EPHRIN PATHWAY & BREAST CANCER

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EPHRIN OVERVIEW

- Guidance of axon growth
- Tissue boundary formation
- Cell migration
- Membrane bound proteins
- Activation only through cell-to-cell interaction
- 2 subclasses - A & B
NORMAL EPHRIN FUNCTION

- Axon guidance
- Retinotopic mapping
- Migration factor in intestinal epithelial cell migration
- Reverse signaling
- Angiogenesis: EphB2 and B4

Picture (Arvanitis & Davy, 2008)
EPHRIN PATHWAY & BREAST CANCER

- EphB2 & EphB4 implicated in breast cancer development
- EphB2 & B4 expression mainly cytoplasmic
- B2 expression is negatively correlated with disease survival
- B4 expression is positively correlated with tumor stage
- EphB4 shown to increase tumor proliferation and migration by blocking apoptotic pathways
- High levels of ligand stimulates adhesive forces between tumor cells
Treatment: How does EphA2 stimulation via selective monoclonal antibodies act as a tumor suppressor?

- EphA2 overexpression in epithelial cell tumors
- Inability to bind ephrinA1 in tumors

(Carles-Kinch et al.)
EphB6, Kinase deficient receptor binds to EphB4 and EphA2. Tumor Suppression

- Inhibition of EphB6 leads to overexpression of EphB4/A2 leading to cell growth and migration

- Highly expressed in normal mammary epithelial cells and noninvasive neoplasms
  - (Kaenel, 2012)

- Down regulated in metastatic cancer

- So Should we Activate it?
Summary

- Largest of the RTK families
- Emanate bidirectional signaling
- Regulate developmental processes and tissue homeostasis
- EphB6 is involved in suppression of cancer
- Overexpression of EphB4 or EphA2 leads to stimulation of cell growth and migration
References:


