



Supplemental Figure 2: A subset of the functional modules predicted by mining highly-connected clusters from functional relationship networks. These modules are organized into a partially overlapping hierarchy, similar to that of the Gene Ontology. Each module consists of genes predicted to be related based on multiple informative genomic datasets. Here, a specific module consisting of PIAS3, MITF, and PAX6 generalizes through two main branches into modules enriched for various transcriptional regulation activities in the cell cycle, apoptosis, and intercellular signaling. The most specific module in the hierarchy links the transcriptional regulators PIAS3, MITF, and PAX6 with very strong evidence drawn from multiple direct binding assays in the BioGRID (Stark et al. 2006). This module has two main branches of more general parents in the hierarchy. The first contains several cell growth, death, and differentiation transcriptional modulators, including JUN, NFKB1, and BCL3. The second contains multiple cell cycle related oncogenes, oncogene activators, and TGF- β family mediators, almost all of which are also transcriptional modulators (Kim et al. 2000). This is likely indicative of two interrelated regulatory programs, the former focused on cell development and differentiation and the latter responding more specifically to extracellular signaling. We have automatically mined and hierarchically organized ~17,000 functional modules of varying specificities from our integrated data.