Tissue Bias – Database Project

Case Study I: TF *POU3F2*

* Question: Would we find similar pathways enriched for *POU3F2*-regulated gene clusters if KEGG, REACTOME, or BIOCARTA were used for pathway enrichment analysis instead of Gene Ontology?
* Sample paper: Genome-Scale Transcriptional Regulatory Network Models of Psychiatric and Neurodegenerative Disorders (Pearl)
* Summary: Brain diseases are associated with transcriptional regulatory changes in the brain but the effects of specific transcription factors (TFs) is unknown. In this study, a TRN model for the human brain was constructed. Identified key regulator TFs whose predicted target genes are enriched for genes differentially expressed in brain diseases, including TF *POU3F2*.
* Results: studied gene expression profiles from human subjects with schizophrenia (SCZ), bipolar disorder (BD), major depression disorder (MDD), autism (ASD), and Alzheimer’s disease (AD) and non-diseased controls. Differentially expressed genes between cases and controls were identified. Then they tested for over-representation of each transcription factor’s target genes among differentially expressed genes to find TF-disease associations (Pearl, pg. 126)
* **By matching enriched gene clusters regulated by TF *POU3F2* to Gene Ontology pathways, the study found that *POU3F2* affects the transition from proliferative (cell cycle pathway) to non-proliferative cell states (transcription pathways) (Pearl, pg. 129-130).**
* Conclusion**:** “We validated key network predictions that *POU3F2* target genes are over-represented among differentially expressed genes in PFC from SCZ and BD cases versus controls and that a risk-associated SNP near VRK2 influences gene expression through an interaction with *POU3F2*…anti-proliferative effects are consistent with two recent reports linking *POU3F2* to neural proliferation phenotypes in stem cell models of ASD (Belinson et al., 2016; Marchetto et al., 2017)…convergent evidence presented here adds *POU3F2* to a very short list of well-supported BD risk genes” (Pearl, pg. 131)