The Department of Pharmaceutical and Biomedical Sciences

Research Seminar Series

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"Role of p38 gamma and ErbB2 in alcohol-induced aggressiveness of breast cancer"

Dr. Luo's lab focuses on the major health problems of alcoholism, alcohol abuse, and the medical complications of excessive drinking. Among his lab's research projects, Dr. Luo is interested in elucidating the cellular/molecular mechanisms underlying alcohol-promoted tumor progression, particularly the metastasis of breast cancer cells.

Both epidemiological and experimental studies indicate that excessive alcohol exposure increases the risk for breast cancer and enhances metastasis/recurrence. However, the underlying mechanisms remain unclear. Cancer stem cells (CSCs) play a critical role in cancer metastasis and recurrence. We used MMTV-neu transgenic mice and *in vitro* models to investigate the tumor promoting effects of alcohol. Chronic alcohol exposure increased breast CSC population and enhanced the lung and colon metastasis in MMTV-neu transgenic mice. Alcohol exposure caused a drastic increase in CSC population and mammosphere formation in cultured breast cancer cells overexpressing ErbB2/HER2. Alcohol exposure stimulated the phosphorylation of p38γ MAPK (p-p38γ) and ErbB2, and increased CSCs in the mammary tumor tissues. Alcohol activated ErbB2/HER2 and selectively increased p-p38γ MAPK as well as the interaction between p38γ MAPK and its substrate, SAP97 in cultured breast cancer cells. However, alcohol did not affect other isoforms of p38 MAPK, such as p38α/β MAPKs. Blocking p38γ MAPK signaling significantly inhibited an alcohol-induced increase in CSC population, mammosphere formation and migration/invasion of breast cancer cells overexpressing ErbB2. Therefore, p38γ MAPK is downstream of ErbB2 and plays an important role in alcohol-enhanced aggressiveness of breast cancer.