribution to the pathophysiology of GAD should be investigated in greater detail. *The authors marked with an asterisk equally contributed to the work.

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Tight junction proteins and inflammation in obsessive-compulsive disorder severity: the role of MarvelD3 and tricellulin in children and adolescents

K. Ünal^{*I}, Y. Taş Torun^{*II}, M. E. Erol^{*III}, Z. K. Kurt^{*IV}, C. Özbaş^{*V}
^IGazi University, Medical Biochemistry, Ankara, Türkiye, ^{II}Gazi University, Child and Adolescent Mental Health and Diseases, Ankara, Türkiye, ^{III}Gazi University, Institute of Health Sciences, Department of Medical Biochemistry, Ankara, Türkiye, ^{IV}Ankara Etlik City Hospital, Child Adolescent Psychiatric Clinic, Ankara, Türkiye, ^VGazi University, Faculty of Medicine, Department of Public Health, Ankara, Türkiye

Obsessive-compulsive disorder (OCD) is a chronic neuropsychiatric condition in which individuals experience