

Whole-genome array-based methylation analysis was performed on two cohorts of kidney allograft biopsies: 95 obtained at implantation (82 brain-dead donors and 13 living donors), using EPIC BeadChips and 67 obtained after reperfusion (58 brain-dead donors and 9 living donors), using Infinium 450K Beadchips. Donor age ranged from 16 to 73 years, and from 16 to 79 years, respectively. Comb-p was used to identify differentially methylated regions (DMRs). The genes mapped to DMRs with a FDR q-value < .0001 were selected for ingenuity pathway analysis.

Donor age associated significantly with methylation levels at 89,293 cpgs (10% of all probes) in the implantation cohort and 87,393 (20% postreperfusion (q-value < 0.05), adjusted gender cold ischemia time. q-value < 0.0001 corresponded to 17,077, respectively 15,225 differentially methylated regions. both cohorts, top enriched was wnt signalling pathway, which is involved kidney injury, repair fibrosis, as well renal senescence.

There a strikingly pervasive association between DNA changes kidney. These occur preferentially genes suggesting link advanced chronic allograft dysfunction.

INTRAVENOUS ADMINISTRATION OF MESENCHYMAL STROMAL CELLS MODULATES RENAL LIPID METABOLISM IN RATS.

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Mesenchymal stromal cells (MSC) have been shown to attenuate renal ischemia/reperfusion (I/R) injury in rodents. Still, the mechanisms of such a nephroprotection remain unclear. Here, rats were intravenously infused with MSC (1.5×10^6 cells in 1 ml saline; MSCD-7 group, n=6) or equivalent volume of saline (SD-7 group, n=6) 7 days before kidney sampling. High-throughput RNA sequencing technology was used to compare transcriptomic renal profiles, using TopHat and Cufflinks open-source software tools. A total of 494 and 256 genes were found to be significantly (q-value < .05) down- and up-regulated in mscd-7 versus sd-7 groups, respectively. Hierarchical cluster analysis by "david" "webgestalt" softwares highlighted that the metabolic pathways mostly affected msc included adipogenesis, insulin signalling, fatty acid (fa) biosynthesis, il-6 b-cell receptor il-3 pathway nuclear receptors involved lipid metabolism. Real-time qpcr immunoblotting analyses confirmed pivotal enzymes of fa biosynthesis were significantly downregulated group, whereas expression ppar alpha, a transcription factor oxidation, was induced msc. Additionally, fat />CD36 – a key regulator of membrane uptake of FA – was increased in MSCD-7 kidneys, with a preferential localization in proximal tubules (PT). As a whole, our data suggest that MSC infusion causes critical modifications of lipid metabolism, including (i) down-regulation of FA biosynthesis; (ii) activation of PPAR alpha pathway, and (iii) prioritization of FA as sources of energy in PT cells, which may eventually prevent lipid peroxidation and attenuate renal I/R damage.

A GLYCOMIC SERUM MARKER ANALYSED ONE WEEK AFTER LIVER TRANSPLANTATION IS AN INDEPENDENT PREDICTOR OF GRAFT LOSS DURING THE FIRST YEAR AFTER LIVER TRANSPLANTATION.

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Poor graft function after liver transplantation (LT) remains a challenge for transplant professionals and sometimes requires retransplantation. Pretransplant estimation of graft function using scores like donor risk index has limited use in individual patients. Graft loss is increased in patients showing early allograft dysfunction after liver transplantation. However, biomarkers that reliably identify patients at risk for graft failure after LT are lacking. Analysis of N-glycans in serum (glycomics) has shown to reflect the underlying liver function in liver disease but has never been assessed after liver transplantation. The aim of this study was to assess the potential of serum glycomics as predictive markers for graft and patient survival after liver transplantation.

In this monocentric prospective cohort 127 liver transplant patients were included between 1 December 2012 and 31 December 2014. Serum samples were collected just before and on daily bases during the first 2 weeks after liver transplantation. Glycomic profiles were analysed using an optimized glycomic technology on a DNA sequencer. The major outcome parameters (graft and patient survival during 1 year) were related to the observed glycomic alterations and the best predictive association was searched for using cox regression analysis.

The assessment of 2 serum glycans NG1A2F (an agalacto, core-alpha-1,6-fucosylated biantennary glycan structure) and NA3 (a triantennary glycan), combined as $\log(\text{NG1A2F}/\text{NA3})$ on day 7 after liver transplantation was strongly associated with graft loss (hazard ratio = 7.222; $p < 0.001$; 95% CI 2.352-22.182) and patient death (hazard ratio =