NORTHEASTERN

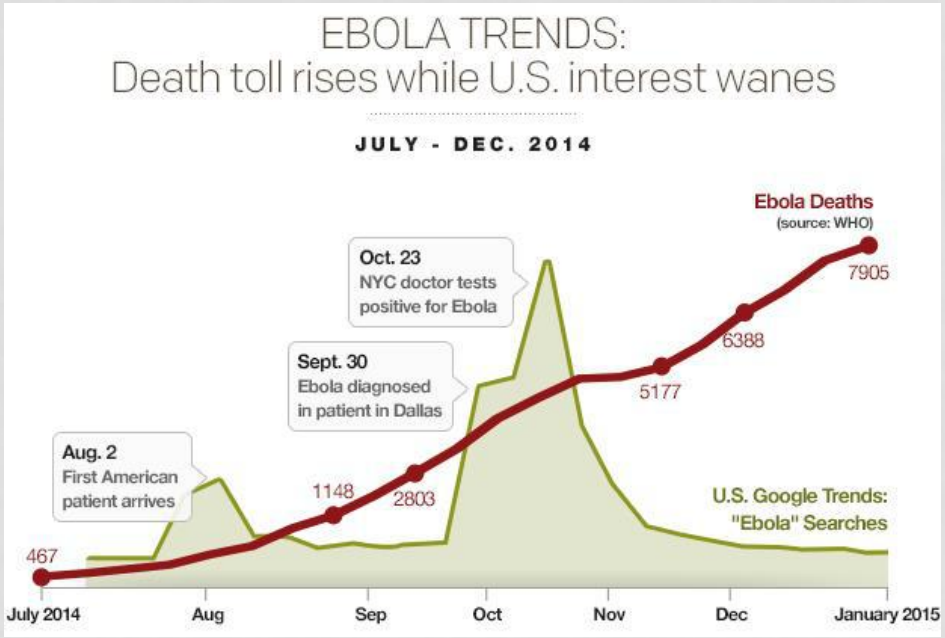
IGEM 2015

IN LIGHT OF THE 2014 EBOLA OUTBREAK

"Dr. George D. Yancopoulos, chief scientific officer of Regeneron, said the crisis had pointed up shortcomings in biodefense. "Nobody is really prepared," he said. "Nobody in the world has rapid response capabilities."

—New York Times, Jan 2015

THE NEED



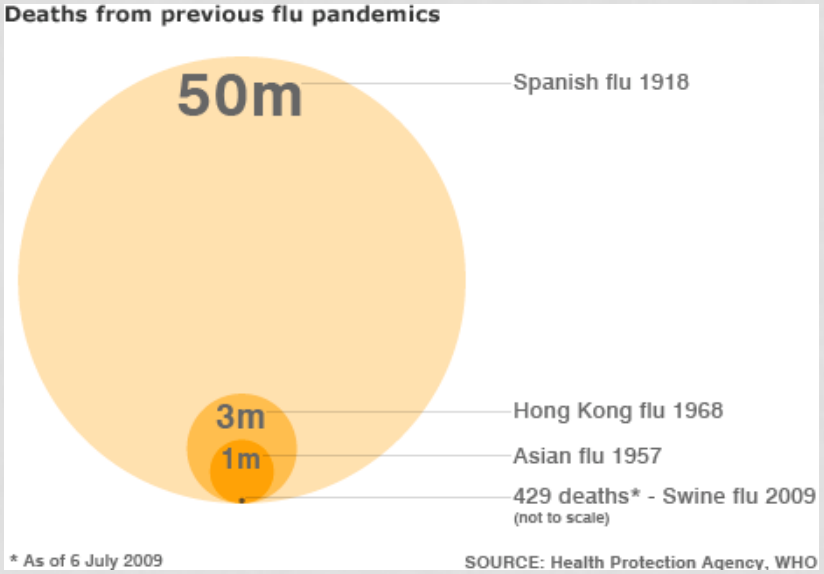
- During that time a potential anti-Ebola antibody cocktail, ZMapp, was going through preclinical studies
- 7 doses available total

POTENTIAL FOR FUTURE OUTBREAKS

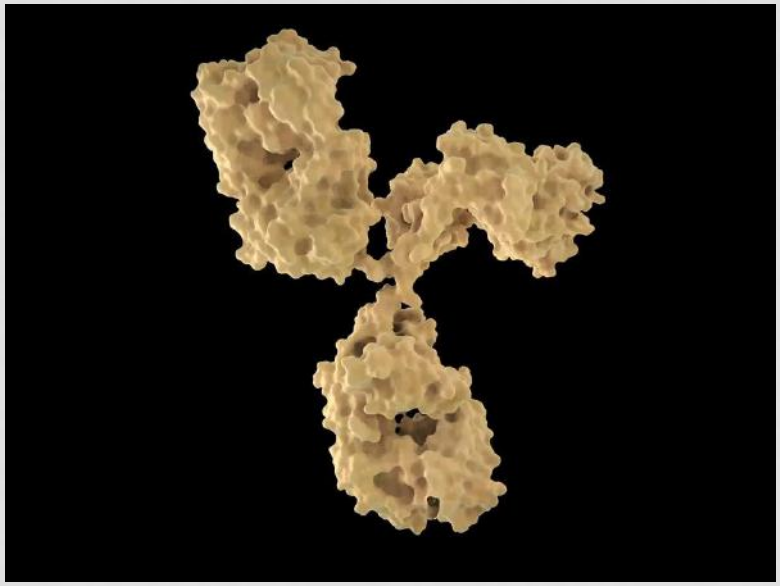
"I rate the chance of a nuclear war within my lifetime as being fairly low. I rate the chance of a widespread epidemic, far worse than Ebola, in my lifetime, as well over 50 percent."

—Bill Gates

POTENTIAL FOR FUTURE OUTBREAKS



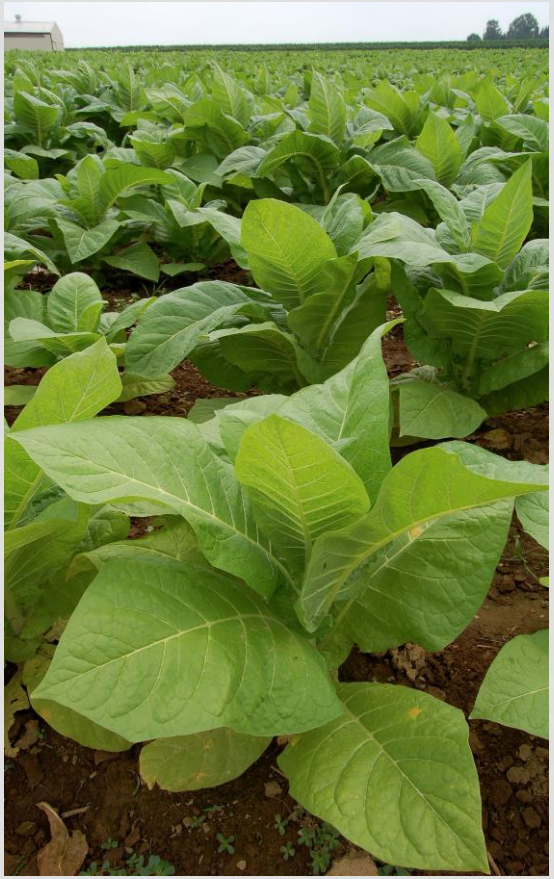
ANTIBODIES



- Antibodies are the best potential solution
- They can be quickly isolated and sequenced from infected patients
- A quickly available supply of antibodies would to paramount to slowing a viral epidemic

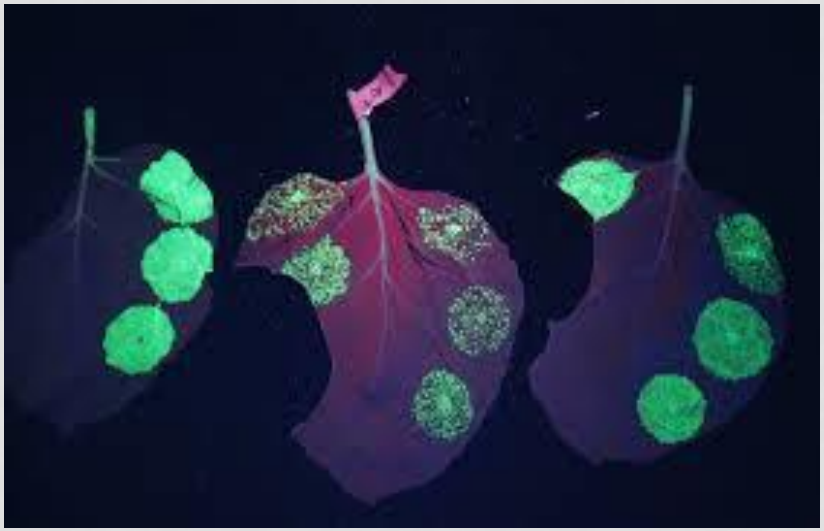
CURRENT PRODUCTION METHODS

>$200M



THE CURRENT "SOLUTION"

- The tobacco plant was a proposed solution to making large quantities of antibody
- Agrobacterium containing the DNA for the therapeutic antibody, was forced into the plant leaves by vacuum infiltration
- The tobacco grows and the antibody is purified from the plant cell lysate



New York Times

THE CURRENT "SOLUTION"

- In theory, this is a quick and inexpensive method for rapidly producing lots of antibody, dependent upon arable land rather than high-sterility CHO vats.
- In practice, it is not.

A BETTER SOLUTION

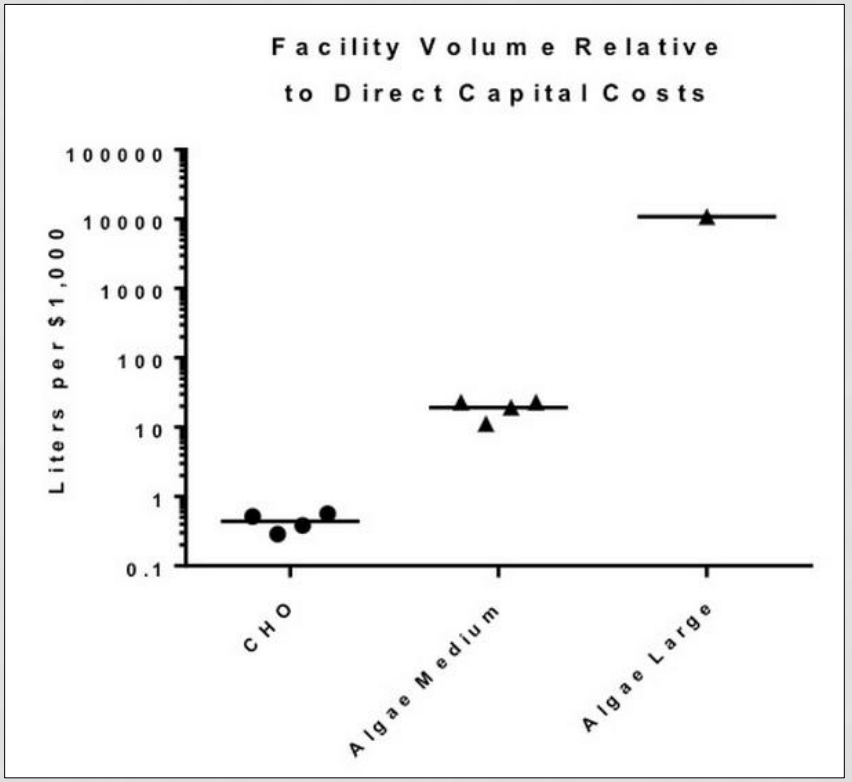
- Use *Chlamydomonas reinhardtii*, the workhorse of microalgae research, as a large scale production platform for antibodies

Mammalian	**Tobacco**	**Microalgae**
• Very high productivity	• High productivity	• Low productivity
• Most expensive	• Less expensive	• Least expensive
• Scalable with sterile vats	• Scalable with arable land	• Most scalable with ponds
• Medium growth-period	• Longest growth-period	• Shortest growth-period

CHLAMYDOMONAS REINHARDTII

- Quickly, cheaply scalable in large raceway ponds
- Unaffected by mammalian pathogens, a constant concern in CHO facilities

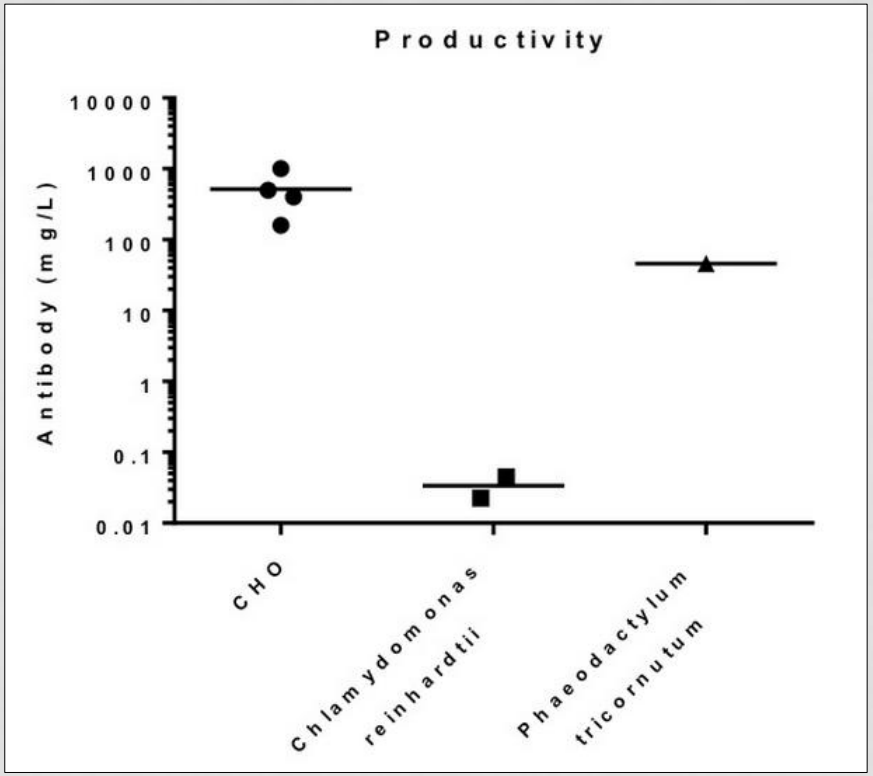
CHLAMYDOMONAS REINHARDTII



http://bit.ly/1YFuHJe

POTENTIAL FOR GLOBAL ALGAE DISTRIBUTION

CHLAMYDOMONAS REINHARDTII



http://bit.ly/1KUpmYC

- Productivity is the current obstacle

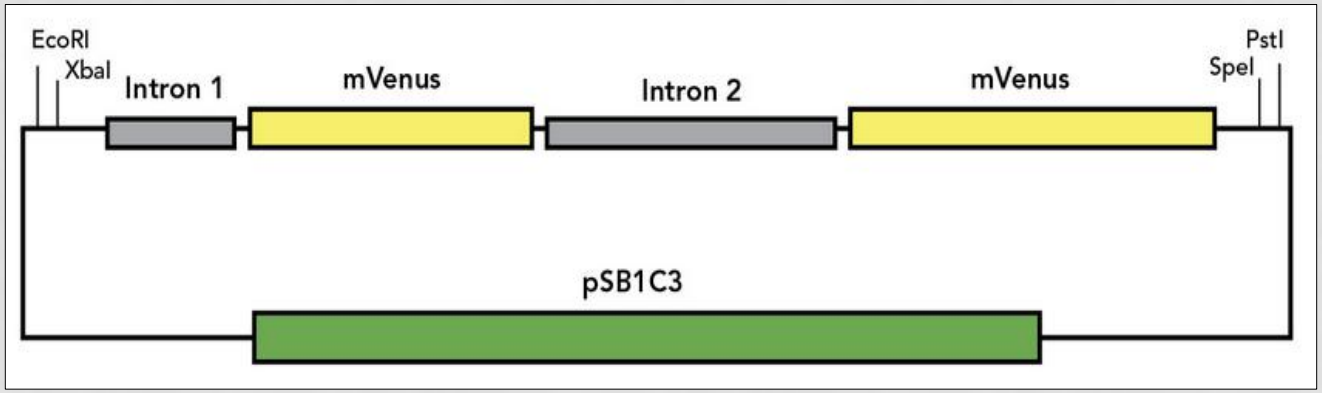
INITIAL APPROACH

- We sought to create a novel high-expression plasmid via Gibson Assembly
- Nuclear codon-optimized and iGEM standardized

FINAL APPROACH

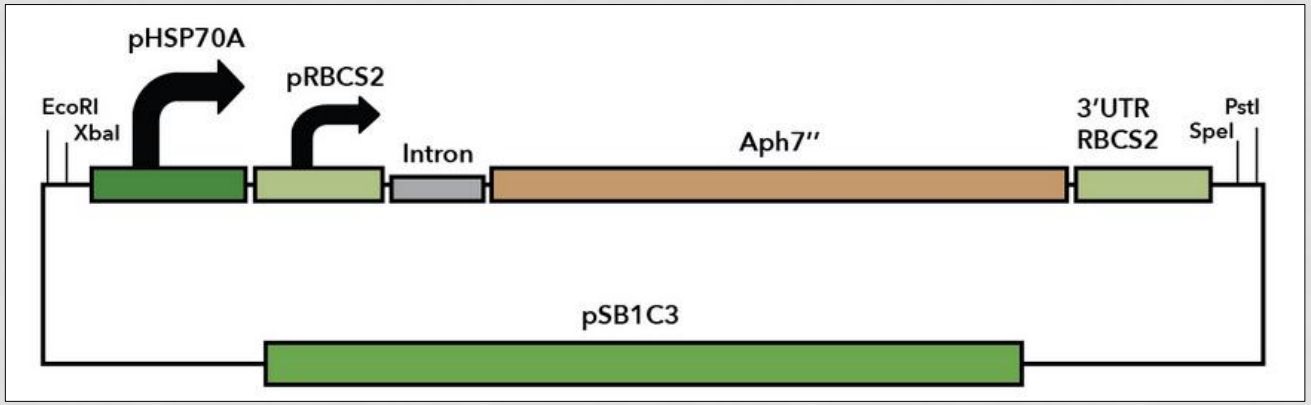
- Recognizing the lack of usable parts, we set out to standardize those that will make work with C. reinhardtii feasible for iGEM

mVenus



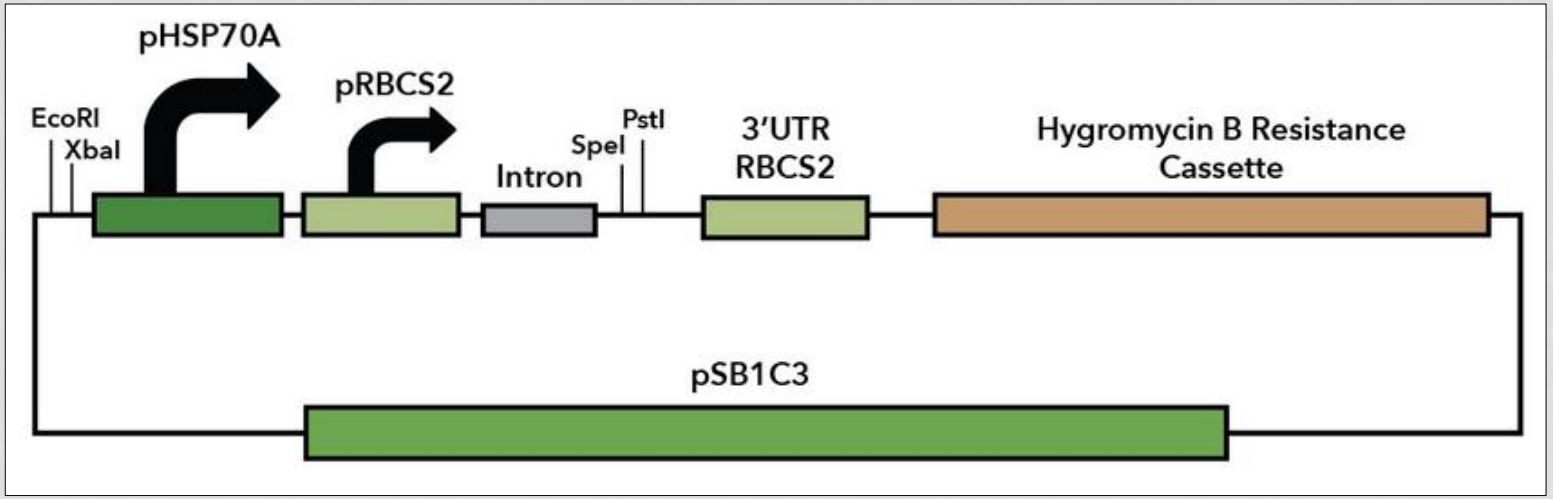
PARTS

HygromycinB Resistance Cassette



PARTS

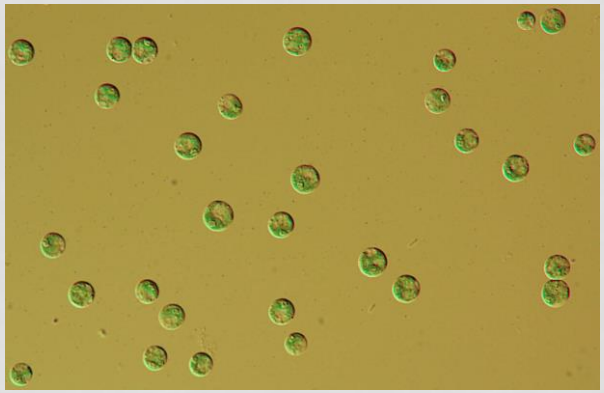
- **Expression Plasmid**: HSP70A-RBCS2 promoter/RBCS2 Intron1 flanked by the iGEM prefix and suffix.
- Useful for 1) heterologous protein production & 2) comparison of promoter strength



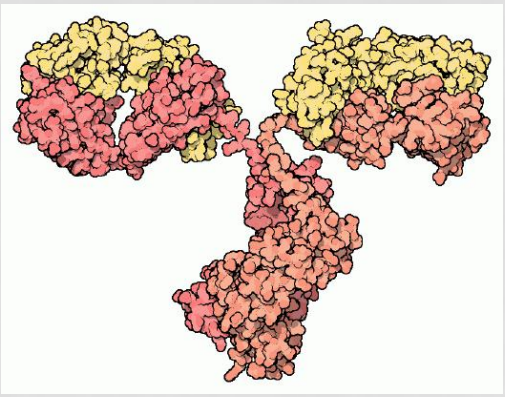
WHY MICROALGAE?

- iGEM teams should experiment with microalgae as their production chassis

Consume CO2



Inexpensive to grow

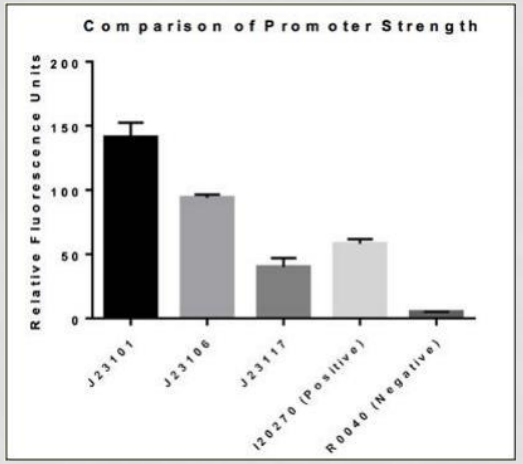


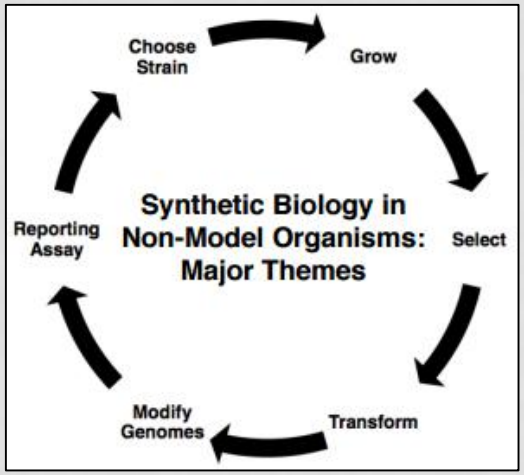
Capable of producing complex proteins

Sapphire Energy, Sunomix & Solazyme

INTERLAB

- Interlab study
- Contributed to the Yale Handbook for non-model chassis



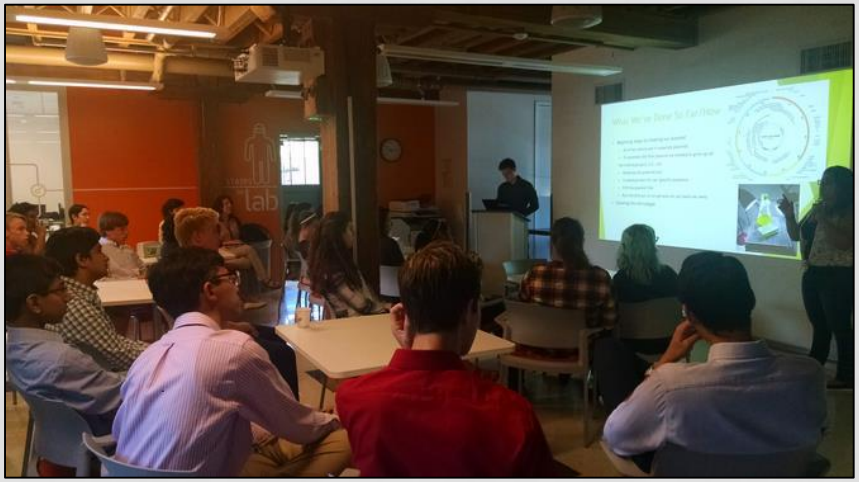


OUTREACH

- Met with other teams at this year's NEGEM
- Spoke to AbVitro, a high-throughput antibody company about the potential for using microalgae

OUTREACH

- Gave a talk about synbio to high school students involved with Biogen's "Adventures in Biotechnology," encouraging them to try iGEM



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