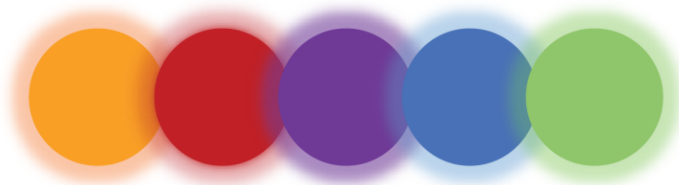
Pearl Bio



Yale Pitchfest
December 6, 2019

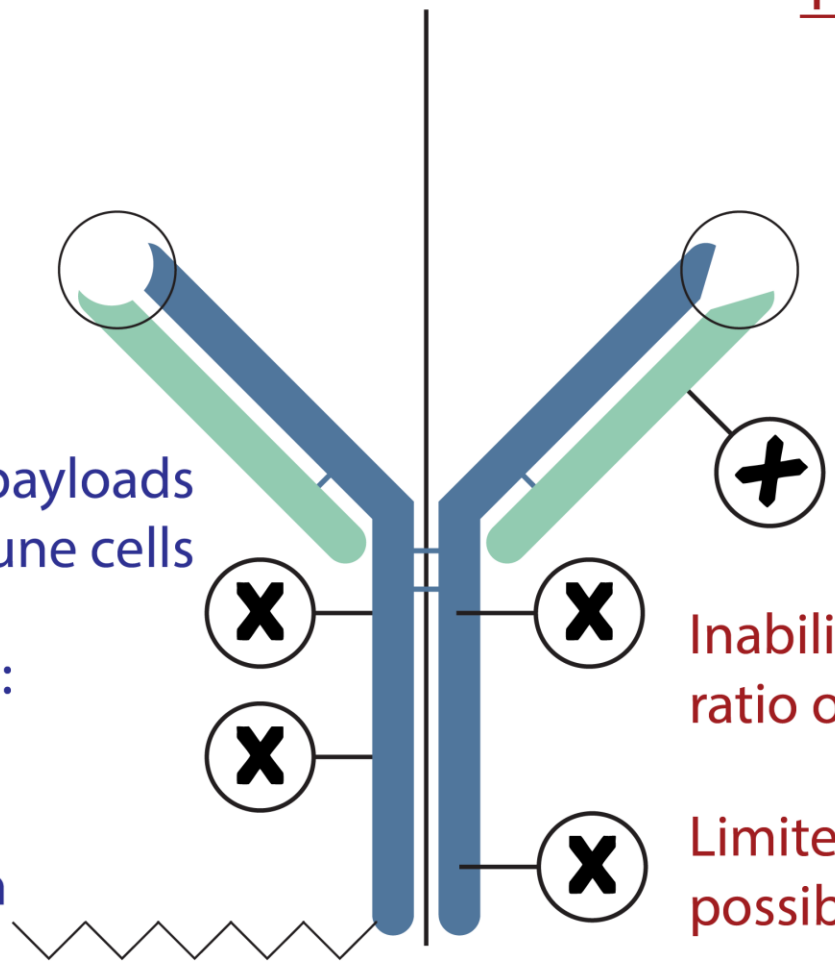
Precise engineering of multi-functional biologics

THE VISION

Modular targeting to tissues, cells, or subcellular locales

Conjugate cyotoxic payloads or recruit immune cells

Tune therapeutic properties:
- Half-life
- Solubility
- Purification



THE STATE-OF-THE-ART

Challenging and time-consuming to design

Imprecise attachment locations that impair function

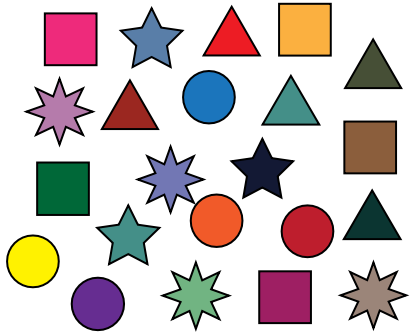
Inability to titrate ratio of attachments

Limited types of modifications possible (e.g., lysine, N-term)

Our Solution: unite chemistry and biology

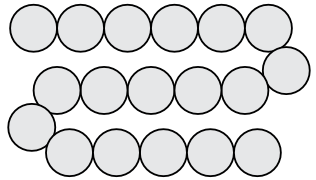
Chemistry-based Synthesis

Generation of polymers with unlimited diversity, but not template-directed



Biology-based Synthesis

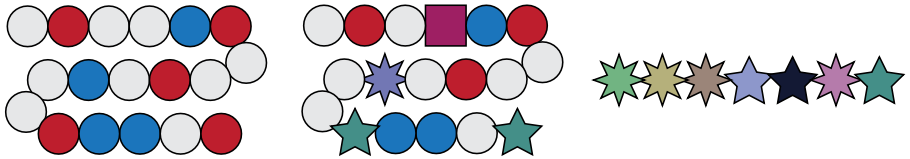
Precise, template-directed protein production, but limited to 20 amino acids



Pearl Bio Synthesis

Unites the diversity of chemistry and the precision of biology to create:

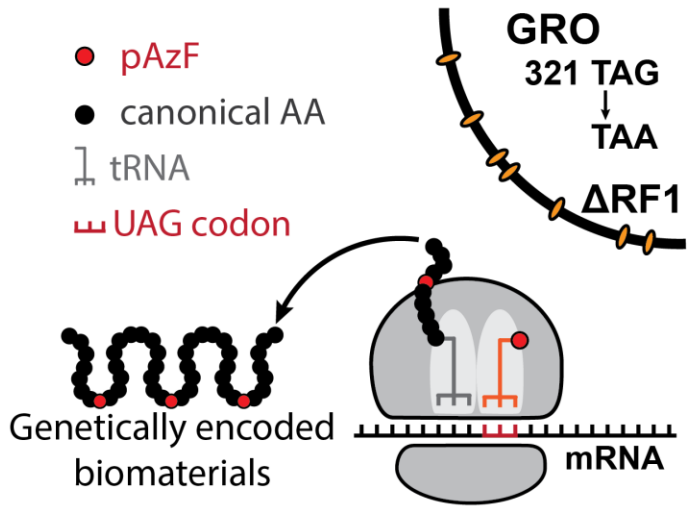
- sequence-defined polymers
- chemically diverse
- tunable



How it works: specific, multisite modification to optimize protein properties

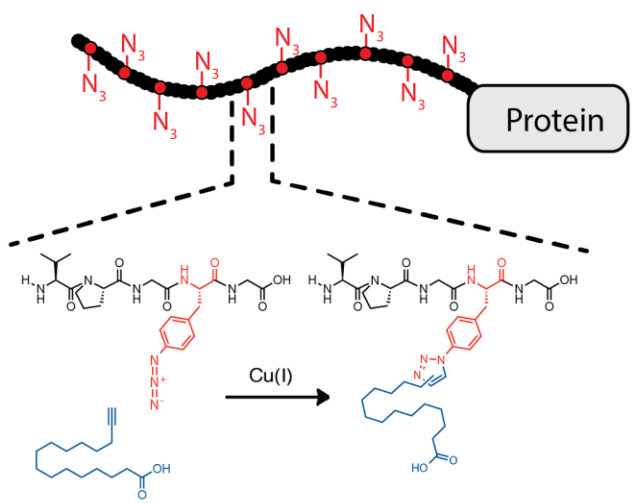
1

Express biologic in Pearl Platform



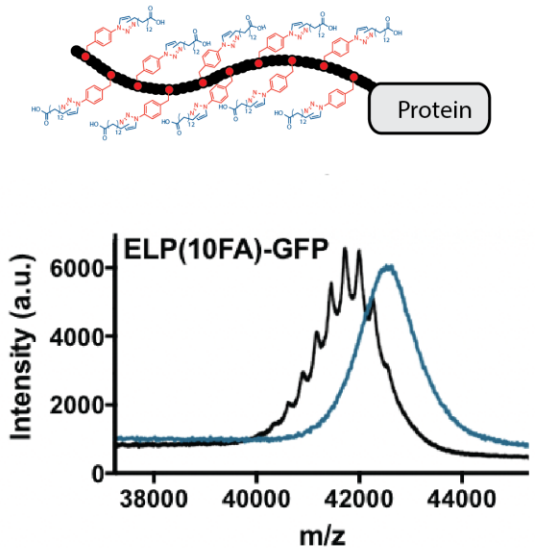
2

Extract and react to functionalize



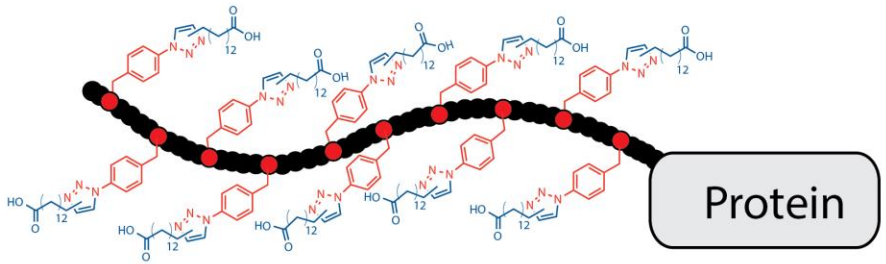
3

Characterize

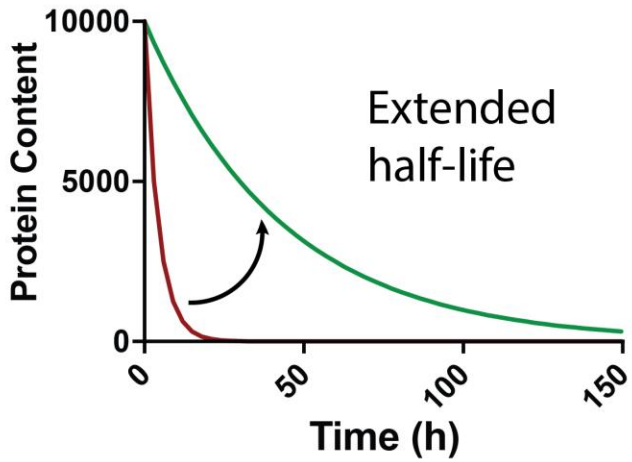


Optimized protein stability via precise fatty-acylation

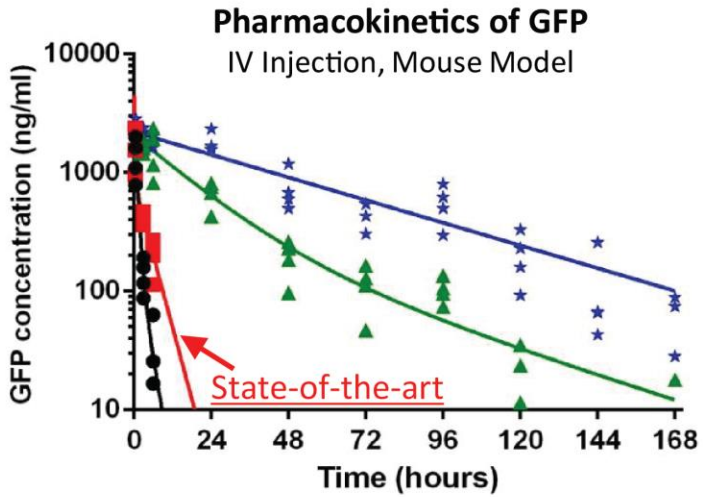
Programmable biologic



Predicted Model



Tuned half-life *in vivo*

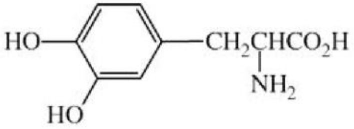


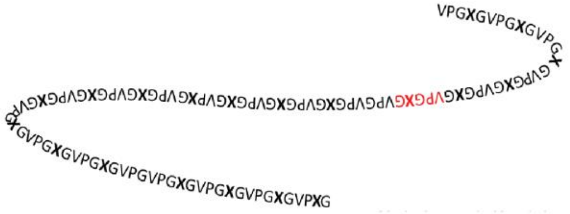
10 fatty acids increases half-life 25-fold

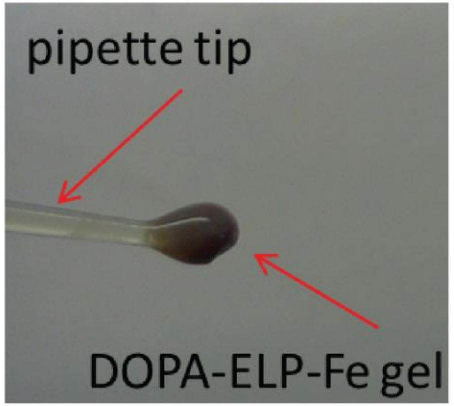
Pearl Bio

Multiple functionalizations reduced to practice

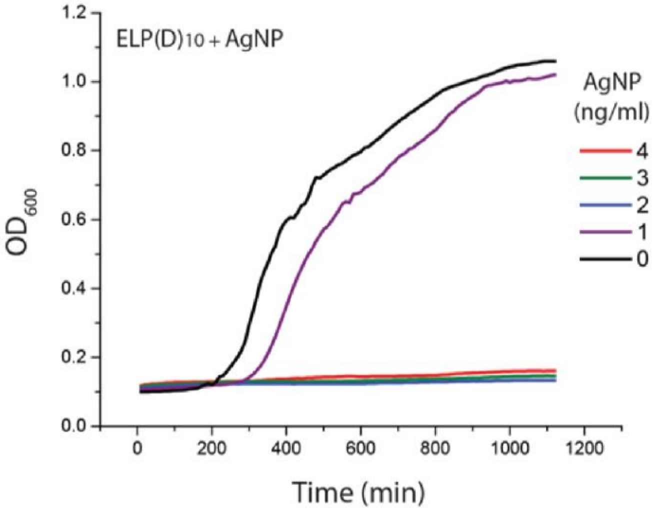
Tunable bioadhesive protein polymer







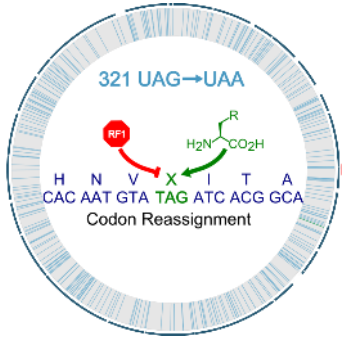
Nanoparticle-conjugated antimicrobial peptides



Growth of *E. coli* in presence of conjugated nanoparticle peptides

Multiple core technologies spanning 8 active patents

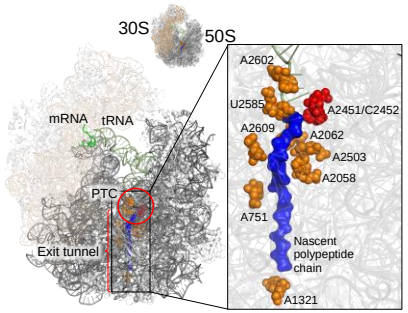
Genomically Recoded Organisms



Encode multiple synthetic amino acids (SAAs) and synthetic monomers for biomaterial production

EXCLUSIVE IP

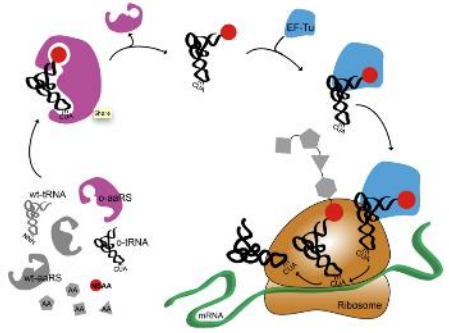
Orthogonal, Tethered Ribosomes



Engineer the ribosome catalytic site to drive polymerization of synthetic monomers

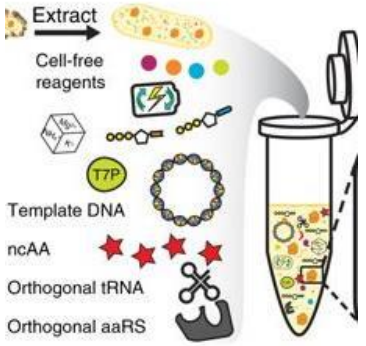
EXCLUSIVE IP

High-yield Biomaterials Synthesis



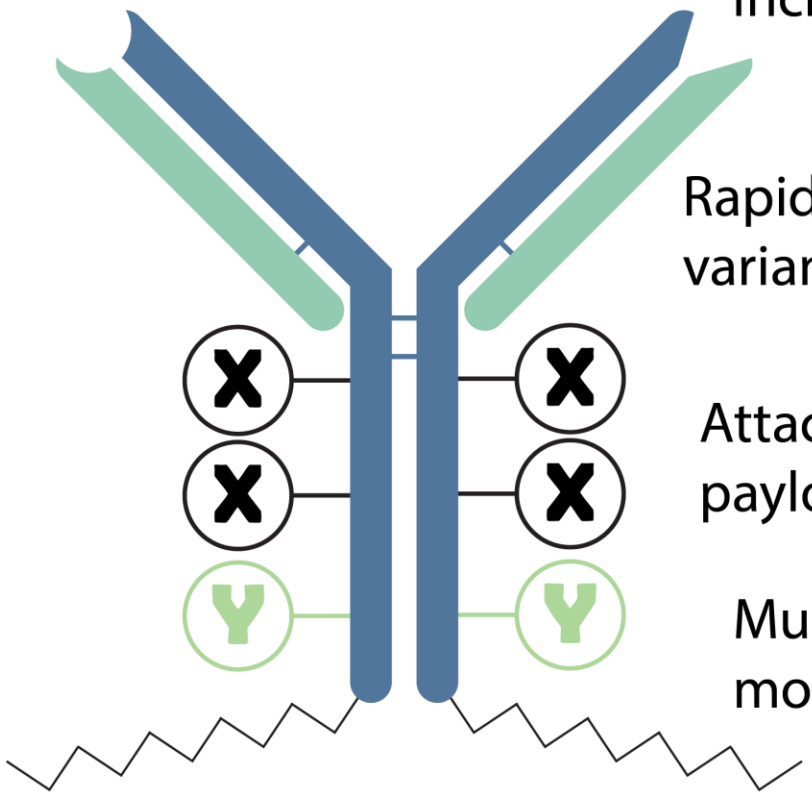
Use multiplex engineering to maximize purity and yield of biomaterials with multiple SAAs and synthetic monomers

Cell-free Synthesis



Produce biomaterials with multi-site SAA and synthetic monomer incorporations at high yields

The future: precise, multifunctionalized therapeutics



Synthetic amino acids increase structural diversity

Rapid expression of many variants at high purity

Attachment of multiple payloads at precise ratios

Multiple different modifications per protein

Differentiated from competition by core capabilities:

1. Many (5+) attachments per protein (Exclusive IP)
2. Multiple different amino acids for functionalization
3. Ability to incorporate more exotic monomers using engineered ribosomes (Exclusive IP)
4. Cell and cell-free expression systems

Potential first applications

Therapeutic Protein	Disease Area	Expression in *E. coli*?
 **Asparaginase/ Arginase**	Oncology	Yes
 **Interleukins**	Oncology and Infectious Disease	Yes
 **Uricase**	Treatment-refractory Gout	Yes
 **Enzyme Replacement Therapy**	Rare Disease (e.g., Gaucher)	Varies

Market research underway to identify first application

Team, Timeline, and Budget

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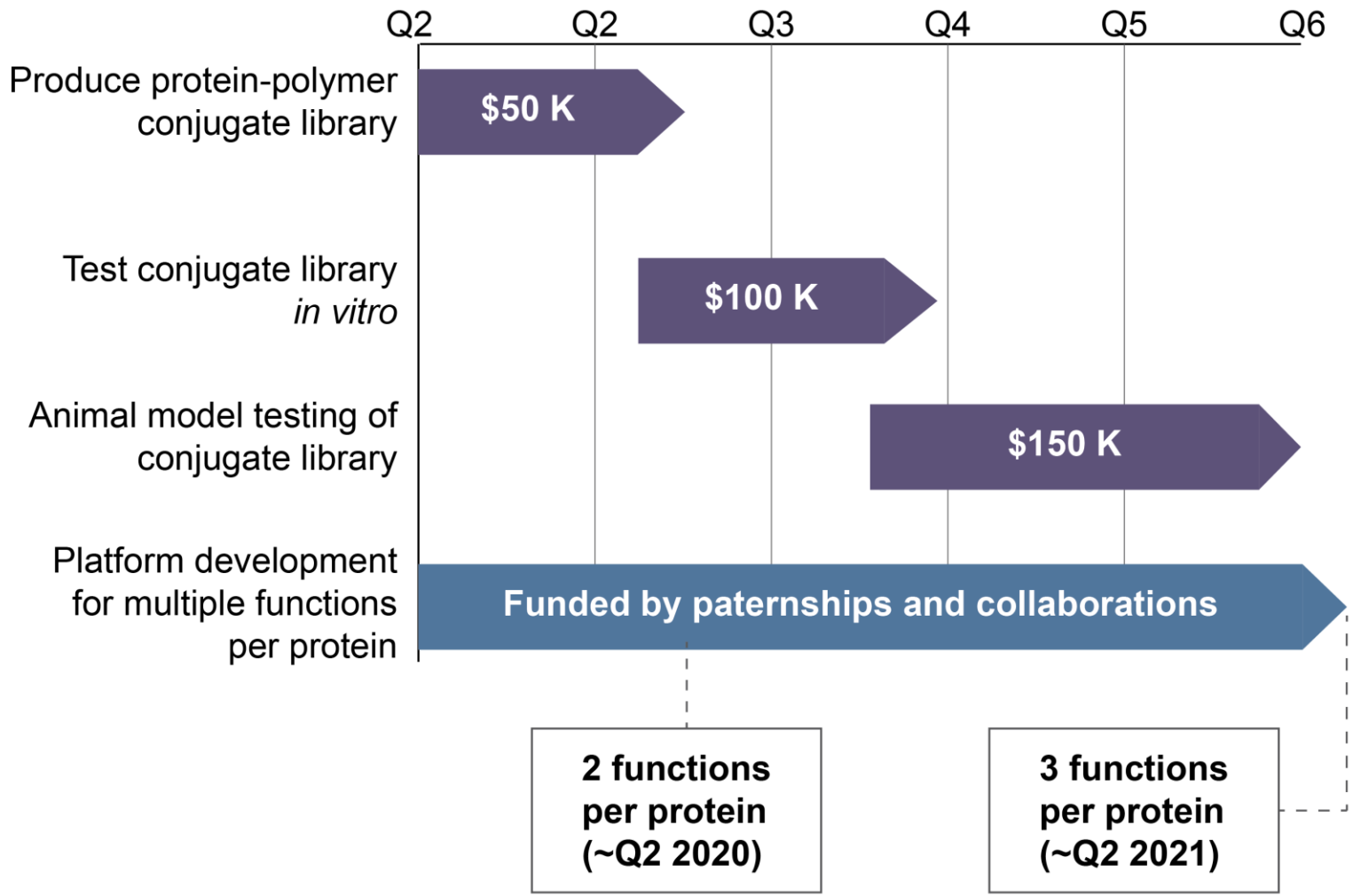
Yale
enEvolv
The Genome Engineering Company

Mike Jewett
Professor
Northwestern
SWIFTSCALE BIOLOGICS

Natalie Ma
Blavatnik Fellow
Yale
CLEARVIEW Healthcare Partners



QUESTIONS?

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