HOW TO MAKE A SCIENTIST

Brian Teague

Whitehead Seminar Series for Highschool Teachers
12/1/2014
First, a shout-out.
What is a scientist?
A scientist is ...

... a practitioner of the scientific method.

... an accurate, independent thinker.

... a big nerd.
What is iGEM?
iGEM is a synthetic biology competition.
Make it or Break it:

Diesel Production

and Gluten Destruction

the Synthetic Biology Way
iGEM 2010 Winner: Slovenia

DNA coding beyond triplets

Team Slovenia 2010
Bacterial Biosensors: How to build a bacterial biosensor with these parts
iGEM 2009 Winner: Univ. of Cambridge

BioBricks: Colour Generators
iGEM makes synbio accessible.
iGEM HQ provides
• parts
• instructions
• infrastructure
• oversight

iGEM promotes
• education
• community
• openness
The MIT iGEM Cycle

- Nov/Dec: Advertise, recruit, choose the team (12)
  - Across all disciplines and majors
- January: IAP “iGEM bootcamp”
- Spring semester: meet twice weekly
  - Continue skills development
  - Project selection
  - Begin designing experiments and DNA
- Summer semester: in the lab daily
- Fall: develop wiki, poster & presentation
- End of October: International Jamboree
A Day in the Life

• 9:15 morning meeting
  – Discuss results, difficulties
  – Coordinate the day's activities, short-term plans

• 10:30 – noon: SCIENCE

• 1:00 professional development
  – Read papers, Writing Lab, weekly review

• 2 - ??: more SCIENCE
Making undergraduates that are...

... practitioners of the scientific method....

... accurate, independent thinkers....

... big nerds....

support

ownership

success
How do you support development?

- Resources
- Daily feedback
  - Professional standards.
- Structure and prioritization
- Experiential support
The iGEM Experience

Synbio is cool!

The first day in the lab!

Define a project

Man, science is hard.

Present at the Jamboree!

Grrr, nothing is working.

It's .... working!
Ownership drives learning, nurtures motivation.
A story from Biology I

**EXPERIMENT**
- **P Generation**
- **F₁ Generation**

- Female: ![Red-eyed female]
- Male: ![Red-eyed male]

Females × Males → All offspring had red eyes

**RESULTS**
- **F₂ Generation**

A story from Biology I

Challenge: a gifted class full of strategic learners
Solution: a high-stakes experience with very little support
- Organogenesis
- Heart cells → pacemakers (oscillators!)
- Cure Parkinson's (Genome editing)
- Cure mad cow (prions & protein folding)

- Cure cancer (detect & destroy)
  - A "protein primer"
  - Proteins by design
  - Modularity/composable
  - Extracellular → biomaterials
  - 1 μM scale
Ownership drives learning, motivation

- Choose the project
- Choose the approach
- Do *all* the work
- When you get up to present....
Nothing succeeds like success.

- Confidence
- Pride
- Fun!
- Requires careful targeting of the problem
  - (and lots of support.)
Outcomes
iGEM Improves Skills
iGEM Changes Attitudes

Percent with Indicated Response

Did the iGEM experience affect your interest in lab research?
- My interest/confidence has not changed
- I'm now more interested/confident

Did the iGEM experience affect your interest in biological engineering?
- My interest/confidence has not changed
- I'm now less interested/confident

Did the iGEM experience change your thinking about your career path?
- My interest/confidence has not changed
- I'm now more interested/confident
MIT iGEM 2014
Improving the Diagnosis & Treatment of Alzheimer's Disease
Non-Amyloidogenic

s-APPα

P3 γ-secretase

α-secretase

AICD

C83

Amyloidogenic

s-APPβ

β-Secretase inhibitors

β-secretase

Aβ40; Aβ42

γ-secretase

C99

AICD

Plaques

Oligomers

Discovery Medicine / Can Zhang, 25 Sept 2012
Healthy Brain  Severe AD

National Institutes of Health
Medline Plus
In vitro model system
Native receptor detection

**MIT iGEM**

β-AMYLOID

miRNAs

miRNA SENSORS

miRNA GENERATOR

BACE1

BACE2

miRNA TRANSCRIPTIONAL ACTIVATOR

ENGINEERED BCR

NATIVE RECEPTORS

DETECT ➔ TREAT
Native receptor detection

LilrB 2 or PirB

β-AMYLOID

TEV CLEAVAGE SITE

TRANSCRIPTIONAL ACTIVATOR
BBa_K1391114
BBa_K1391113

BBa_K1391115

COFILIN

TEV PROTEASE

RESPONSE

4Kim et al., Science, 2012
5Barnea et al., PNAS, 2007
Immunostaining to detect receptor expression
Immunostaining shows LilrB2 expression

(-) LilrB2

(+) LilrB2

[Images of cell staining with DAPI nuclear stain and LilrB2]
Immunostaining shows PirB expression
Flow cytometry indicates receptor localization to membrane.
Biotin-streptavidin assay to detect β-amyloid binding
β-amyloid binding to LilrB2: confocal microscopy

(-) LilrB2

(+ ) LilrB2

28 µm

DAPI nuclear stain

β-amyloid
Testing native receptor activation

- LilrB
- 2 or PirB

- TEV CLEAVAGE SITE
- BBa_K1391114
- BBa_K1391113

- β-AMYLOID

- COFILIN
- TEV PROTEASE
- BBa_K1391115

- TRANSCRIPTIONAL ACTIVATOR

- mKate2
Native receptor activation: unexpected results

**Transfection Marker (eBFP)**

**Inactive:** 
- \((-\) \(\beta\)-amyloid)

**Active:** 
- \((+\) \(\beta\)-amyloid)

**LilrB2**

**PirB**
Open Questions

• Scalability
  – Resource-intensive – money, time, people

• Transferrability
  – Level-appropriate?
  – (though there is an HS division......)

• Democratization and social impact