Identification Of In-Common Molecular Pathway In Acute Kidney Injury Using Global Gene Expression Analysis

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Background and goal of study

Acute kidney injury (AKI) may be caused by a number of different diseases through several different physiological processes that either affect glomerular filtration, urine production, or cause tissue damage. Common biomarkers for AKI of any cause suggest a common underlying pathway. The goal of this study was to identify such a pathway using published microarray data.

Materials and methods

Six high-quality microarray studies of gene expression after AKI caused by gram negative sepsis, gram positive sepsis, ischemia reperfusion, malignant hypertension, rhabdomyolysis and cisplatin toxicity were analyzed and compared using R/Bioconductor and Ingenuity Pathway Analysis.

Results and Discussion

A total of 5254 genes were differentially expressed in at least one of the AKI models. 66% we only found in one of the models, but there were in-common features. Four genes were differentially expressed in all six models, 49 in at least five of the models, and 215 were in common to at least four models.

Left: Network of 29 connected genes in-common for at least five models. Genes in squares were in-common to all models.

Right: Hierarchical network showing connected genes in-common to all six, five, and four AKI models.

The in-common genes included many of the known biomarkers and were connected in a central network of three, 29, and 114 in the respective levels of six, five and four models. MYC was the most highly connected gene. This indicates that there is a common molecular pathway in AKI regulated through MYC. This may be useful for identifying new potential biomarkers and for understanding the progression from AKI to chronic kidney disease.

Further, 3464 out of the identified genes were found in only one of the six experimental models. This indicates that these different etiologies of AKI do indeed have substantial unique features that may be useful to understand different ways to activate the central MYC-regulated network.

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Conclusion

A diverse collection of diseases can cause AKI through a limited number of physiological pathways that converges on a common molecular pathway in AKI where MYC activation is a central gene expression regulator.

Identification of in-common genetic regulation in acute kidney injury (AKI) presents a new synthesis of the mechanism behind renal tissue damage and progression of renal dysfunction after AKI.