DIXDC1: A New Role in Metastasis of Cancer Cells

INVENTION: A critical question in cancer biology is the relationship between tumor-initiating mutations, including oncogenes and tumor suppressor genes, and the propensity for tumors to metastasize. LKB1 is a kinase that is a tumor suppressor, which when lost shows increased metastatic potential. Investigators at Salk together with their collaborators entered into a research effort to define molecular signatures of metastasis caused by loss of LKB1, and identified an AMPK-independent pathway revealing a central role for the scaffold protein DIXDC1. When DIXDC1 is present, cells are less mobile and stay adhered to the surface through large focal adhesion complexes; and when absent, cells are less adhesive due to smaller adhesion complexes and thus more likely to spread. DIXDC1 is also frequently downregulated in human cancers, which correlates with poor survival likely due to the increased probability of metastasis. These results further illuminate the link between tumor suppressor molecules and metastatic events and may well provide new targets for more effective treatments for cancer.

APPLICATIONS:
• Potential biomarker to predict if a tumor will respond to FAK or Src kinase inhibitors
• Possible target for activators of DIXDC1 or its upstream components to modulate metastasis

ADVANTAGES:
• DIXDC1 is a direct substrate of the LKB-1 dependent kinases connected to metastatic progression
• DIXDC1 alone shows a significant influence over the metastatic phenotype

STAGE OF DEVELOPMENT: DIXDC1 is shown to suppress lung colonization by metastatic lung tumor cell lines in mouse models.

BACKGROUND: Non-small cell lung cancer (NSCLC), even when discovered early, has an aggressive tendency to spread through the body (metastasis), and is thus one of the leading causes of cancer-related deaths. There is an urgent need to understand what causes a lung tumor to metastasize and the connection between mutations that initiate tumor formation and metastasis, with the goal of preventing metastasis to increase the probability of survival.

INVENTORS: Dr. Reuben Shaw & Jonathan Goodwin

PATENT STATUS: PCT patent application WO2016/011065 is pending


CONTACT: Melissa Rodgers; mrogers@salk.edu; (858) 453-4100 x1481

TECHNOLOGY ID: RD1390; S14009