ESTABLISHING A FRAMEWORK TO INFER GENE REGULATORY NETWORKS FOR KIDNEY DEVELOPMENT.

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During nephrogenesis cells in the metanephric mesenchyme (MM) are induced to acquire an epithelial phenotype upon interaction with the ureteric bud. This is a reiterative process, in which different developmental steps simultaneously take place in different anatomical regions. To understand this process, we devised a two-tiered approach: 1) *in vitro* analysis of conditionally immortalized E11.5 mouse MM cell line (46m) in which mesenchymal-to-epithelial transition (MET) was induced with LiCl; 2) gene expression analysis of post-natal murine kidneys after the end of nephrogenesis.

We demonstrated a consistent time change profile in gene expression patterns after LiCl induction in 46m cells and identified a set of 685 genes differentially expressed throughout the time course experiment (fdr-adjusted p value < 0.05). Differential expression was validated in a subset of genes using real time RT-PCR. For one of them, a transcription regulator previously not known to be involved in murine kidney development, we showed, by immuno-fluorescence staining, expression in a subset of cells in mouse embryonic kidneys (E14.5). We have also recently identified a developmental switch in post-natal kidney maturation (Piontek et al., Nat. Med., 2007). We showed a clear change in the gene expression pattern of early (P11 and P12) versus late (P14 and P15) kidneys and identified 827 differentially expressed genes between these groups ($p<0.001$).

In conclusion, we have developed a framework to study MET, which could be used to identify a potentially important factor for the early stages of kidney development and that can be used to understand post-natal kidney maturation. Further studies using Chip-on-chip, gene knock-down and characterization of epigenetic modifications and microRNA expression patterns will provide enough data to build and test accurate networks, increasing our understanding of relevant gene regulatory networks important for kidney development.