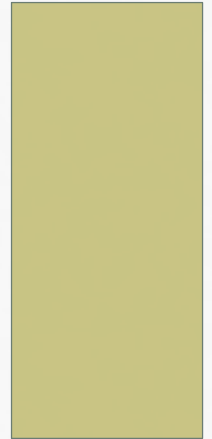




NORTHEASTERN

IGEM 2015



IN LIGHT OF THE 2014 EBOLA OUTBREAK

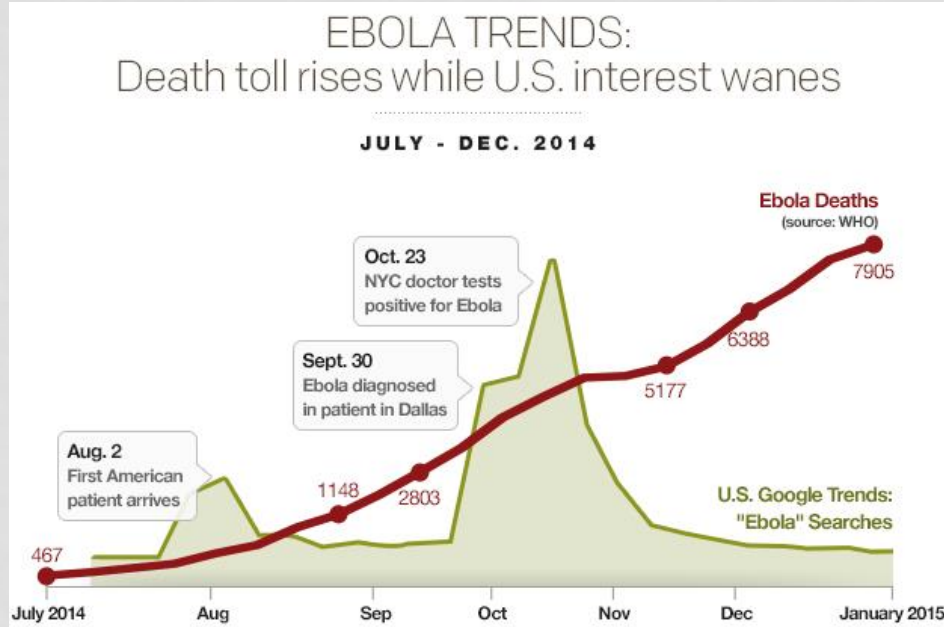
"Dr. George D. Yancopoulos, chief scientific officer of Regeneron, said the crisis had pointed up shortcomings in biodefense.

"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

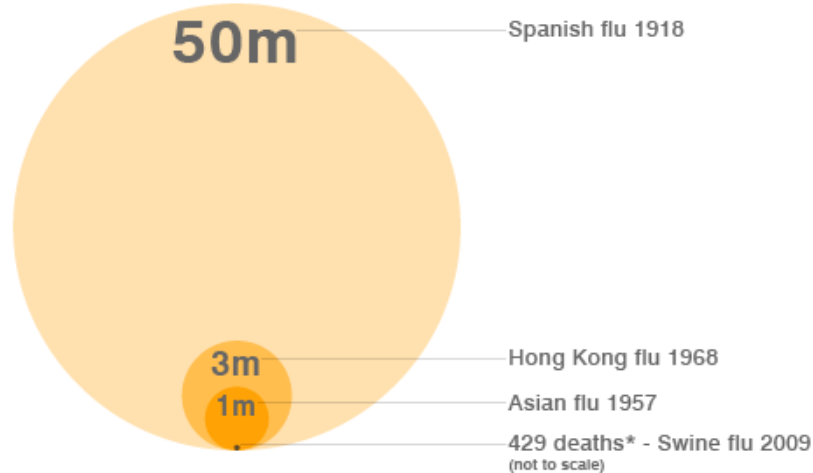
"I rate the chance of a nuclear war within my lifetime as being fairly low. I rate the chance of a widespread epidemic, far worse than Ebola, in my lifetime, as well over 50 percent."

—Bill Gates



POTENTIAL FOR FUTURE OUTBREAKS

Deaths from previous flu pandemics

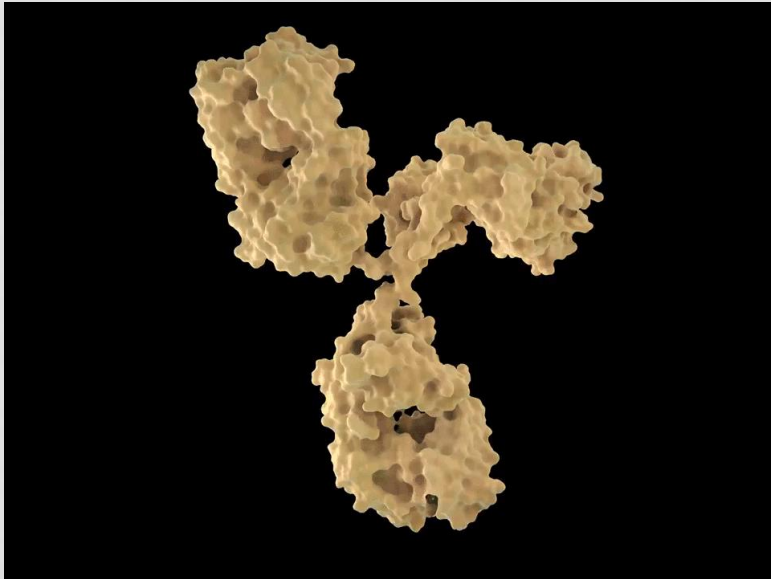


* As of 6 July 2009

SOURCE: Health Protection Agency, WHO



ANTIBODIES



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

CURRENT PRODUCTION METHODS

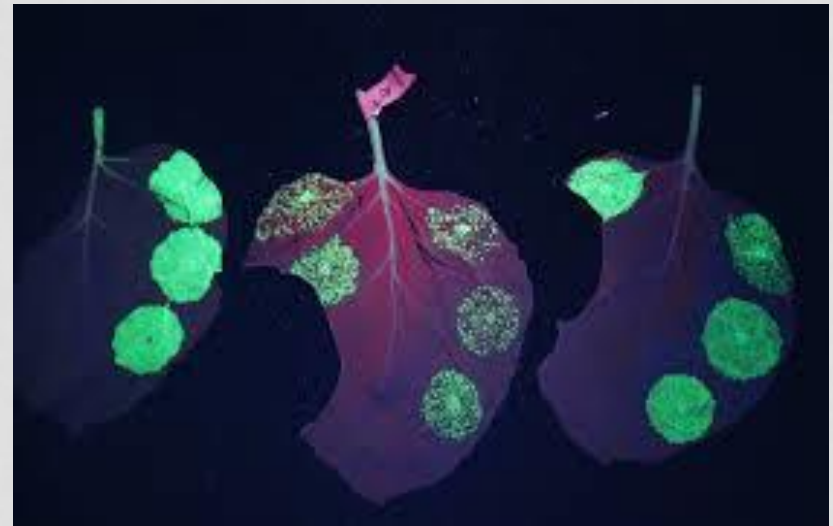


>\$200M



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

- Very high productivity
- Most expensive
- Scalable with sterile vats
- Medium growth-period

Tobacco

- High productivity
- Less expensive
- Scalable with arable land
- Longest growth-period

Microalgae

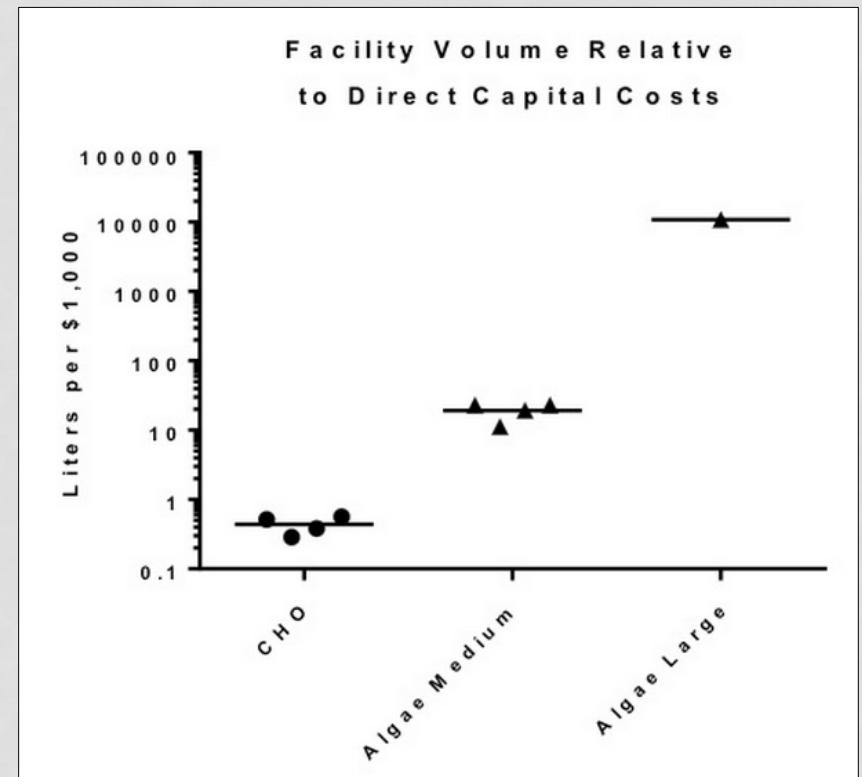
- Low productivity
- Least expensive
- Most scalable with ponds
- Shortest growth-period

CHLAMYDOMONAS REINHARDTII

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



CHLAMYDOMONAS REINHARDTII

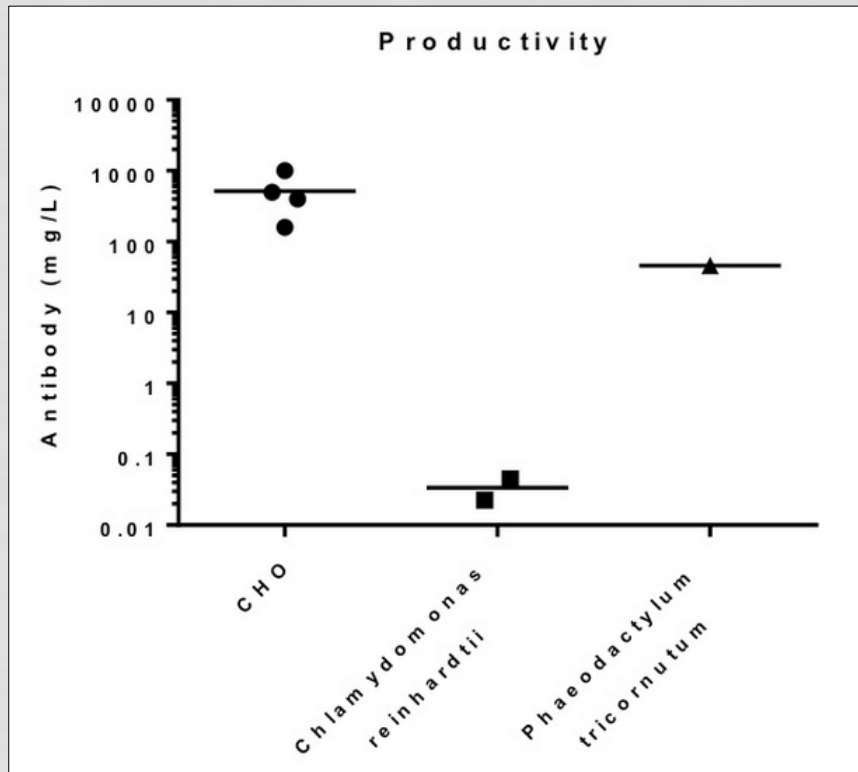


<http://bit.ly/1YFuHJe>

POTENTIAL FOR GLOBAL ALGAE DISTRIBUTION



CHLAMYDOMONAS REINHARDTII



- ❖ Productivity is the current obstacle

<http://bit.ly/1KUpmYC>

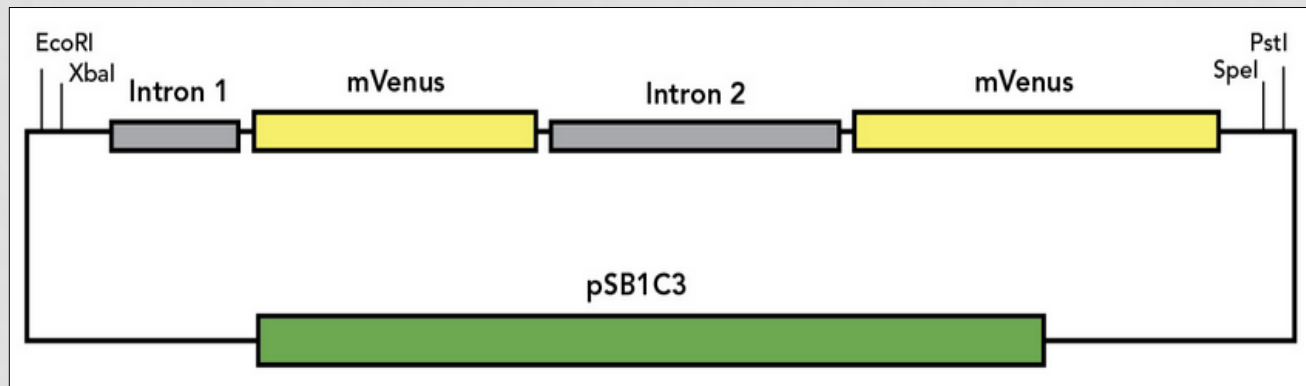
INITIAL APPROACH

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

FINAL APPROACH

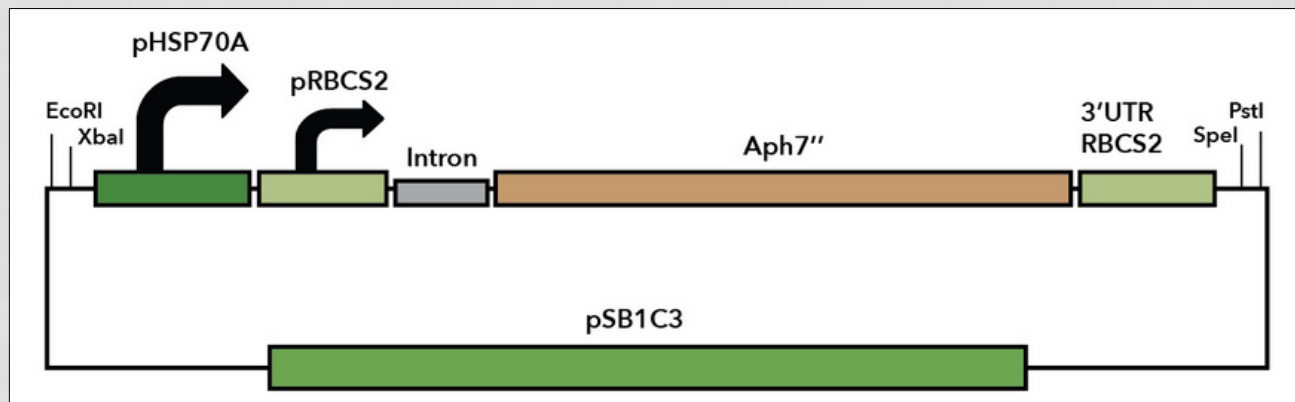
- ❖ Recognizing the lack of usable parts, we set out to standardize those that will make work with *C. reinhardtii* feasible for iGEM

mVenus



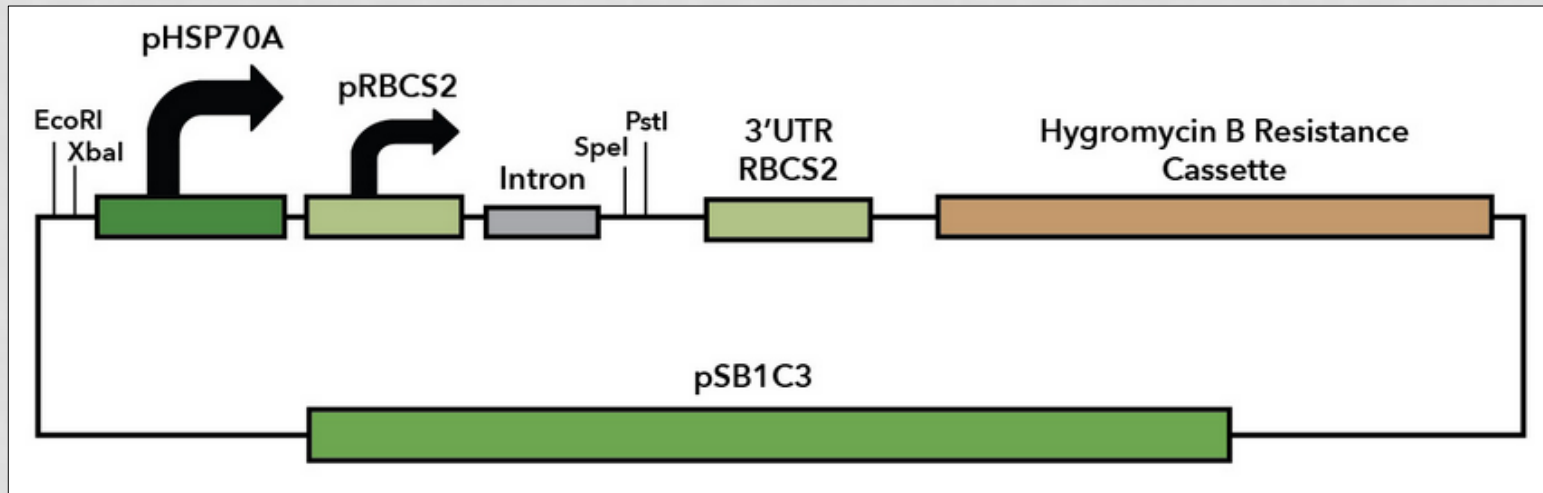
PARTS

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

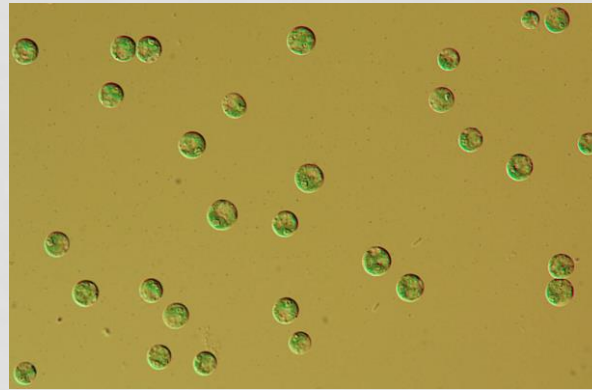


WHY MICROALGAE?

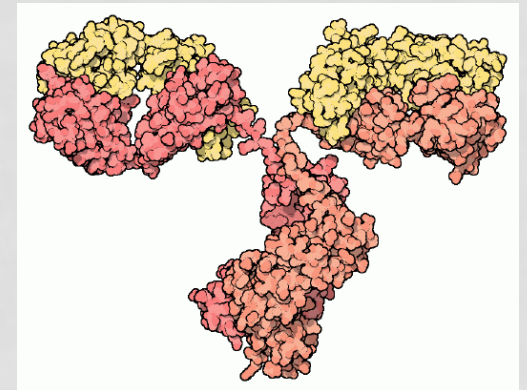
- iGEM teams should experiment with microalgae as their production chassis



Consume CO₂



Inexpensive to grow

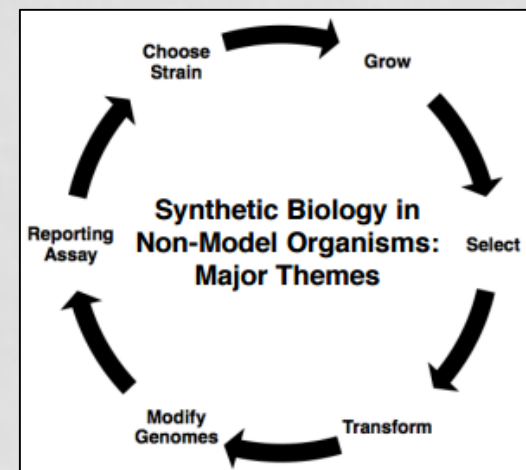
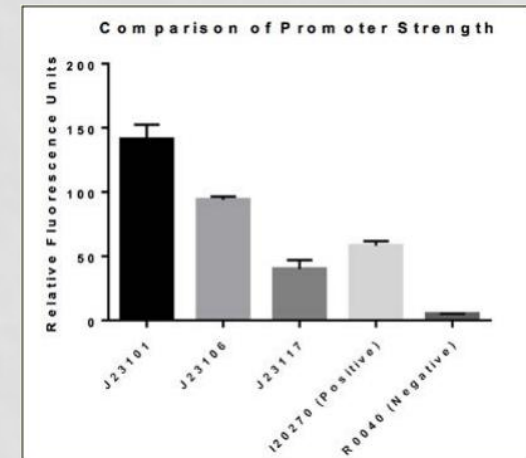


Capable of
producing complex
proteins

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



ACKNOWLEDGEMENTS

Members

David Adams
Josh Colls
Ariela Esmurria
Josh Timmons
David Urick

Mentors

Jeff Bouffard
Hema Madaka
Caitlin Kramer
Sanjin Hosic
Marissa Puzan
Alison Wirshing

Northeastern University
College of Science

DEPARTMENT OF
Bioengineering



DEPARTMENT OF
Chemical Engineering



Advisors

Dr. Lee-Parsons
Dr. Godoy-Carter