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FGFR1 lentivirus lung cancer cell model for anti-cancer drug discovery and the study of FGFR1 signaling pathway

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Introduction & Aim: Lung cancer is the most common diagnosed cancer worldwide, with the highest cancer death rate. Prognosis of lung cancer patients is still poor despite recent advances in treatment, thus more effective methods for lung cancer management are urgently needed. Overexpression of fibroblast growth factor receptor 1 (FGFR1) is associated with high incidence and mortality in lung cancer. FGFR1 signaling is implicated in oncogenic traits such as proliferation, cell survival, angiogenesis and migration. FGFR1 and its ligand basic FGF (bFGF) are promising new therapeutic targets. This study aimed to develop a simple, effective in vitro lung-cancer cell model for cancer therapy development and to study FGFR signaling in lung cancer.

Methodology: An overexpressing FGFR1 cell line was developed by inserting lentiviral constructs encoding the FGFR1 gene into A549 human lung adenocarcinoma cells and validated by PCR, gel electrophoresis, and gene sequence. FGFR1 overexpression was characterized using a unique bFGF mAb developed in our laboratory and assayed for adhesion, invasion, migration, clonogenicity, cell cycle and apoptosis. PI3K/Akt/mTOR signaling pathway was examined by Western blots.

Results: A stable lentiviral FGFR1 A549 cell model was established with >20-fold higher expression of FGFR1 protein and mRNA compared to A549 parent. Ligand binding to FGFR1 activated the PI3K/Akt/mTOR signaling pathway increasing adhesion, invasion, migration and apoptosis. The overactive PI3K pathway, associated with negative metastatic signaling, can be effectively blocked by unique bFGF mAb. The bFGF mAb not only neutralized free bFGF but also inhibited the endogenous bFGF.

Conclusions & Significance: This model provides an effective and simple screening kit for anti-FGF1 drug compounds for lung cancer treatment and a tool for understanding the molecular mechanisms of the FGFR1 signaling pathway in lung cancer. Furthermore, this basic FGFR1 lentiviral toolkit is transferrable to study FGFR1 signaling in any type of cancer cell.

Biography

Yiguang Lin is a Medical Graduate and has completed his PhD in Pharmacology from the University of New South Wales and Post-doctoral training at Prince Henry Hospital, Australia. He was a Visiting Professor at the University of Michigan working with Dr. Peter A Ward and Yale University with Dr. Paul Lizardi. Since 2003, he has been a Tenured Faculty Member at the University of Technology Sydney. He has published widely in many reputed international journals. His research interest has long been in the area of pharmacology of anti-inflammatory drugs, anti-cancer drugs and natural compounds while he recently shifted his interest to cancer biology and medicine with a focus on liver and lung cancer.

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