Supplement 5
Web Server "HMRI" (Human Membrane Receptor Interactome)

Receptors are attractive drug targets because they mediate the communication between the cell and its environment. Figure S6.1 illustrates the two types of human membrane receptors.
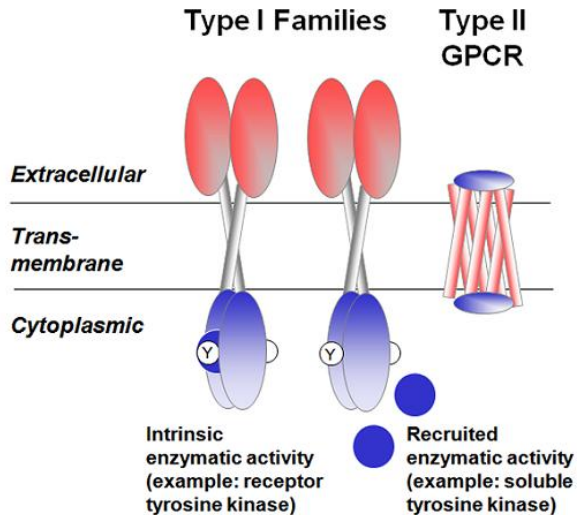

Figure S5.1   Known human membrane receptor types. Type I receptors contain one or two transmembrane helices, and usually exert their signaling function as dimers. There are 18 different families of type I receptors, defined by the enzymatic activity inherent to or recruited to the cytoplasmic domains of the receptors. Type II receptors are G protein coupled receptors, characterized by a seven-transmembrane helical bundle and their interaction with G proteins.

A web server for the human receptor interactome has been implemented and is freely available to the research community. Its URL is:
http://flan.blm.cs.cmu.edu/HMRI/index.html

It provides four basic functions:

1. Check the query protein
This service would perform a check on the input protein to see if the query is a receptor protein or not. If yes, we further check if the input belongs to the GPCR family or not.

2. Search interaction partners for the query protein
This service would search on the whole predicted receptor interactome to find interaction partners for the query. The output is a table listing the retrieved interaction partners scored with higher values than a score cutoff specified by the user.

3. Search interaction pairs among the set of input proteins
This service would search the potential pairs among a group of input proteins. The returned pairwise interaction scores are higher than an input score threshold specified by the user. The output is a table including the retrieved interaction pairs and a graph representation of the pairs, similar to the example shown in Figure S5.2.

4. Check the predicted interaction score and related feature vector for a pair of input proteins
This service would retrieve the predicted interaction score for a pair of input proteins. At the same time, we check if this pair existed in HPRD[1] or not. In addition, we also retrieve the features vector of this requested pair.

5. An example output from HMRI
Here we give an example of using HMRI. We use the above function three as the case study to show. You can input a group of genes to search for their subnetworks on our membrane receptor interactome. For example, "EGFR, DNM2, HCK, TEK", choose your favorite cutoff (for example, 1.5), click "retrieve" ➔

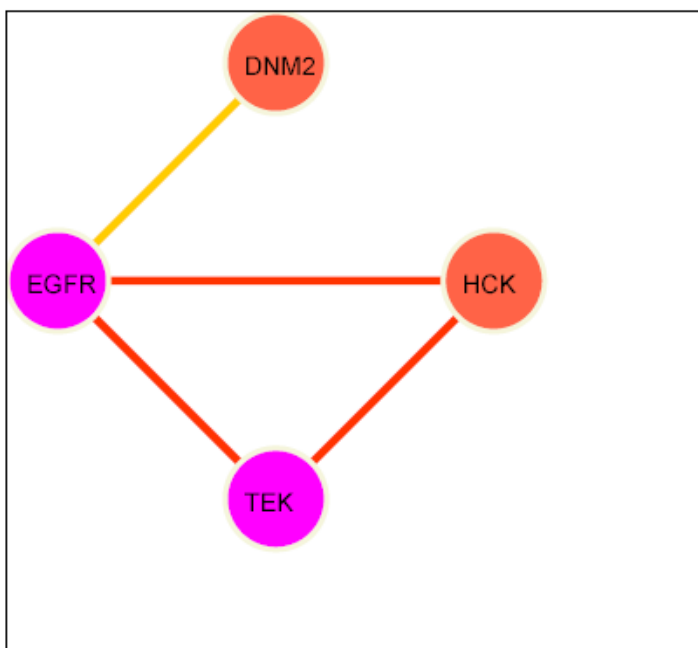| Partner 1	Partner 2	Interaction Score	HPRD-06 Label	Check PairFeatures
HCK: ID-3055 (ncbi)	TEK: ID-7010 (ncbi)	1.80077	No	CheckFeatures
TEK: ID-7010 (ncbi)	EGFR: ID-1956 (ncbi)	2.05351	No	CheckFeatures
HCK: ID-3055 (ncbi)	EGFR: ID-1956 (ncbi)	2.73452	No	CheckFeatures
DNM2: ID-1785 (ncbi)	EGFR: ID-1956 (ncbi)	3.10006	No	CheckFeatures

Figure S5.2   An example output (table and graph) representation from the web server "HMRI". The node labels are the gene names in NCBI and the edge colors refers to edges with different score ranges. The nodes are color coded based on the family of proteins (different colors for type I receptor, GPCR, non-receptor, and ligands).

Bibliography

1.   Mishra GR, Suresh M, Kumaran K, Kannabiran N, et al. and Pandey A. Human protein reference database--2006 update. Nucleic Acids Res 2006 Jan 1; 34(Database issue) D411-4.