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NOVEL INTEGRATIVE METHODS TO IDENTIFY THERAPEUTIC TARGETS AND COMPOUNDS FOR TREATING KIDNEY FIBROSIS

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INTRODUCTION: Chronic kidney diseases (CKD) characterised by renal fibrosis leading to gradual decline of renal function. Despite the urgent medical need there is still no effective therapy to inhibit or reverse the diseases. However, so far only a few therapeutic targets and compounds have been identified in the preclinical and clinical studies for the treatment of kidney fibrosis. Our aim was to develop an integrative framework to improve the identification possible target molecules and compounds which may have anti-fibrotic effects.

METHODS: Comprehensive literature research was performed to identify those genes that have a role in renal fibrosis based on gene knockout (KO) animal studies. Moreover, genes of an extensive human microarray study that correlated with the severity of chronic kidney diseases were listed. Finally, the overlapping set of the two lists were generated and coupled with known compounds altering the function of the investigated genes in anti-fibrotic manner.

RESULTS: Based on KO animal studies we found 91 pro-fibrotic and 73 anti-fibrotic genes which influenced the amount of extracellular matrix (ECM) depositions in the fibrotic kidney. Among them the expression of 54 gene were altered in the human kidney biopsies from patients with CKD as well. More than 300 compounds were identified that affecting these genes may exert anti-fibrotic effect.

CONCLUSIONS: We established an effective method to identify new drug targets and possible compounds that can be repurposed for the treatment of renal fibrosis.

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