# CALIFORNIA STATE SCIENCE FAIR
## 2012 PROJECT SUMMARY

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**Project Number**
**S1737**

**Project Title**
# Structural Integrity of the Cytoskeleton in Response to Myosin Inhibitors

**Abstract**

**Objectives/Goals**
For cancer, diabetes, and other diseases, myosin inhibitors offer potential prevention and treatment by blocking cell migration and stopping diseased cells from spreading. The myosin inhibitors Blebbistatin, ML-7, and Y-27632 reduce signaling by non-muscle myosin II (NMII), myosin-light chain kinase (MLCK), and Rho-associated protein kinase (ROCK), respectively. These signaling pathways play significant roles in disease development and regulation of the cytoskeletal structure. Here, I studied a mechanism of controlling cell mobility by evaluating the effects of these myosin inhibitors on cytoskeletons. I hypothesized
(1) that Y-27632 would be the most effective in reducing cytoskeletal integrity, and
(2) that higher drug concentrations would weaken the cytoskeleton the most.

**Methods/Materials**
Cells were passaged and cultured in fresh media. After drug treatment, cells were fixed and permeabilized. Signal enhancer reduced nonspecific binding. Cells were immunostained with antibodies and imaged with fluorescence microscopy. Microtubule and stress fiber integrity with respect to drug concentration was analyzed.

**Results**
Y-27632 was the most effective drug in reducing actin and tubulin expression. ML-7 inhibited microtubule formation, while Blebbistatin weakened stress fibers. Y-27632 caused disassembly of central stress fibers. ML-7 caused disruption of peripheral stress fibers, as well as the cells' loss of spread morphology. No consistent correlation between cytoskeletal integrity and drug concentration was evident.

**Conclusions/Discussion**
As I hypothesized, Y-27632 is the most effective drug in weakening cytoskeletal integrity by affecting both stress fibers and microtubules. Blebbistatin inhibits the formation of stress fibers, while ML-7 weakens microtubules. ML-7 degrades peripheral stress fibers critical in maintaining the rounded cell shape, whereas Y-27632 reduces the number of central stress fibers. Therefore, cytoskeletal integrity depends mostly on ROCK expression, as well as the strength of peripheral stress fibers and microtubules. My other hypothesis that higher drug concentrations resulted in weaker cytoskeletal integrity was partially supported.

**Summary Statement**
Cytoskeletal integrity was observed in response to the myosin inhibitors Blebbistatin, ML-7, and Y-27632 which inhibit NMII, MLCK, and ROCK, respectively.

**Help Received**
Used lab equipment at University of California, Los Angeles under the supervision of Dr. Chih-Ming Ho.