Identification and Characterization of a Rare Subpopulation with Cancer Stem Cell Properties in Lung Cancer

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Lung cancer is the leading cause of cancer-related mortality in the US, and over 70% of patients experience metastases in non-small-cell lung cancer (NSCLC). Systemic therapy treatment is often used, but there is minimal success due to recurrence. Cancer stem cells (CSCs) are known to be chemoresistant and to drive tumor movement in many cancers, and are key to addressing this issue via CSC-targeted therapy. Prior research has suggested several CSC markers in NSCLC, but some are controversial and none have had truly adequate sensitivity and specificity. Aberrant activation of the Hedgehog signaling pathway has been implicated in malignancies such as basal cell and pancreatic carcinomas, but its role in lung cancer has been poorly described. Thus, I hypothesized the role of SHh as a CSC marker. The project was conducted with both in vitro and in vivo studies, including FACS, ddPCR, IF staining, qPCR, mice treatments, MTS and migration assays. A small subpopulation of NSCLC cells was found to secrete SHh on the cell membrane, and is solely responsible for producing the SHh protein. These SHh+ cells have paracrine capabilities, demonstrating CSC features. Furthermore, they maintain CSC features in vivo, and greater SHh+ cell proportions are correlated with greater chemotherapeutic resistance. Finally, higher SHh+ percentages are linked to advanced cancer stages and shorter patient TTP, and have clinical significance as an indicator for NSCLC disease progression. These results strongly suggest the potential in creating SHh+ CSC-targeted drug therapeutics. My studies elucidate the role of Hedgehog signaling in CSC maintenance, and provide a foundation for improved chemotherapy, targeted drug treatment, and prognostic tools for lung cancer patients.

Awards Won:

Second Award of $2,000