Module 2: Systems Engineering

Technical
- Shannon Hughes (Mod 2, T/R)
- Agi Stachowiak (W/F)
- Aneesh Ramaswamy (T/R)

Teaching Assistants
- Module 2: Kim Davis

Communications
- Atissa Banuazizi
- Leslie Ann Roldan

Ceri Martina Caroline
Module 2: Systems Engineering

- A few words about 20.109 grading philosophy
- Brain break before thinking more about cell signaling
- Drug resistance & Systems Biology
- Module 2 overview -- in lecture & in the lab
- Short review of the EGFR system
- What we are going to do.
- What we were going to do (discuss M2D4).
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2012 AAAS: Dance your Thesis
http://vimeo.com/50490103
Clinical application: Blocking HER2 signaling decreases breast cancer progression...

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Modified from Pohlmann et al.
Clin Cancer Res December 15, 2009 15; 7479
The elephant in that dance:
What happens to patients who take an anti-HER2 drug?

Disease progression resumes in ~ 1 year --
“acquired resistance”
The elephant in that dance: Mechanisms that mediate resistance.

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How can we do better using a systems approach?

Systems biology aims to solve important problems like drug resistance through experiment + mathematical modeling.

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Experimental Context: EGFR System

Design Goal:

Overcome resistance to EGFR inhibition in SKOV3 human ovarian cancer cells.

Approach:

Use mathematical models to make predictions and ‘high throughput’ experiments to test hypothesis.

Themes of the module:

Cancer Systems Biology
High Throughput Screening Technologies
Cool Science Interlude
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Experimental Techniques:
- cDNA library prep + mutation analysis PCR
- DNA sequencing
- Drug/Inhibitor + Growth Factor Stimulation
- Phosphotyrosine Western blot
- High Throughput Cell Viability Assay -- Robots!

Data Analysis Techniques:
- ODE model simulation
- Sanger sequencing analysis
- Densitometry -- IC50
- Handling large data sets -- visualization & quantification
A very communication intensive module:

In lab ‘mock’ Journal Club -- M2D3
Journal Club presentations (individual) -- M2D5/8
In lecture ‘Design-your-own-HTS’ -- M2D6
Full written research report + revision

+ mid-term evaluations (of us)
## Module 2: Systems Engineering

<table>
<thead>
<tr>
<th>Day</th>
<th>Lab:</th>
<th>Lecture:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Explore the System</td>
<td>Where does SB fit in?</td>
</tr>
<tr>
<td>2</td>
<td>Do we have a mutant?</td>
<td>SB &amp; Mutation</td>
</tr>
<tr>
<td>3</td>
<td>Analysis + Planning</td>
<td>Math in drug design</td>
</tr>
<tr>
<td>4</td>
<td>Low-throughput Screen</td>
<td>(Semi)Quantifying activity</td>
</tr>
<tr>
<td>5</td>
<td>Journal Club</td>
<td>HTS Experimentation</td>
</tr>
<tr>
<td>6</td>
<td>Analysis + Planning</td>
<td>Design your own screen</td>
</tr>
<tr>
<td>7</td>
<td>High-throughput Screen</td>
<td>So much data!</td>
</tr>
<tr>
<td>8</td>
<td>Journal Club</td>
<td>HTS in industry</td>
</tr>
</tbody>
</table>

Tuesday, October 8, 13
Today in lab: EGFR pathway model

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