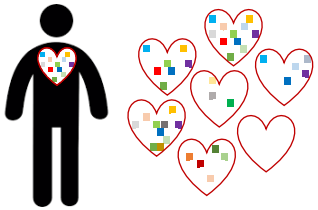
Opportunity

Link SNPs to function
Group SNP combinations
Predict risk and treatment



good		antagonistic	low
bad		additive	medium
ugly		synergic	high

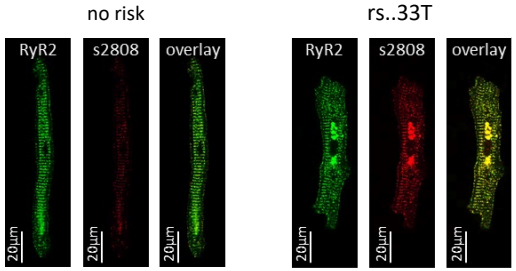
Risk of Arrhythmia

Objectives

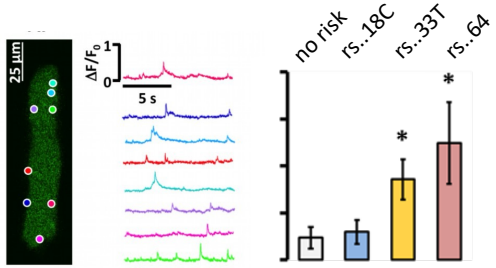
- **Learn Methodology**
  - Use protein labeling to detect their phosphorylation and co-distribution with other proteins
  - Use live-cell imaging to visualize local signals and dynamic changes in calcium
  - Measure ion currents with patch-clamp technique

- **Determine impact of SNPs on function**

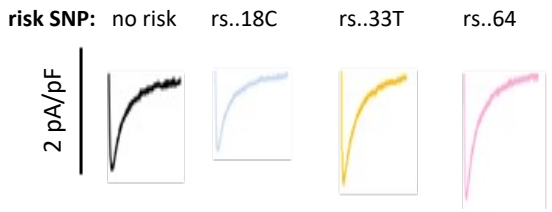
RyR2 phosphorylation at s2808 (labeling)



Calcium sparks (live-cell imaging)



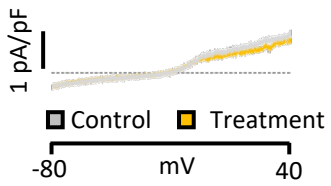
Calcium-current (Patch-clamp)



- **Group SNP combinations according to combined impact and predict risk and therapeutic target**

Mechanism-based Prediction

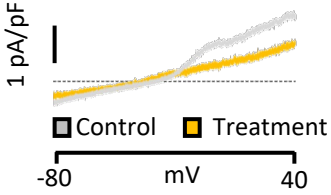
High risk (two risk SNPs; rs..18AC + rs..33CT)
Small control current



Unresponsive to treatment

SK-current (Patch-clamp)

Low risk (no risk SNPs; rs..18AA + rs..33CC)
Normal control current



Responsive to treatment