Supplementary Figure Legends

Supplementary Figure1. Interaction Network of Literature Curated Set of 270 Binary Interactions Mediated By PDZ proteins.

(A) An interaction map of all 270 binary interactions between PDZ proteins and ligands identified by manual literature curation visualized by Cytoscape (Shannon et al. 2003). **(B)** The interaction map of a subset of interactions is illustrated. The PDZ domain containing proteins and ligands are shown as nodes and physical interactions as edges. The nodes are colored according to the type of ligand with the PDZ encoding proteins as red and (green=ClassI; yellow=Class2; blue=Class3; turquoise=PDZ domain to non-Class1,2,3; empty circle=non-PDZ domain to non-PDZ domain mediated interaction). The red edges denote those interactions between PDZ and ligand which could be found in the neighborhood co-expression index of individual PDZ genes with radius=500 (21% of interactions with both proteins represented on microarrays (n=238). Note that some PDZ genes show strong preference for ligand PDZ binding motif class (e.g. Dlg4).

Supplementary Figure 2. A family of CED-8 Like Proteins Containing Conserved PDZ Binding Motifs

Phylogenetic analysis of family of proteins with homology to C. elegans CED-8; Genbank accession numbers as shown. Family members shown with conserved canonical PDZ Class I binding motifs indicated with bracket.

Supplementary Figure 3. Example of Thirteen Gene Families in PDZCBM

Shown are examples of 13 gene families within PDZ ligands arranged by CLUSTALW protein pairwise alignment and p phylogenetic analysis. Nineteen genes encoding RhoGEFs or RhoGAPs found to be enriched by domain analysis are shown. Supplemental Table III contains gene family and PFAM protein domains information for the entire PDZCBM gene set.

Supplementary Figure-Table I. Integrating Comparative Genomics with Phenotype Information of Model Organisms Suggests Novel PDZ Ligands

Drosophila orthologs were identified by reciprocal best hit strategy for 30%(269/899) of the PDZCBM gene set. This table shows a sampling of 36 Drosophila orthologs where 23 (green) genes have been associated with cell polarity/adhesion/cytoskeletal re-arrangements. 26/36 genes have conserved mammalian C-terminal motifs (red). A full accounting of orthologs and phenotypes is presented in Supplemental Table IV. The asterick (*) indicates a non-canonical PDZ binding motif, which has been found in literature survey of ligands. Green coloring in Fly phenotype column indicates GO, mutant, or RNAi annotation suggestive of involvement in processes related to adhesion/polarity. Also shown for comparison's purposes, are the worm orthologs for these 36 Drosophila orthologs when present.

Supplementary Tables

Table 1: Annotation of 136 Human PDZ genes along with mouse, Drosophila, and C. elegans orthologs

Table 2: Annotation of 270 PDZ-Ligand Interactions Curated From the Literature