The Role of G Proteins in Non-Canonical Wnt Signaling in Non-Small Cell Lung Cancer

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Background

Lung cancer is the leading cause of cancer death of men and women in the United States. The canonical Wnt signaling pathway is highly associated with cancer.

Winn et al.1 showed that Wnt 7a levels are reduced in 80% of NSCLC and restoration inhibits cell proliferation and tumor initiation. Previous work has demonstrated that Wnt 7a signaling, through its receptor Fzd 9, inhibits transformed growth of NSCLC through activation of the tumor suppressor gene PPARγ.

Frizzled (Fzd) proteins have a similar structure to GPCRs. G proteins are a major target of pharmaceutical therapies.

RATIONAL: Given the fact that past literature suggests that canonical Wnt pathway in NSCLC is mediated by GαQ, our purpose has been to define which G proteins mediate the Wnt 7a/Fzd 9 signaling pathway in NSCLC.

HYPOTHESIS: G proteins GαQ and Gα16 mediate non-canonical Wnt signaling.

METHODS: Western Blot: assay used to probe for the protein of interest (from B2B and NSCLC cell lines). Transfection: used to implement foreign plasmids into B2B and NSCLC cell lines. Luciferase Assay: used to detect the protein of interest in a tissue section. IHC: staining assay used to measure cell proliferation. Cell Growth Curve: measure of cell proliferation. MTS: measure of cell viability (not shown).

RESULTS: Co-expression of Wnt 7a/Fzd 9 decreases cell proliferation of NSCLC cell lines. B2B and NSCLC cell lines were screened for decreases cell proliferation of NSCLC cell lines. Transfection of either GαQ or Gα16 decreases cell proliferation in the NSCLC cell lines tested.

CONCLUSION: GαQ or Gα16 are critical mediators of the effects of Wnt 7a/Fzd 9. GαQ or Gα16 are potential therapeutic targets for lung cancer.

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