

A Marker and Therapeutic Target for the PI3K Pathway

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BACKGROUND

GIV (also known as girdin) is an AKT (serine/threonine protein kinase) enhancer that triggers cell migration and cancer invasion. Despite recent studies showing that the expression of genes/proteins associated with PI3K (phosphoinositide 3-kinase)-Akt signaling, actin remodeling, motility, and invasion vary among tumors, most have failed to make a transition into cancer clinics as biomarkers for prognostication.

TECHNOLOGY DESCRIPTION

Researchers from UC San Diego have identified which two phosphotyrosines in GIV interact directly with two domains of PI3K that stabilize receptor association of PI3K and trigger production of PIP3 (phosphatidylinositol-3,4,5-triphosphate) at the plasma membrane during cell migration. Previously, GIV was shown to be a novel metastasis-related protein whose full-length transcript (GIV-fl) is expressed exclusively in highly invasive colon, breast, and pancreatic carcinoma cells and not in their poorly invasive counterparts (Garcia-Marcos et al 2010). This technology includes sequenced defined targets on GIV to which an antibody can be generated and would provide the basis for prognosticating survival in cancer patients. In addition, and more importantly, this could also be the basis of a novel anti-cancer therapeutic.

An exploratory biomarker study conducted on patients with stage II colorectal cancer revealed a significant correlation between GIV-fl expression in tumor epithelium and shortened metastasis-free survival: survival rate for patients with GIV-fl-positive tumors is significantly reduced compared with the patients with GIV-fl-negative tumors (Garcia-Marcos et al 2010). Ongoing work has confirmed that visualization of GIV's phosphotyrosine is an accurate readout of hyperactivation of the growth factor-GIV-PI3K pathway, and the degree of phosphorylation at these residues in GIV indicates the extent of signaling along this pathway. In breast cancers, the degree of phosphorylation correlated with the aggressiveness of tumors.

INTELLECTUAL PROPERTY INFO

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RELATED MATERIALS

- ▶ Garcia-Marcos M, Jung BH, Ear J, Cabrera B, Carethers JM, Ghosh P. Expression of GIV/Girdin, a Metastasis-Related Protein, Predicts Patient Survival in Colon Cancer. *FASEB J.* 2010 Oct 25. [Epub ahead of print]
- ▶ Ghosh et al. A G α -GIV Molecular Complex Binds Epidermal Growth Factor Receptor and Determines Whether Cells Migrate or Proliferate. *Mol Biol Cell.* 2010 Jul;21(13):2338-54.
- ▶ Garcia-Marcos M, Ghosh P, Farquhar MG. GIV Is a Nonreceptor GEF for G Alpha i with a Unique Motif That Regulates Akt Signaling. *Proc Natl Acad Sci U S A.* 2009 Mar 3;106(9):3178-83.

PATENT STATUS

| Country | Type | Number | Dated | Case |
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OTHER INFORMATION

KEYWORDS

G proteins, girdin, growth factor receptor tyrosine kinases, Src kinase, epidermal growth factor receptor, cell migration, PI3K, Akt

CATEGORIZED AS

- ▶ **Medical**
- ▶ **Disease: Cancer**

RELATED CASES

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