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Integrated bioinformatic analysis showing Lcn2 is a key molecular in Autosomal Dominant Tubulointerstitial Kidney Disease-UMOD

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Objectives : Autosomal Dominant Tubulointerstitial Kidney Disease (ADTKD) is a clinical syndrome characterized as the progressive decline of kidney function and tubulointerstitial lesion. However, the pathophysiological mechanism is unclear with limited studies and various. We aimed to analyze essential molecular and pathway functions in the development of the ADTKD.
Methods : We searched the "Autosomal Dominant Tubulointerstitial Kidney Disease" as the Mesh terms in the GEO database. Differentially expressed genes (DEGs) were analyzed and enrichment pathways were conducted based on gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) database. We constructed protein–protein interaction (PPI) using online tool STRING, and Cytoscape with plug-ins to find hub genes and modules. We constructed the mutant UMOD (C195R) transiently transfected cell lines and examined the expression level of the common DEG.
Results : We selected 2 datasets (GSE139585 and GSE97093) to analyze. GSE139585 is C105F mutation with 5 wild-type mice and 6 mutant mice, while GSE97093 is the UMOD ^{C147W} with 4 wild-type mice vs 4 mutant mice in female and male, respectively. 18 DEGs were identified in GSE139585, while 17 DEGs (gender=F) and 85 DEGs (gender=M) were identified for GSE97093. GO and KEGG pathway enrichment analysis can acquire response to stimulus, multicellular organismal process, and metabolic process pathways, etc. We acquired 78 nodes and 208 edges in the PPI network. Top10 hub genes are cyp2e1, cyp2a5, cyp4a12a, cyp2a4, ugt2b36, ugt1a5, ugt1a2, cyp4a14, ugt3a1, and cyp2b9. Three hub modules were identified. Lipocalin 2 (Lcn2) was the common DEG and a member of the hub modules. The mRNA level of the Lcn2 is elevated in the UMOD^{C195R} transfected cell.
Conclusions : Our study first integrated analysis of the expression profiles of the ADTKD-UMOD and identified key pathways and hub genes. Further in vitro experiment showed that Lcn2 is upregulated in the UMOD^{C195R} transfected cell.

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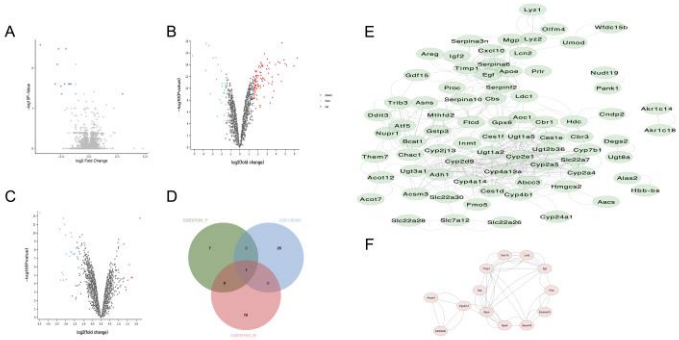
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