# Abstract

## Statement of problem to be addressed

The flow of information through signaling pathways in stem and progenitor cells triggers events such as proliferation, differentation, and programmed cell death. A disruption in signaling, as can caused by a gene mutation or environmental factor, influences cell behavior in a way that can precipitate diseases like cancer and neurodegenertion. It stands to reason that if we can monitor and influence signaling events in stem and progenitor cells with sufficient resolution, we will be able to counter the effects of such diseases. Significant technical advances over the last decade in our ability to monitor and control cell state has yielded speculation of a coming wave of rational and targetted therapies. However, the landscape of therapeutics in use today is populated overwhelmingly by classes of molecules that long pre-date the modern era of genomics and proteomics focused research.

## Obstacles experienced in similar projects

Studying cell signaling is difficult

* The massive diversity in signaling molecules present in cells causes a 'needle in the haystack' problem for finding those responsible for a particular mechanism.
* The intertwined nature of signaling pathways impedes our ability to study a single pathway in isolation.
* Difficulty translating between domains

Stem cell populations have diverse contexts

* Melanoma Cancer Stem Cells
* Human Embryonic Stem Cells
* Adult Neural Progenitor Cells

## Approach and results

Focus on Wnt/ß-Catenin signaling.

* turns out to be key regulator in many interesting stem cell contexts
* restriction which gives individual projects a constraint in scope can turn out to be beneficial
* practical ramifications, in house domain expertise in both perturbation and measurement of the pathway

Use of automated data acquisition and analysis.

* applies to both discovery of mechanism and generation of therapeutic leads
* unbiased approaches overcome pain-points inherent to studying cell-signaling
* work within thesis is proof-of-concept that high throughput techniques can be adapted to difficult to culture cell-types such as hESCs and aNPCs

Parallel experimentation in multiple stem cell based models.

## Impact to the Field

As I applied these approaches to research, I contributed to peer reviewed publications accounting:

* the repurposing of FDA approved drugs to modulate Wnt signaling in disease relevant contexts using in vitro and in vivo stem cell models
* identification of disease mechanisms centered around Wnt misregulation in stem and progenitor cells