

Molecular mechanisms underlying kidney damage in a rat anti-thy-1 model of glomerulonephritis: A Gene expression analysis.

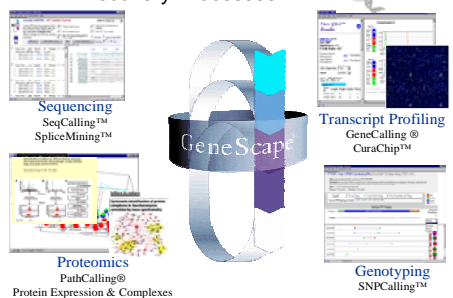


Amitabha Chaudhuri, Glenda Smithson, Gary C. Starling, Carol Pena, Frank Spriggs, Brian Godwin, Faheem Niazi, Mark TrailSmith, Flavia Cruz, Pascal Bouffard, Traci Mansfield, Jeffrey L. Barnes², Veronique L. Barnes², George Yuan³, John Chant and Loic Giot
 CuraGen Corporation, 322 East Main Street, Branford, CT 06405/Probetex Inc. San Antonio, TX 78229
 3Paradigm Array Labs, a unit of Icoria, Inc. 108 T.W. Alexander Drive, Research Triangle Park, NC 27709

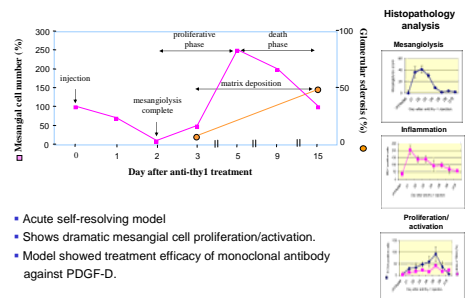
Introduction

- IgA and Lupus nephritis are associated with mesangial cell proliferation.
- The α -Thy-1 induced glomerulonephritis in rats is associated with dramatic mesangial cell proliferation.
- The relevance of the rat model to human proliferative nephropathy is controversial.
- Molecular characterization of kidney damage in α -Thy-1 induced nephritis is likely to reflect differences and similarities between the rat model and the human disease.
- Gene expression analysis using the rat model revealed that the molecular mechanisms underlying kidney damage is similar between rats and humans.

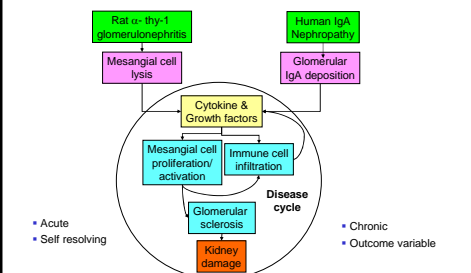
CuraGen's Integrated Discovery Processes



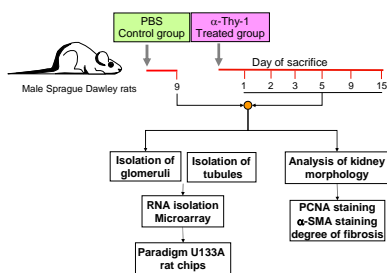
Rat α -thy-1 model of glomerulonephritis



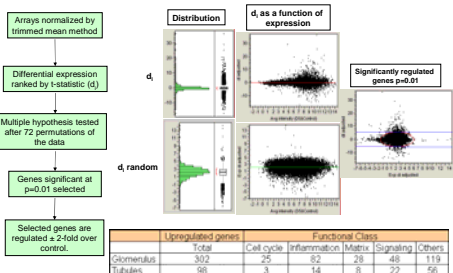
Disease cycle in the rat model has similarities with human IgA nephropathy



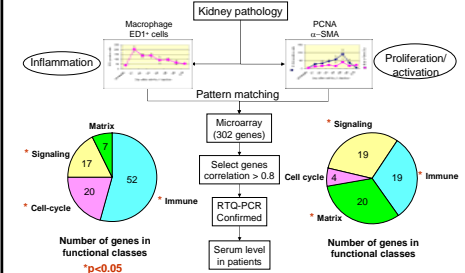
Study design



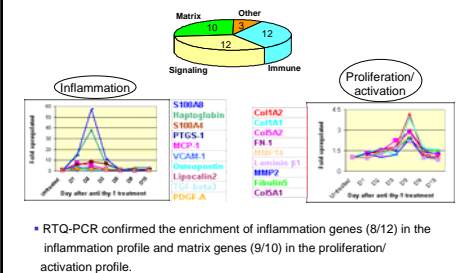
Statistical analysis of the microarray data



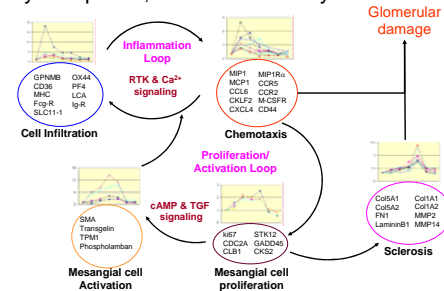
Profile matching segregated genes involved in different processes in the glomeruli



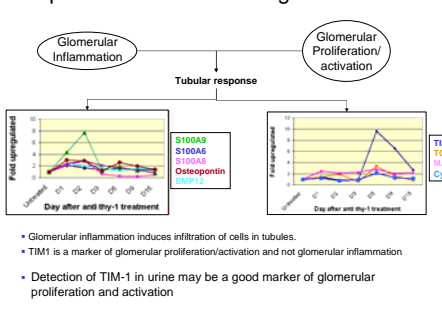
Confirmation of temporal expression of glomerular genes by RTQ-PCR



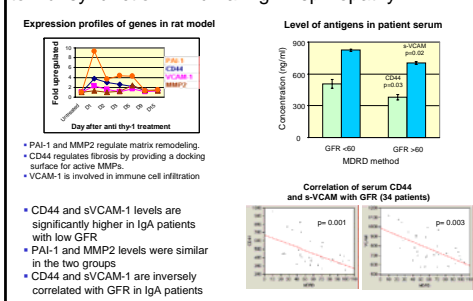
Events leading to Glomerular damage in anti thy-1 nephritis; A molecular analysis



Response of tubules to the glomerular insult



Markers of kidney damage in the rat model are linked to kidney function in human IgA nephropathy



Conclusion & Future studies

- Gene expression analysis revealed that glomerular inflammation precedes glomerular matrix deposition.
- A significant number of genes identified in this study are known to be involved in the patho-physiology of human IgA nephropathy.
- CD44 and s-VCAM1 identified in the rat model were found to be significantly higher in the serum of IgA patients with GFR <60 strongly implicating their involvement in kidney damage.
- Future studies will look into the effect of human monoclonal antibody against PDGF-D in the rat model to identify genes that are regulated by the growth factor.