AI-POWERED DIAGNOSTICS

Mining Public Genomics Data Identifies Potential Kidney Injury Biomarkers

Anders Wallqvist US Army

Background: Acute kidney injury (AKI) is a military-relevant disorder associated with high mortality rates. There is a critical need to identify novel sensitive and specific AKI biomarkers that can improve current clinical outcomes.

Objective: Develop computational approaches to mine kidney genomics data and experimentally validate identified candidate biomarker genes.

Methods: We developed a computational protocol that integrates co-expression modules and network analysis to extract candidate genes from DrugMatrix, a large publicly available rat kidney omics database with millions of data points. We performed in vivo validation experiments using mercuric chloride exposure on guinea pigs.

Results: We utilized the iterative signature biclustering algorithm and generated a compendium of rat kidney gene co-expression modules after exposure to diverse toxicants. We performed network analysis by integrating these modules with a high-confidence, protein-protein interaction network and identified the involvement of immunoproteasome in AKI. Mining of other independent gene expression data showed immunoproteasome upregulation in rat kidney following gentamicin exposure. We further performed validation experiments using mercuric chloride-induced kidney injury on guinea pigs and observed upregulated immunoproteasome subunits (PSMB9 and 10).

Conclusion: We developed a computational protocol to mine toxicogenomic big data that enabled identification of immunoproteasome as a potential AKI biomarker. We demonstrated that immunoproteasomes are upregulated during AKI across two distinct species, rat and guinea pig. The unique peptides produced by these immunoproteasomes could serve as non-invasive urine-based biomarkers.