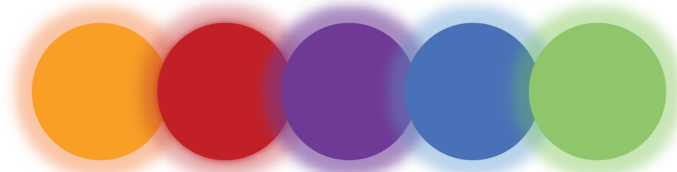


Pearl Bio



Yale Pitchfest
December 6, 2019

Precise engineering of multi-functional biologics

THE VISION

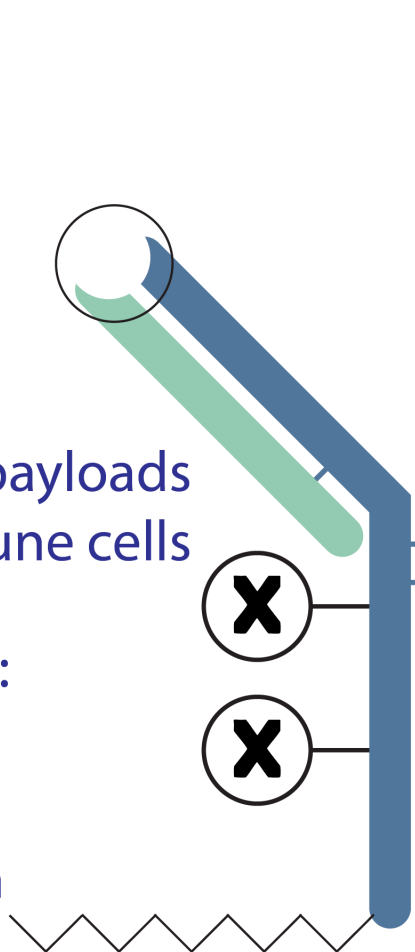
Modular targeting
to tissues, cells, or
subcellular locales



Conjugate cytotoxic payloads
or recruit immune cells

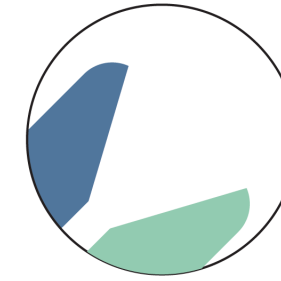
Tune therapeutic properties:

- Half-life
- Solubility
- Purification



THE STATE-OF-THE-ART

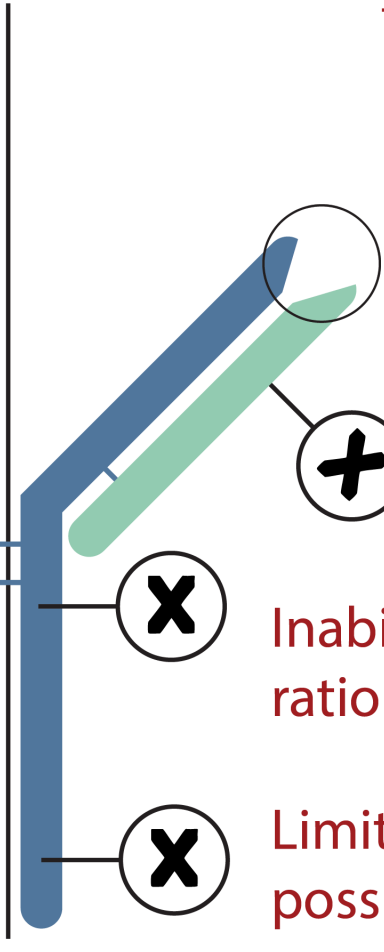
Challenging and
time-consuming
to design



Imprecise attachment
locations that impair function

Inability to titrate
ratio of attachments

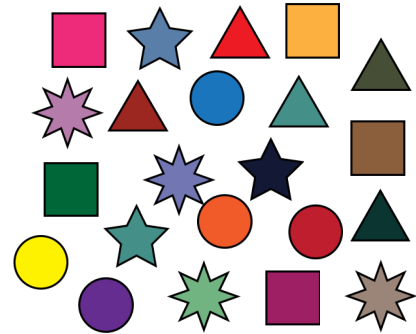
Limited types of modifications
possible (e.g., lysine, N-term)



Our Solution: unite chemistry and biology

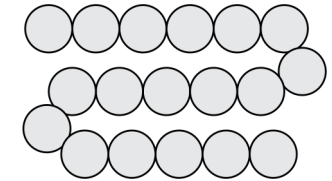
Chemistry-based Synthesis

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



Biology-based Synthesis

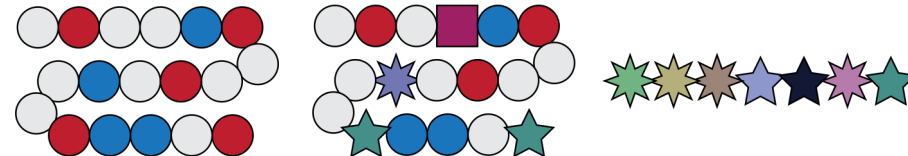
Precise, template-directed protein production, but limited to 20 amino acids



Pearl Bio Synthesis

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

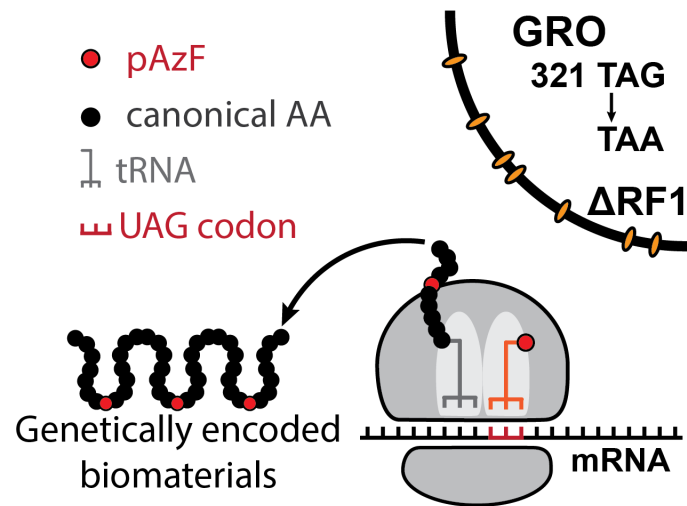
- sequence-defined polymers
- chemically diverse
- tunable



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

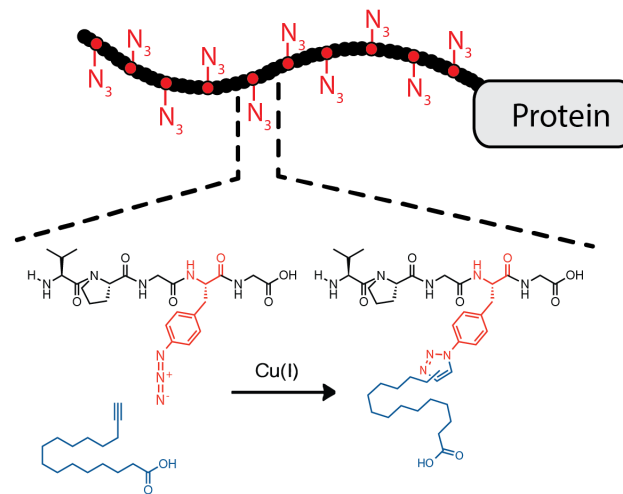
1

Express biologic in Pearl Platform



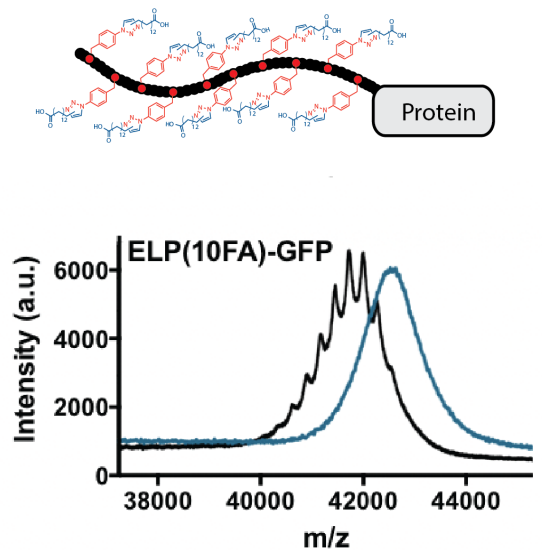
2

Extract and react to functionalize



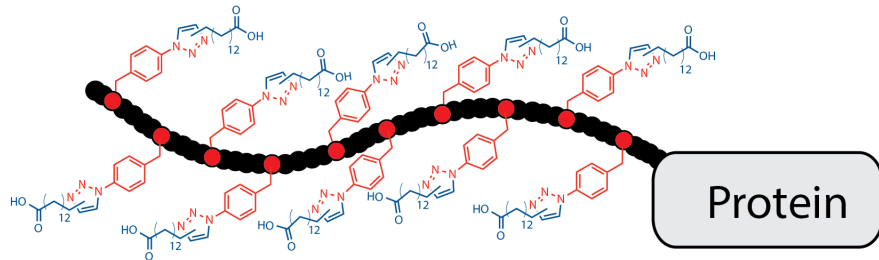
3

Characterize

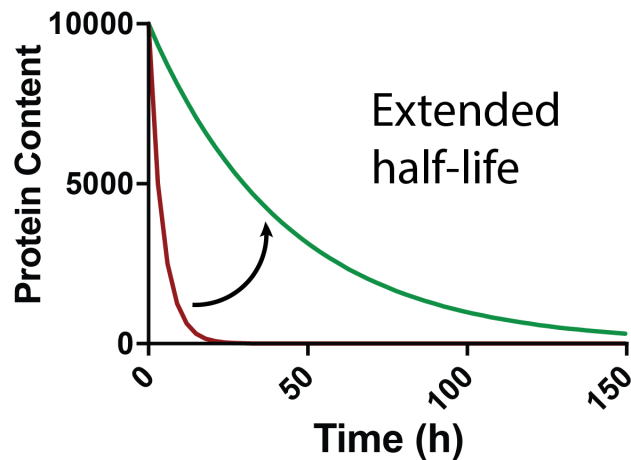


Optimized protein stability via precise fatty-acylation

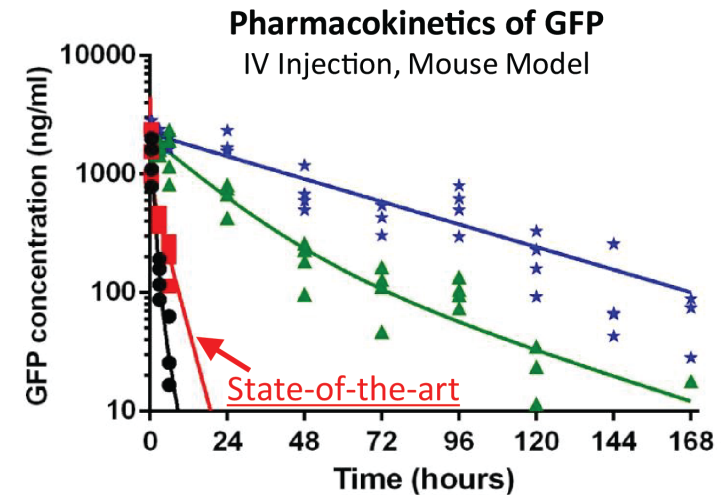
Programmable biologic



Predicted Model



Tuned half-life *in vivo*

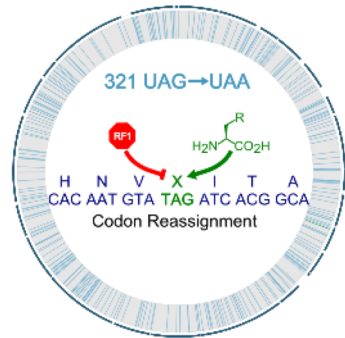


- no fatty acids
- 1 fatty acid
- 5 fatty acids
- 10 fatty acids

10 fatty acids increases half-life 25-fold

Multiple core technologies spanning 8 active patents

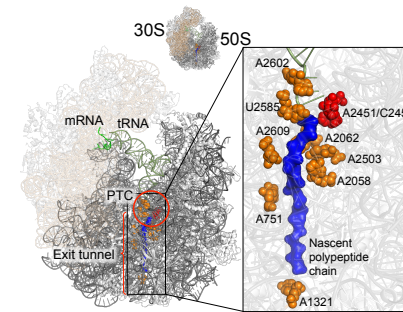
Genomically Recoded Organisms



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

EXCLUSIVE IP

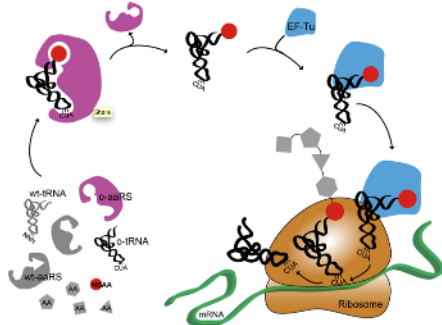
Orthogonal, Tethered Ribosomes



Engineer the ribosome catalytic site to drive polymerization of synthetic monomers

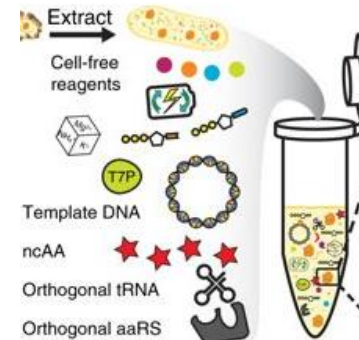
EXCLUSIVE IP

High-yield Biomaterials Synthesis



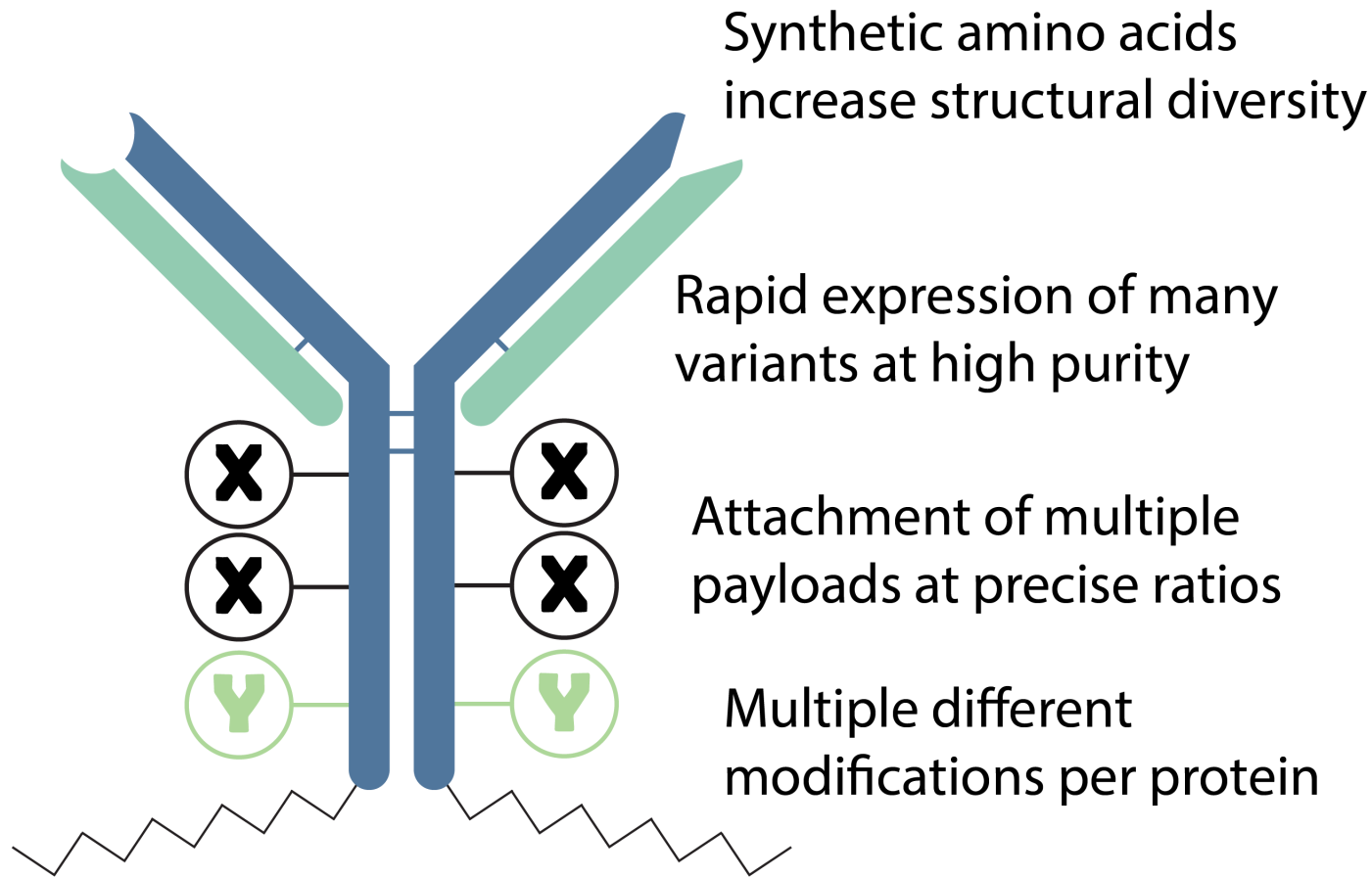
Use multiplex engineering to maximize purity and yield of biomaterials with multiple SAAs and synthetic monomers

Cell-free Synthesis



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

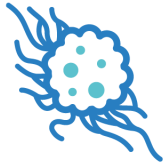



The future: precise, multifunctionalized therapeutics



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 <i>E. coli</i> ?
	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



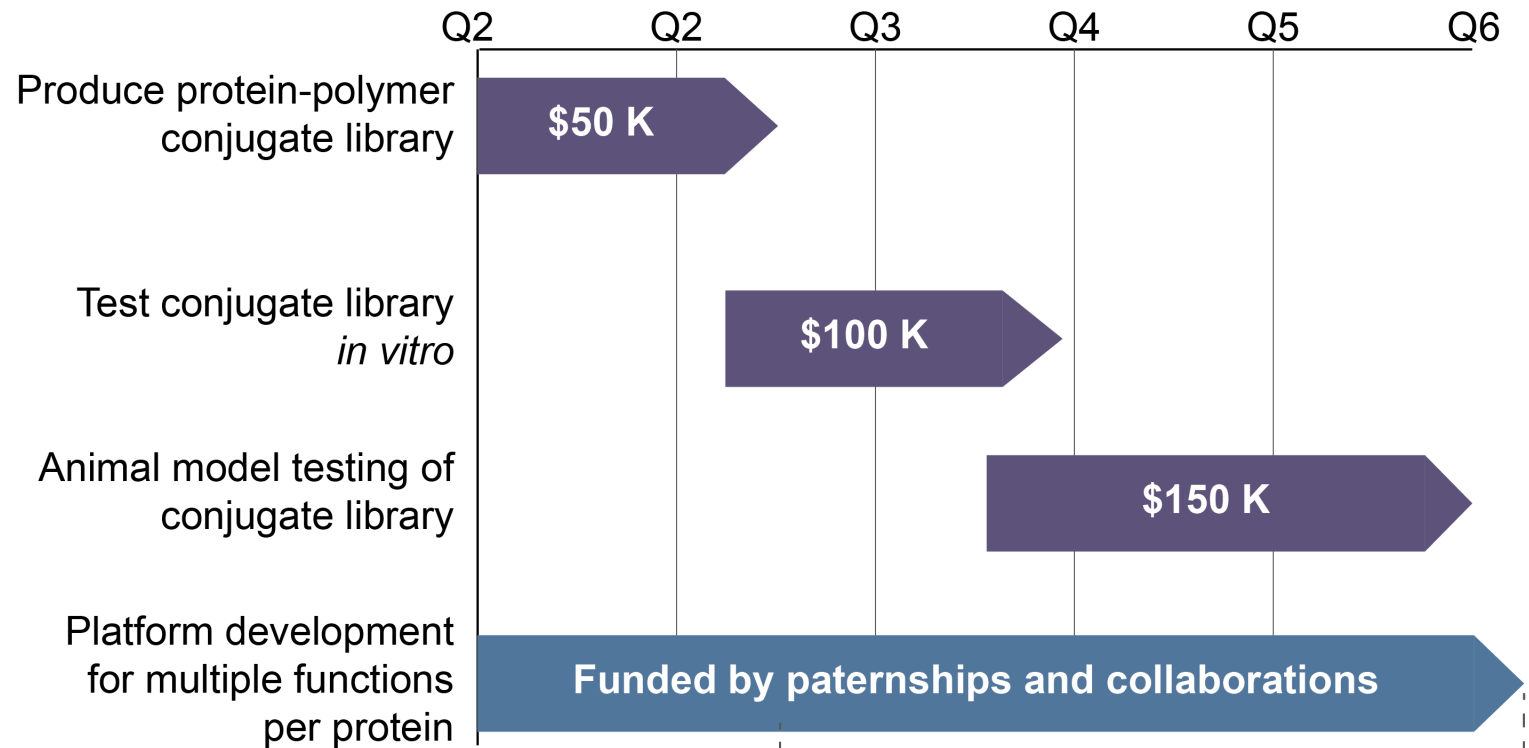
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SWIFTS
BIOLOGICS



Natalie Ma
Blavatnik Fellow
Yale
CLEARVIEW
Healthcare Partners



2 functions per protein (~Q2 2020)

3 functions per protein (~Q2 2021)

QUESTIONS?

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