Identification of DDR2 as a Critical Molecule in Breast Cancer Stem Cells

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More than 90% of breast cancer patient mortalities are attributed to cancer metastasis and chemoresistance, for which underlying mechanisms remain unclear. In recent years, accumulating evidence suggests that cancer stem cells contribute to metastasis and chemoresistance. Meanwhile, several receptor tyrosine kinases (RTKs), well-known cell signaling mediators in human cells, were found to be involved in breast cancer progression and metastasis. I thus hypothesized that specific RTKs may contribute to the characteristics of breast cancer stem cells. These RTKs can act as tumor markers or therapeutic targets for breast cancer. In this project, I found that when human mammary epithelial cells overexpress the transcription factor Foxq1, they showed apparent epithelial to mesenchymal transition (EMT). The overexpression of Foxq1 also led to the development of stem cell characteristics including an increase in CD44+/CD24- cell population as well as mammosphere formation. A Q-RT-PCR screening to determine the expression levels of all RTKs identified that DDR2 had the highest expression in Foxq1-induced stem cells. Furthermore, I found that the expression of DDR2 was highest in Basal B human breast cancer cell lines, which is the breast cancer subtype most commonly associated with the stem cell/progenitor cell. Lastly, I determined that the expression of DDR2 was significantly high in the metastatic 4T1 mouse tumor cells. In summary, DDR2 was shown to be highly expressed in stem cell models and metastatic cells. Thus, DDR2 is a potential critical molecule in cancer stem cells, which contributes to cancer metastasis and chemoresistance. Targeting DDR2 will provide a novel approach to the treatment of Basal-like breast cancer, for which targeted therapy is currently unavailable.

Awards Won:

Second Award of $2,000