Predicted Cancer Invasion Gene Network

Membrane and Protease Genes

The genes furthest upstream in the network consist of membrane-bound genes and proteases. Invasion involves both coordinating signals from outside the cell, often facilitated through membrane-bound genes, and the degradation of the extracellular matrix proteins via proteases.

- ADAM21, ADAM9, and UBE2L6 are all related to protein degradation.
- SCN5A is a sodium channel known to control muscle and neural tissues.
- CD53 is a cell surface marker.

Calcium Signaling

Both calcium-dependent enzymes and a front-to-back intracellular calcium gradient are known to play important roles in cell motility. At the bottom of the pathway is the calcium activated protease CAPN12. CCR9 is a receptor that elevates calcium levels upon binding its ligand. The NARG1 homolog in *Xenopus* (frog) has been found to be activated by calcium and Wnt signaling and is essential for cell migration and adhesion during gastrulation.

MAP Kinase Signaling

Mitogen-active Protein (MAP) Kinases perform roles in a large number of cellular processes, including cell migration. The yeast homolog of STK24 is necessary for invasive growth, and appears to play a similar role in colon cancer. GNAI3 is in a family of MAP kinase signaling modulators.

Membrane Remodeling/ Secretion

We predict the interaction of several genes used in membrane remodeling and/or secretion. The role of this in cancer invasion is previously unreported, and we hypothesize that this is a novel connection.

Invasion Network

Network Frontier

SCN5A
UBE2L6
ADAM21
CD53
ADAM9
NARG1
STK24
AK091308
NARG1
GNAI3
FAM43A
RPL32
KRT20
TFDP1
GLS
DHX32
GAS1
Negative Regulation of Mitotic Cell Cycle
SLC1A4
Carboxylic Acid Transport
CCR9
EIF2AK2
NRCAM
Cell Migration
PPP2R1A
Regulation of Wnt signaling
AA099748
CHMP4C
CTGF
Ectoderm Development
SCRN3
CAPN12
Response to Virus
IFITM1

Legend

Round 1 Knockdown
Round 2 Knockdown
Round 3 Knockdown
GO Term
Activation
Inhibition
E-gene
Functional category enrichment in frontier genes

Network Frontier Functional Categories

Our current invasion network predicts more than 1000 additional genes to be potentially involved in the invasion process, and each connects to the network at one location. To determine if the frontier at any one location is enriched for a particular biological function, we overlapped the frontier genes with functional categories from the Gene Ontology (GO) database. The heatmap below shows the significance of overlap for every point in the network and the top-scoring GO function categories. Darker rectangles correspond to more statistically significant overlap, while lighter rectangles show insignificant or no overlap.