ABSTRACT: Cyclic AMP-dependent protein kinase A (PKA) and the Src Family Kinases (SFKs) are important signaling proteins in the field of cell biology. When these proteins become dysregulated, abnormal cells survive, proliferate, and migrate uncontrollably. Recently, data showed that PKA-dependent phosphorylation and activation of SFKs during chronic stress is correlated with higher mortality rates in ovarian cancer patients[1]. This study was unique in that it explicitly showed the collaboration of PKA and SFKs in promoting tumor invasion and metastasis. Preliminary data in the Deming laboratory has shown that SFKs can tyrosine-phosphorylate the catalytic subunit of PKA (PKA-C) and subsequently increase the activity of PKA-C *in vitro*. Therefore, we hypothesized that SFKs and PKA-C participate in a feed-forward loop that further promotes tumour growth and invasion in SKOV3 cells.

To begin to test our hypothesis, we aimed to determine 1) whether SFKs tyrosine phosphorylate PKA-C in SKOV3 cells and 2) the impact of SFKs on PKA-C activity. We report that Fyn, a SFK family member, tyrosine phosphorylates PKA-C in SKOV3 cells, specifically at Y69. In addition, we were able to recapitulate the results observed in the stress-induced ovarian cancer cell model system described by Armaiz-Pena et al[1] demonstrating PKA-mediated SFK activation in the presence of the stress hormone norepinephrine. Importantly, when SFK activation was inhibited pharmacologically, there was a decrease in norepinephrine induced PKA activity in the SKOV3 ovarian cancer cells. These findings illustrate novel aspects of the complex norepinephrine-induced signaling network between SFKs and PKA *in vitr*o.

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[1] Armaiz-Pena G.N., J. K. A., A. Cruz, et. al. (2013) Src activation by β-adrenoreceptors is a key switch for tumour metastasis. *Nature Communications* **4**