Researchers use metagene 'portraits' to reveal distinct stages of kidney formation

December 11 2008

In the art world, the most successful portraits are often those that reveal the true essence of the subject – a subject that on canvas, at least, will never age. In the science world, researchers are relying on portraits of gene expression patterns – but, in this case, the images are helping to reveal how various tissues form.

Now, a multi-disciplinary team at UC San Diego has used novel computational methods to gain insight into kidney formation. By performing time-series analyses of global gene expression, and clustering these genes into larger groups known as metagene portraits and also calculating entropy values, the researchers have identified distinct stages of organ formation.

The research, published in the December 9 edition of *Science Signaling*, is also significant in that it suggests additional genes that had not been previously implicated in orchestration of kidney development.

"The approach may also be helpful for understanding tissue regeneration and pathological states," said Sanjay K. Nigam, Professor of UC San Diego's Department of Pediatrics, Department of Medicine (Nephrology-Hypertension) and the Department of Cellular and Molecular Medicine. "Analysis of the metagene portraits suggested points of stability and transition which are not as evident using conventional methods."

Additional research members in the study include Igor F. Tsigelny, a project scientist with UC San Diego's Department of Chemistry and

Biochemistry and the San Diego Supercomputer Center at UC San Diego; and Valentina L. Kouznetsova; Derina E. Sweeney; Wei Wu; and Kevin T. Bush; all with UC San Diego's School of Medicine.

In efforts to provide a more comprehensive view of organogenesis, the researchers compared and analyzed visual representations of gene expression patterns during kidney development. Approximately 30,000 genes were organized into 650 groups called metagenes, or gene clusters known as self-organizing maps (SOMs).

Essentially acting as unsupervised learning neural networks, SOMs cluster genes with similar temporal expression profiles into metagene portraits. In this case, the SOMs were collected using microarray gene expression data and a high-dimensional data analysis program called Gene Expression Dynamics Inspector, or GEDI. UC San Diego scientists then performed a detailed time-series analysis of the kidney SOMs reflecting various stages of organogenesis. That was followed by entropy calculations for each SOM to measure the differences in states during the various stages, before correlating these results with morphometric parameters and specific gene networks.

Taken together, analysis of the metagene portraits suggested that kidney formation could be divided into as many as eight distinct stages.

"Although there is morphological support for the notion of stages, the beginning and end points of those stages can be difficult to define because many basic morphogenetic processes occur simultaneously," said Tsigelny. "Our research suggests that with the metagene analysis and entropy calculations, global gene expression can be used to more clearly define these stages and allow us to have a fuller understanding about how organs form."

Source: University of California - San Diego