RENAL TRANSPLANTATION. EXPERIMENTAL, IMMUNE-TOLERANCE OF ALLOGENIC AND XENOGENIC TRANSPLANTS

TRANSSCRIPTOME ANALYSIS OF ZERO KIDNEY GRAFT BIOPSIES REVEAL A ROLE OF METALLOTHIONEINS IN RENAL AGEING

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Introduction and Aims: Human life span is increasing continuously while structure and function of the kidney deteriorate with age. Age-related diseases contribute to this process and about one third of the population older than 70 years suffers from chronic kidney disease. Despite some similarities the aging kidney and CKD differ and it is unclear, whether the loss of renal function represents an intrinsic ageing process or is due to the accumulation of disease associated damage. Thus biological markers for age might be useful tools to dissect the specific pathologies and gene expression analysis of healthy aged kidneys might be a reasonable approach to avoid confounding by disease.

Methods: Age-associated gene expression changes in zero hour donor kidney biopsies were determined using microarray technology followed by ANOVA and SAM analysis. Expression changes of selected genes were confirmed by quantitative real-time PCR. In situ hybridization and immunohistochemistry was used to localize mRNA and protein expression in zero hour biopsies. Functional aspects were examined in vitro in RPTEC/TERT1 cells.

Results: Donors were classified into 3 age groups (younger than 40, 40-59, older than 59 years). In Microarray data age-associated transcriptional changes were identified: 16 transcripts were found to be significantly upregulated in age group 3 as compared to age group 1. 8 of these transcripts encoded for metallothionein (MT) isoforms. In situ hybridization demonstrated localization of MT mRNA in renal proximal tubular cells. RPTEC/TERT1 cells overexpressing MT2a were less susceptible towards CdCl2 induced cytotoxicity.

Conclusions: Metallothioneins (MTs) play a role in the ageing kidney. As MTs contribute to detoxification of heavy metals and homeostasis of essential metals, protect from ROS mediated oxidative stress and prevent apoptosis their upregulation with ageing might represent an intrinsic protective mechanism.

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