

## **Gita Byraiah**

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*Mentor:* Kaylee Schwertfeger, Microbiology, Immunology, and Cancer Biology

## ***The Role of Osteopontin in FGFR1 - Mediated Breast Tumorigenesis***

Osteopontin is a protein secreted by tumor cells and cells of connective tissues that is known to mediate breast tumor formation. This protein is secreted into the microenvironment where it interacts with cell surface proteins and changes cellular processes, ultimately resulting in tumor formation. The fibroblast growth factor receptor-1 (FGFR1), a receptor that is amplified in approximately 8-10% of human breast cancers, triggers a cascade that results in generation of osteopontin. To study the mechanisms of FGFR1 activation *in vitro*, our laboratory uses mammary epithelial cells with a modified version of the receptor that is activated using a synthetic dimerizer. We have demonstrated that the activated cells express and secrete high levels of osteopontin.

Furthermore, we found that osteopontin in the media of these cells was cleaved into fragments. It has been hypothesized that cleavage of osteopontin by extracellular proteases called matrix metalloproteases (MMPs) is an important step in tumor formation. Therefore, we hypothesized that expression and cleavage of osteopontin are key mediators of the FGFR1-mediated tumorigenic properties of these cells. Initial studies examined the ability of MMPs to cleave osteopontin in our cell culture system using an MMP-specific inhibitor as a control.

To further study the effects of FGFR1-induced osteopontin on tumor-forming properties, osteopontin production was inhibited using small-interfering RNA (siRNA) to prevent translation of osteopontin mRNA into protein. We hypothesize that osteopontin is associated with key properties of tumor formation: cell proliferation, migration, and invasion and we expect these properties will be diminished with inhibition of osteopontin. By studying the role of osteopontin in tumor formation, we can potentially develop therapies designed to target osteopontin in breast cancer patients.

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