MO038 SCARF EXPRESSION IN KIDNEY DISEASE

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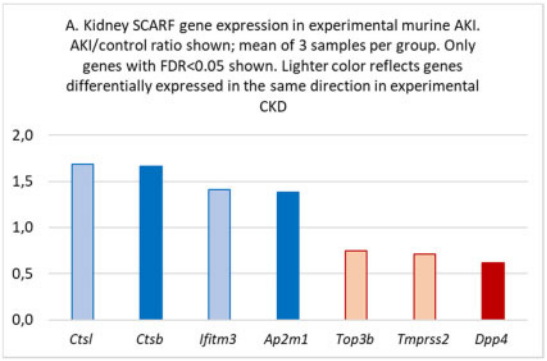
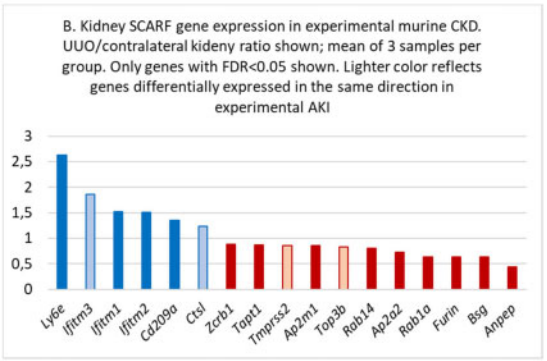
BACKGROUND AND AIMS: Chronic kidney disease (CKD) is the most common risk factor for lethal COVID19 and the risk factor that most increases the risk of death of COVID19 patients. Additionally, acute kidney injury (AKI) is frequent in COVID19 and AKI increases the risk of death. However, the underlying cellular and molecular mechanisms of such increased risk are unclear. SARS-CoV-2 and coronavirus-associated receptors and factors (SCARFs) are required for and/or regulate (in a positive or negative manner) coronary cell entry and/or viral replication. We have now studied changes in the expression of genes encoding for SCARF in the context of acute and chronic kidney disease.
METHOD: Data mining of in-house (experimental models of AKI -folic acid nephropathy- and CKD -Unilateral ureteral obstruction- in mice) and publicly available databases (Nephroseq, published single cell transcriptomics studies) of kidney tissue transcriptomics as well as the Protein Atlas database.
RESULTS: Out of 28 SCARF genes identified by Singh et al (Cell Reports 2020), 26 were represented in the experimental AKI database. Of them 7 (27%) were differentially expressed during AKI (FDR <0.05), 4 of them upregulated and 3 downregulated (Figure 1.A). Additionally, 27 were represented in the experimental CKD database. Of them 17 (63%) were differentially expressed during experimental CKD, 6 of them upregulated and 11 downregulated (Figure 1.B). Two genes were consistently upregulated (Ctsl and Ifitm3) and two consistently downregulated (Tmprss2 and Top3b) in both experimental AKI and CKD (Figure 1.A and B). They encode cathepsin L, interferon induced transmembrane protein 3, transmembrane serine protease 2, DNA topoisomerase III beta, respectively. Single cell transcriptomics databases localized Ctsl expression mainly to podocytes and tubular cells while protein atlas showed clear tubular staining. The main site of Ifitm3 was endothelium in both datasets and it was also localized to leukocytes by single cell transcriptomics. Tmprss2 was mainly localized to tubular cells in both datasets while Top3b was widely expressed in parenchymal renal cells, endothelium and leucocytes in single cell transcriptomics. Increased kidney expression of Ifitm3 and decreased expression of Tmprss2 and Top3b were confirmed in diverse CKD datasets in Nephroseq.





CONCLUSION: Both AKI and CKD are associated with differential expression of SCARF genes in kidney tissue, the impact of CKD appearing to be larger. Characterization of these changes and their functional impact in kidney tissue and

beyond the kidneys may provide clues to the increased risk of severe or lethal COVID19 in kidney disease patients.
Kidney SCARF gene expression