

## **Focal Adhesion Kinase and Isometric Tension**

**Presenter** Miede, Kimberly

**Advisor** Wysolmerski, Robert

**Collaborators:** Goeckeler, Zoe

Focal adhesions are multi-protein complexes that allow the cell to adhere and interact with the extracellular matrix. Proteins in focal adhesions link the actin cytoskeleton to the extracellular matrix providing the physical linkage needed for the cell to generate tension. One of the major components in focal adhesions is focal adhesion kinase (FAK). FAK is a nonreceptor tyrosine kinase known to regulate cell growth, adhesion, migration, and cytoskeletal organization. Since FAK is important in linking the actin cytoskeleton to the extracellular matrix at sites of focal adhesions, we hypothesized that the loss of FAK modifies focal adhesions and disrupts the cell's ability to generate maximal tension. FAK knockout (FAK  $-/-$ ) mouse embryonic fibroblasts (MEFs) and wild-type littermate fibroblasts (FAK-WT) were utilized in the experiments. Data shows that loss of FAK induces a rounded morphology with few cellular protrusions. In FAK  $-/-$  MEFs, the F-actin assumes a cortical distribution while in the FAK-WT MEFs actin is localized to central stress fibers that traverse the long axis of the cells. Focal adhesions in FAK  $-/-$  MEFs are larger compared to control cells. Expression of FAK in FAK  $-/-$  MEFs rescues this phenotype. Cells expressing FAK appear more spread, exhibit a greater number of cell processes and have more organized actin stress fibers. Isometric force measurements indicate that FAK  $-/-$  MEFs have a 50% reduction in basal tension compared to FAK-WT MEFs. Interestingly, agonist stimulated FAK  $-/-$  MEFs only produce a 3-5 dyne increase in tension compared to the 50-70 dyne increase in force by agonist stimulated FAK-WT MEFs. Despite changes in isometric force production, myosin II localization in FAK  $-/-$  MEFs appears similar to control cells. These findings implicate an important role for FAK in cellular tension production. This work was supported by NIH grants: T-32HL090610, HL45788, and RR016440