CONNECTING THE DOTS: A NETWORK ANALYSIS OF CKD AND AKI GENES

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Abstract

This research project was done to analyze and connect the genes of chronic kidney disease (CKD) and acute kidney injury (AKI) and how we can treat kidney disease from that information. Tools like Dignet, Python, ShinyGO, and ChatGPT were used to compare genes from both conditions and identify shared and unique pathways. We may find better treatment options for kidney diseases by targeting these pathways.

Introduction

The reason I chose to do my project on kidney diseases was because I was intrigued to learn about the severity of kidney diseases, and the fact that we were still trying to find effective goals pulled me in. Kidney diseases are classified into two main types: CKD and AKI. CKD is a gradual loss of function in the kidney, which is often caused by diabetes and high blood pressure (long-term conditions). It is not curable. AKI, on the other hand, is a sudden loss of function in the kidney, often happening because of dehydration, blood loss, or urinary tract infection. It is curable once the underlying cause is cured. Both CKD and AKI are significant health problems, affecting >10% of people worldwide combined, either directly or through the cost and complications such as death. So, the main question I want to answer is, **"How can we better understand the differential gene interactions in CKD and AKI to discover improved treatment options for kidney failure?"**

Methods

The gene pairs associated with CKD and AKI were downloaded from Dignet, a part of Ignet (https://ignet.org), an ontology-based biomedical literature mining system. Custom Python scripts were written to filter and process the downloaded gene-pair data, keeping those pairs with more than three supporting publications. The CDK- and AKI-related genes and gene pair overlaps were determined and visualized using VennDetail. Networks of gene pairs were built, and key genes with the most connections to other genes were identified in Cytoscape. ShinyGO was used to analyze and visualize the significantly enriched top 25 biological functions in terms of KEGG pathways. ChatGPT was then used to assist in interpreting the results.

Results

Dignet returned 86,023 papers for CKD and 77,050 papers for AKI. For gene pairs, CKD had 14,508 unique pairs, AKI had 237 unique pairs, and 561 genes were shared (Fig. 1A). These gene pairs included 3,037 unique genes in CKD, 41 unique genes in AKI, and 414 shared genes (Fig. 1B). For pathways, CKD had 59 unique, AKI had 7 unique, and they shared 233 significantly enriched pathways. After analyzing the unique pathways (Fig. 1C), ChatGPT suggested "insulin secretion", unique to CKD (Fig. 2A), and "systemic lupus erythematosus", unique to AKI (Fig. 2B), as potentially the most relevant results. "AGE-RAGE signaling pathway in diabetic complications" was the top shared pathway between CKD and AKI. The network analysis showed CKD's gene interaction network was more extensive and complex, with significant genes like TNF and INS. In contrast, AKI's smaller network highlighted stress response genes like lipocalin-2 (LCN2).

Conclusion and Discussion

There were more genes and gene pairs in the CKD dataset, likely because there are more research papers about CKD. The gene pair networks show different molecular interactions in CKD and AKI, which could help in developing different treatments. AGE-RAGE signaling pathway was the main shared pathway between CKD and AKI, while insulin secretion was unique to CKD, and systemic lupus erythematosus was unique to AKI. Even though CKD and AKI share many biological functions, important differences should be considered when developing treatments.
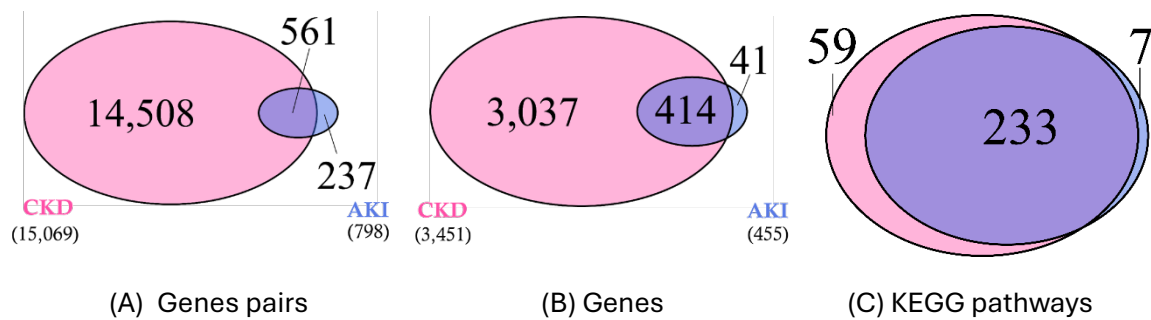
(A) Genes pairs (B) Genes (C) KEGG pathways

Fig. 1. Venn diagram comparing the numbers of unique and common KEGG pathways of CKD and AKI. CKD-Pink, AKI-blue.
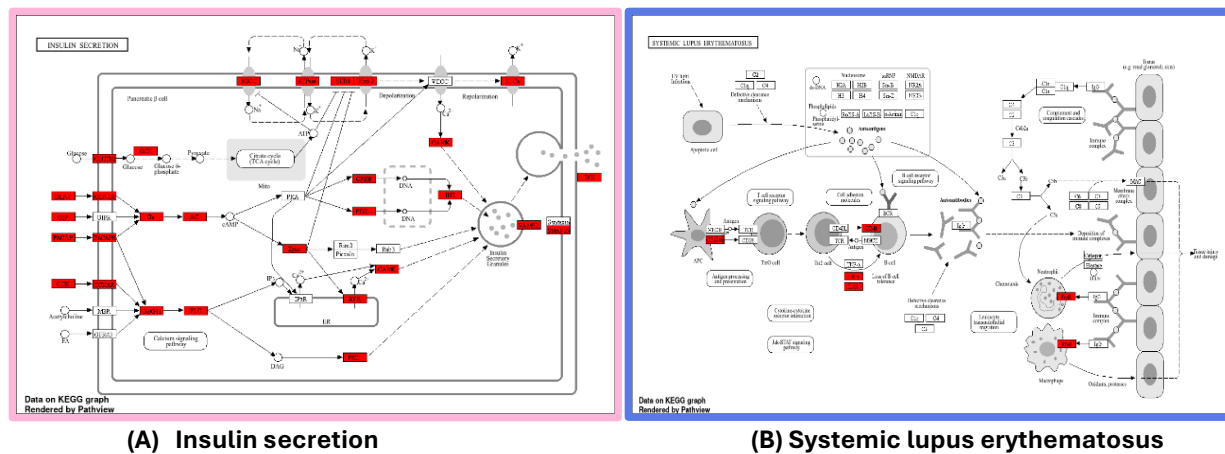

(A) Insulin secretion **(B) Systemic lupus erythematosus**

Fig. 2. KEGG Pathways. Genes included in the Dignet-derived CKD and AKI data are highlighted in red. CKD-Pink, AKI-blue.
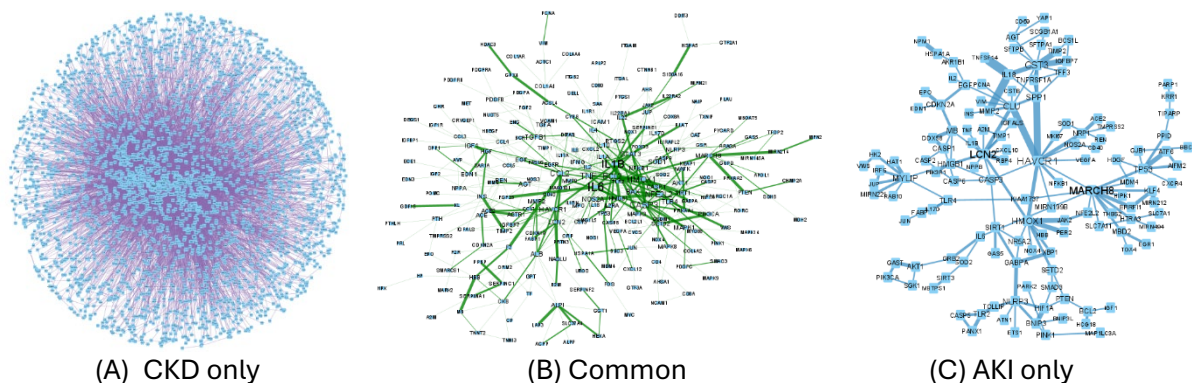

(A) CKD only (B) Common (C) AKI only

Fig. 3. Venn diagram comparing the numbers of unique and common KEGG pathways of CKD and AKI. CKD-Pink, AKI-blue.

References

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