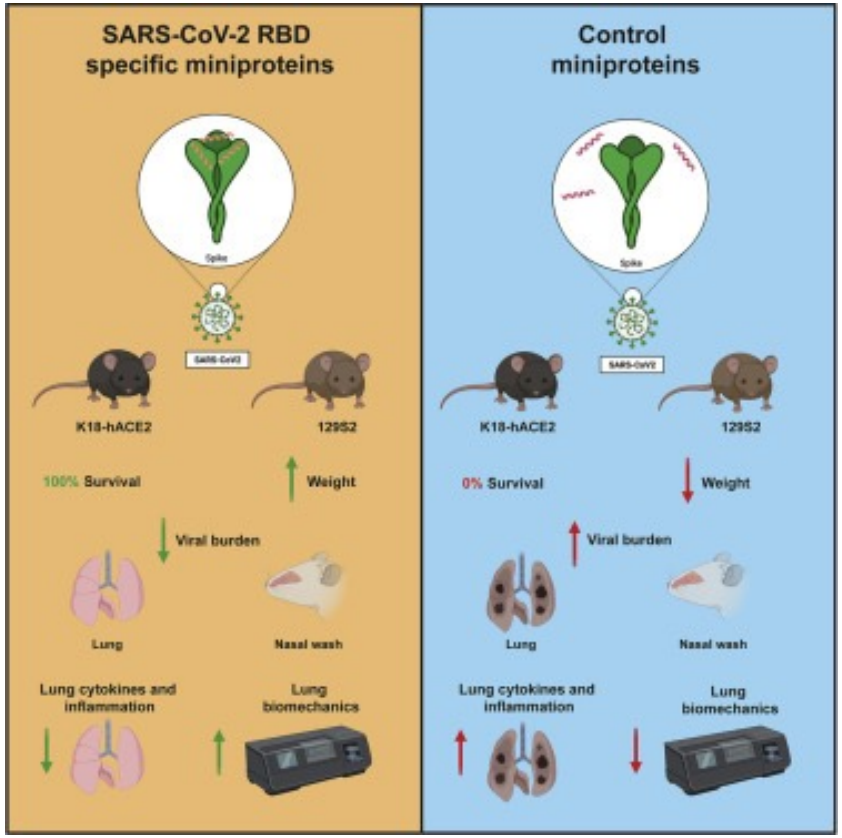
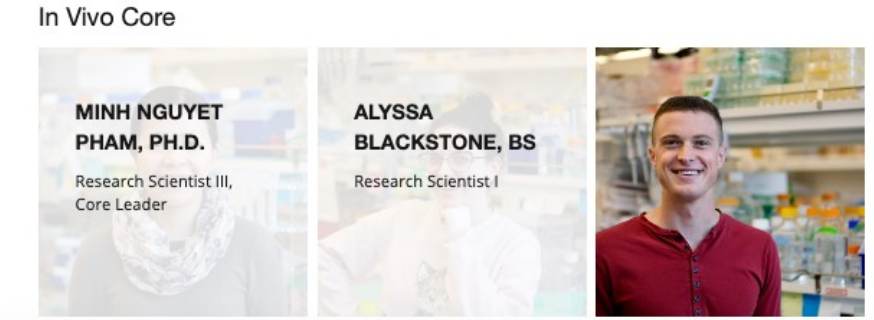
4° Structure – subunit interactions

Computational *de novo* design of proteins that:

1) bind SARS-CoV-2 Spike protein and 2) neutralize virus *in vitro* …

3) and now *in vivo!*





UWO Grad 2020

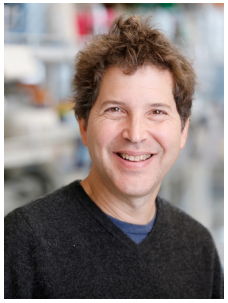
Ultrapotent miniproteins targeting the SARS-CoV-2 receptor-binding domain protect against infection and disease. Case *et al*, Cell Host & Microbe 2021

The Protein Folding Problem

We know the genome sequence of an organism…now what is the structure of a new important enzyme or disease protein?

Can we design new proteins with new useful functions?

Steve Mayo lab, Cal Tech
http://www.mayo.caltech.edu
Computational protein design of antibodies (including broadly-neutralizing antibodies against SARS-CoV-2)



David Baker lab, University of Washington
www.bakerlab.org and Fold.it/
Institute for Protein Design: http://www.ipd.uw.edu/
https://www.ipd.uw.edu/coronavirus/
Rational protein design and structure prediction

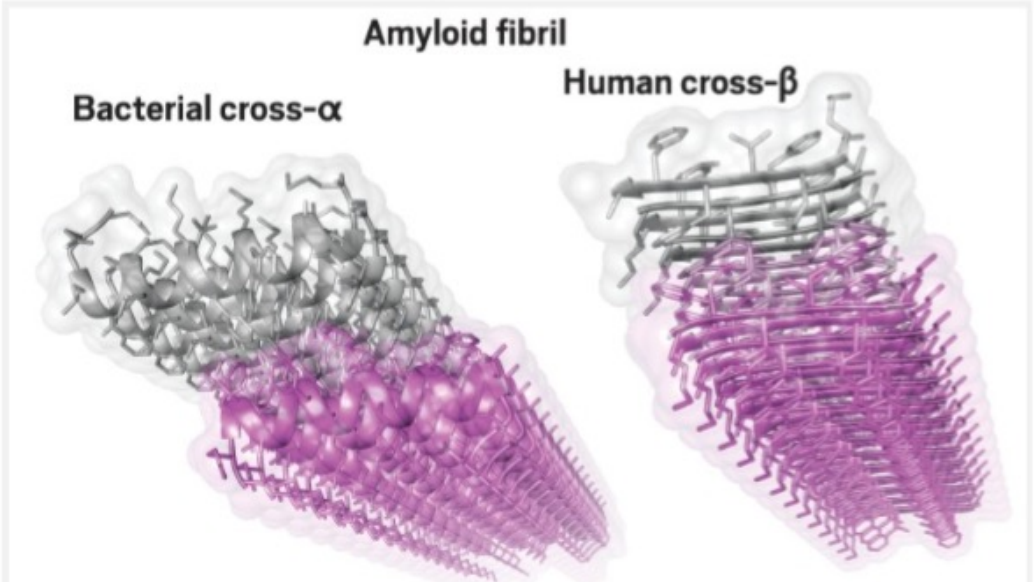
Frances Arnold lab, Cal Tech
http://cheme.che.caltech.edu/groups/fha
Protein engineering and directed evolution for new functions

Amyloids: not just for β-sheets anymore!

Surprising amyloid structure solved

Bacterial peptide forms amyloids with α-helices instead of β-sheets; new structures could be targets for antibiotics

By Celia Henry Arnaud



PSMα3 is the most cytotoxic member of a family of peptides secreted by the bacterium *Staphylococcus aureus*. It's an example of a "functional amyloid," one that is beneficial rather than harmful to the organism that produces it. Involved in disintegrating human cells, PSMα3 is a major contributor to *S. aureus*'s virulence.

The cytotoxic *Staphylococcus aureus* PSMα3 reveals a cross-α amyloid-like fibril

Tayeb-Fligelman *et al*, Science 2017

Meytal Landau lab
Technion-Israel Institute of Technology