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The concept of “cancer stem cells” has emerged as an important theme for cancer research in the past few years. Normal stem cells are defined by their dual capacity to regenerate selves through self-renewal mechanism and to produce mature cells through differentiation. Recent evidence suggests that most cancers, if not all, are sustained by a relatively small population of stem-like cell, referred to as “cancer stem cells”, with the same ability to perpetuate the production of progeny with limited proliferative ability. As well, recurrence or metastasis is orchestrated by the post therapy residual cancer stem cells that escape treatment. Therefore, the selective targeting of cancer stem cells is believed to offer advances in cancer treatment and diagnosis, by attacking the disease at its root. The “stem-like” component of a tumor has been isolated and purified through an experimental strategy that sorts the cells based on the (i) expression, or lack thereof, of surface markers, or (ii) efflux of the fluorescent dye Hoechst 33342 (side population phenotype), or (iii) enzymatic activity of aldehyde dehydrogenase 1 (ALDH1), or (iv) ability to form spheres in an *in vitro* culture assay and then subsequent functional serial transplantation of each fraction into experimental animal models to evaluate the relative capacity to form tumors that recapitulate the original phenotype.

Signaling pathways such as Notch, Wnt, Hedgehog, PI3K/AKT, and PTEN/AKT have been shown to tightly regulate the stem cell state. However, the cell signaling pathways that are preferentially activated in the cancer stem-like cells are not well defined. Research into these pathways may lead to more specific targeted therapies for pediatric malignancies with hopes for improved outcomes and less toxicity. We are interested in the role of the inappropriate maintenance of a stem-like cell phenotype in pediatric tumorigenesis/leukemogenesis.

The questions below provide the gist for our research interests:

1. What are the self-renewal or stem cell-related pathways that are activated and may contribute to the survival of cancer stem cells in pediatrics tumors and promote tumor progression and or relapse?
2. What roles microRNAs (miRNAs) play in the survival (growth) and maintenance of stem-like cancer cells? Using the stem-loop reverse transcription, real-time quantitative polymerase chain reaction (RT-qPCR) assay in a high-throughput 384 wells format, we have identified a number of miRNAs that are differentially express between the stem-like enriched fractions and the non-stem like counterparts in medulloblastoma and hepatoblastoma cell lines. In particular, we found marked up-regulation of miR-21 in medulloblastoma and hepatoblastoma stem-like cells. Functional role of these miRNAs and other genes can be demonstrated using knockout or knockdown strategies as well as pathway specific inhibitors.

Ho MM, Ng AV, Lam S, Hung JY. Side population in human lung cancer cell lines and tumors is enriched with stem-like cancer cells. *Cancer Res.* 2007 May 15;67(10):4827-33.