



Peptide Cues in the Genome-to- Phenome Model

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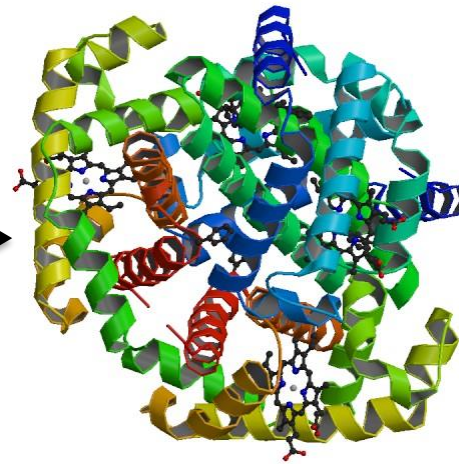
When Genome to Phenome Works

hbb

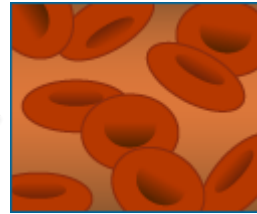
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GAG (glu)

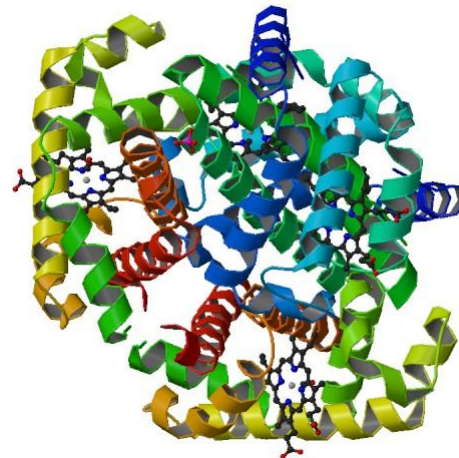
GTG (val)



hemoglobin
(3P5Q)



Normal red
blood cells



sickle cell hemoglobin
(5E6E)

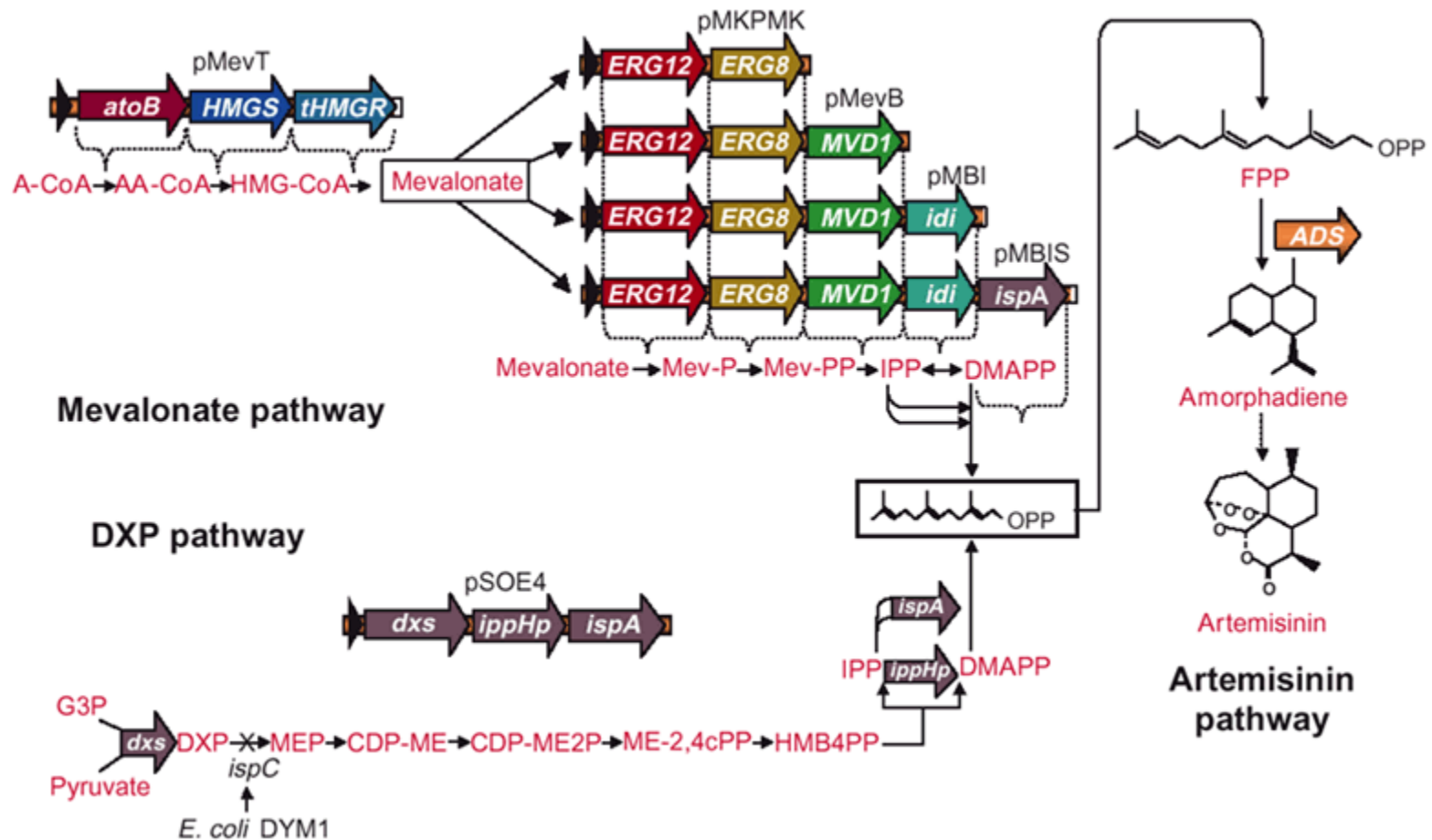


Sickle cell
anemia



When Genome to Phenome Works

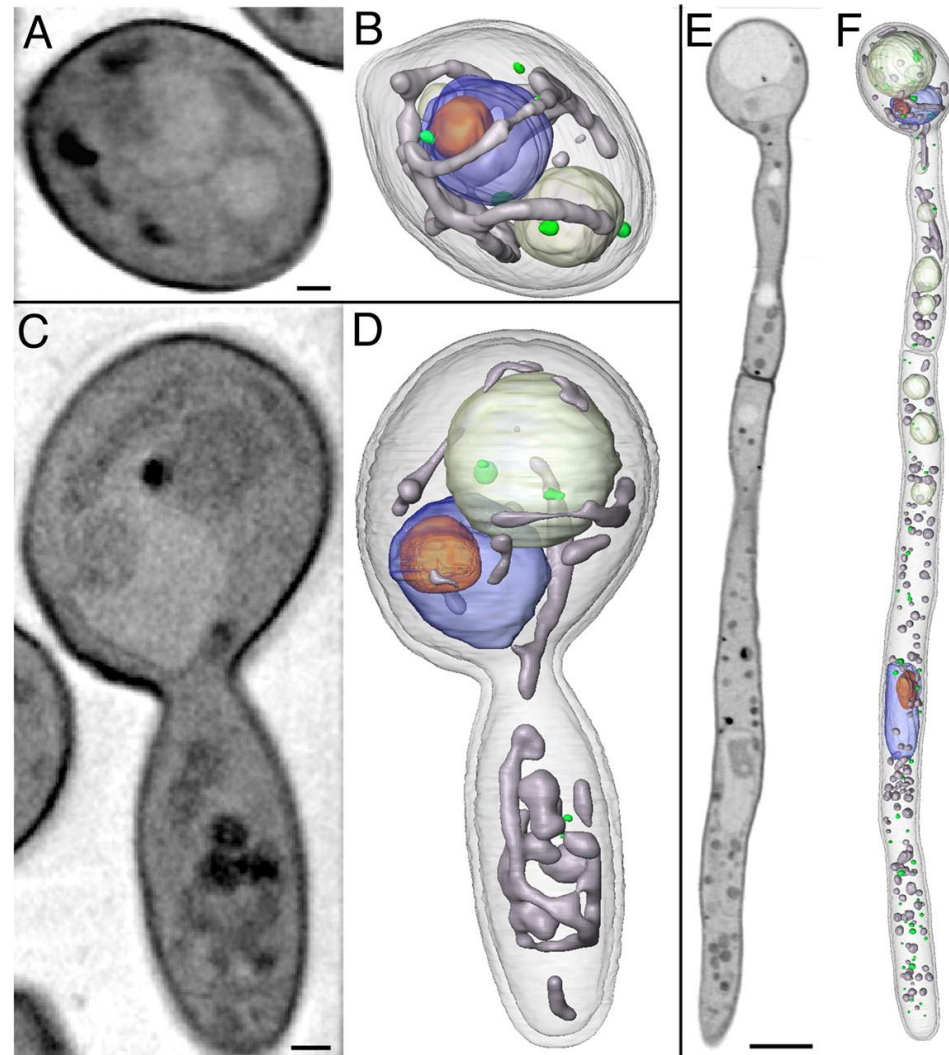
Using synthetic biology/metabolic engineering to produce the antimalarial drug artemisinin





Genetically Identical, but....

- Most of us in this room have *Candida albicans* in us right now
- Based on environmental cues they develop hyphae and become extremely virulent
 - 33%-50% mortality rate upon diagnosis of systemic candidiasis
- Genetically identical
- This is a social behavior

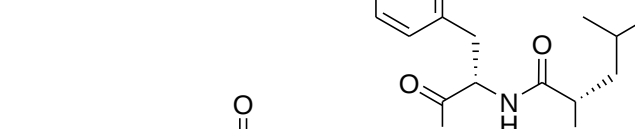


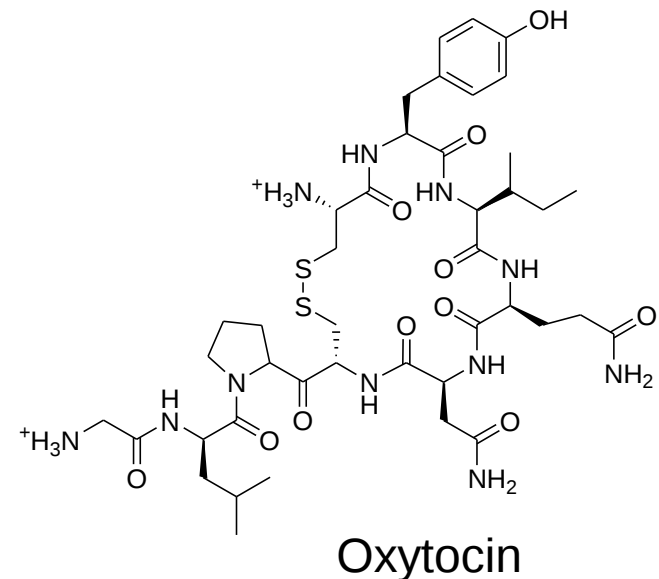
Nature vs. Nurture

- How do environmental cues and social interactions affect development?
- Serial killers, terrorists, and mass murderers are very unlikely to be the product of a genetic mutation
- These two have killed far more people than AIDS has
- HIV: 6,271 US dead in 2014
- Suicide: 42,773 US in 2014





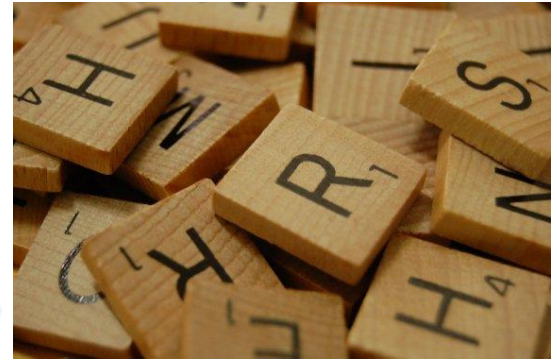
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- The chemical structure of AgrD Peptide is shown. It is a complex polypeptide chain with various side chains, including a benzyl group, a hydroxyl group, and a hydroxymethyl group. The structure is labeled "AgrD Peptide" below it.





Peptides are Rapidly Cleaved

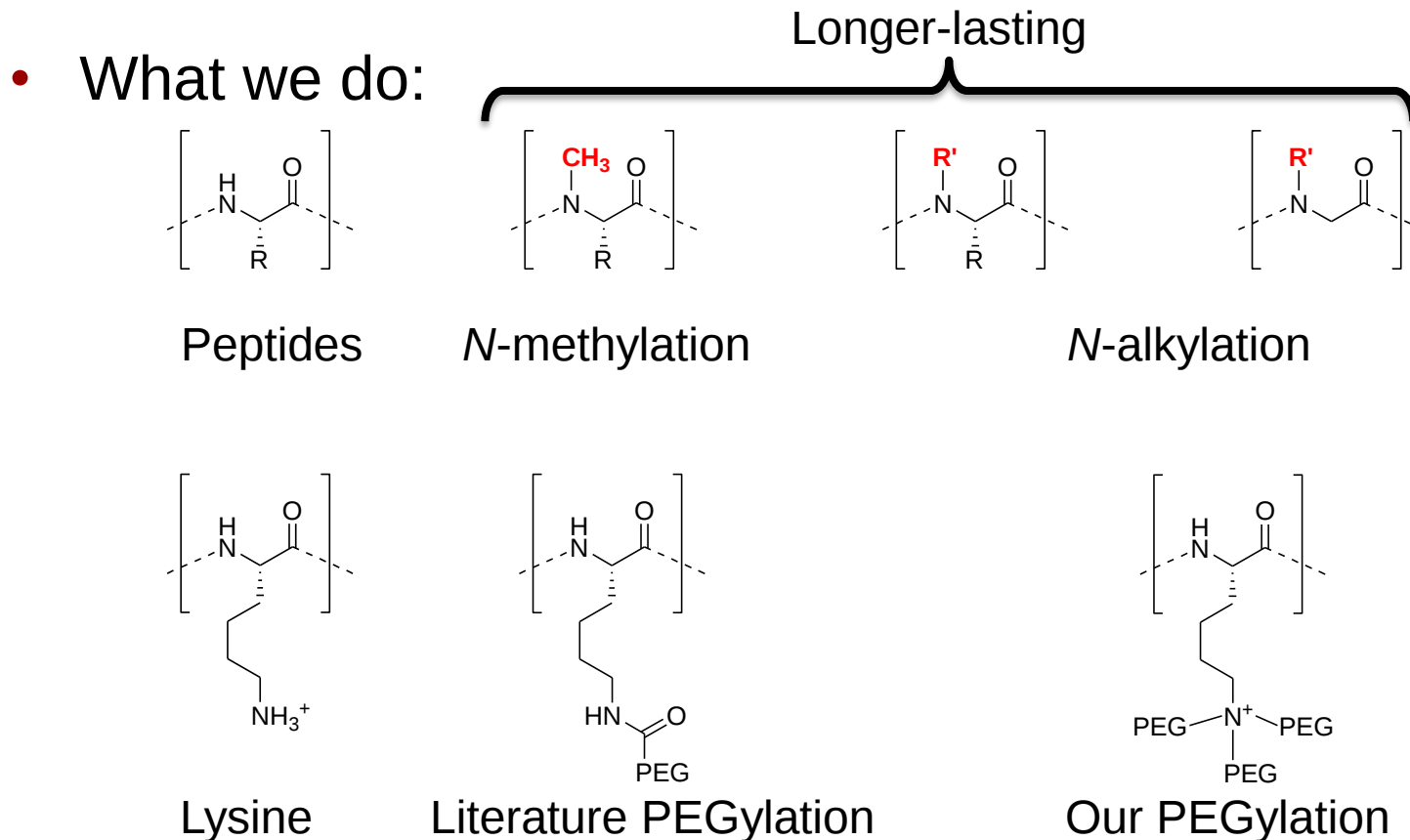
- Grab a fistful of scrabble letters
- Synthesize the peptide they code for
- Inject it into your bloodstream
- Five minutes later it's in your bladder





Need: Longer-Lasting Peptides

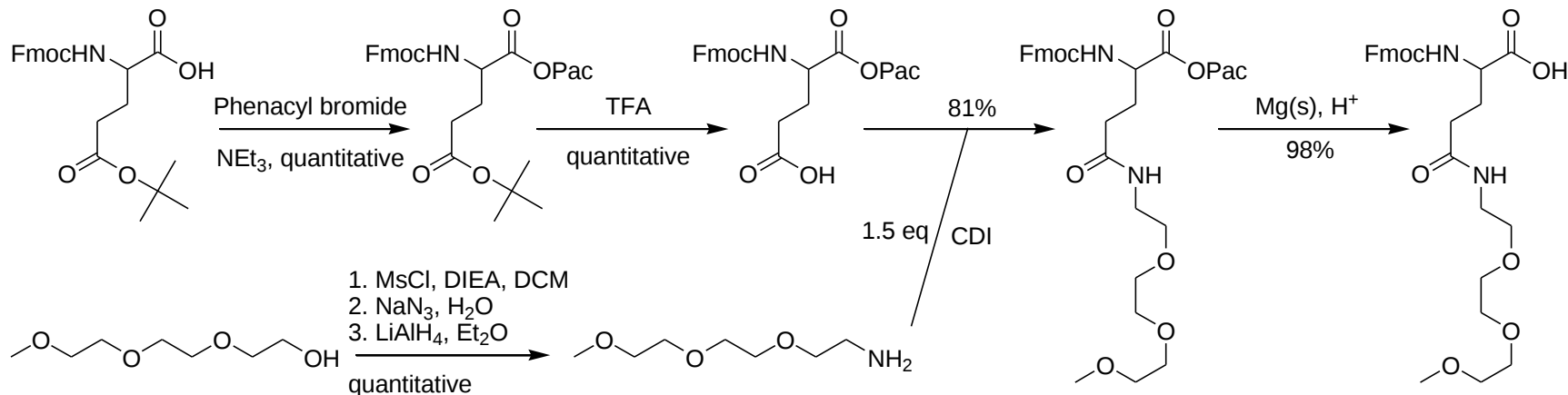
- Longer-lasting peptides would enable turning these social cues on and off and would complete the picture together with genomic tools



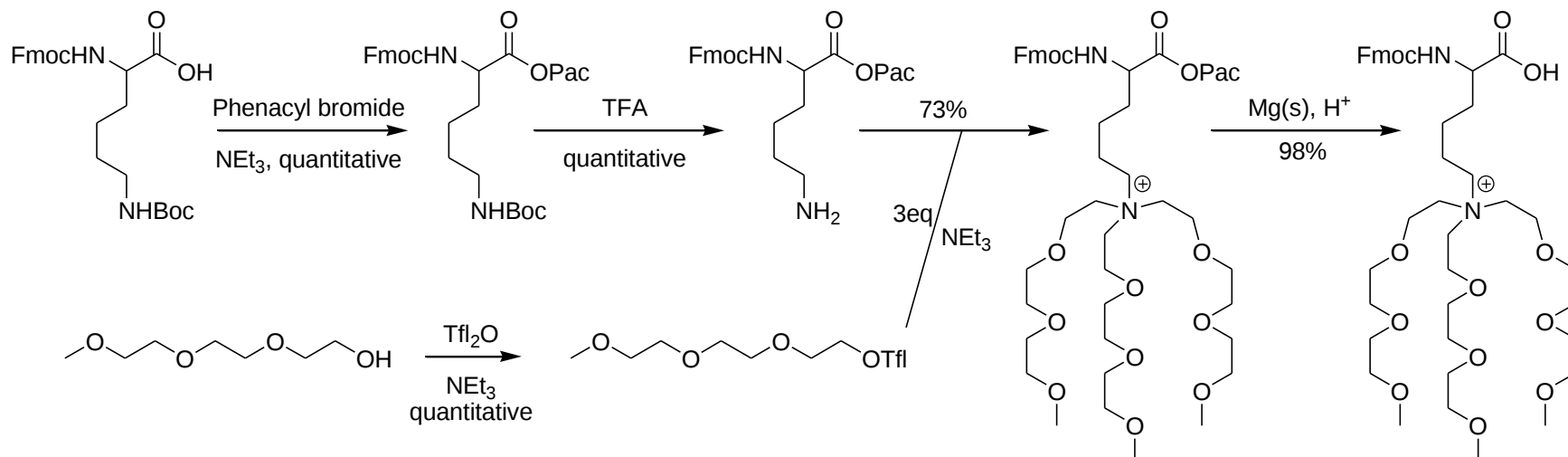


PEGylated Amino Acids

- PEG-Glutamine



- PEG₃-Lysine

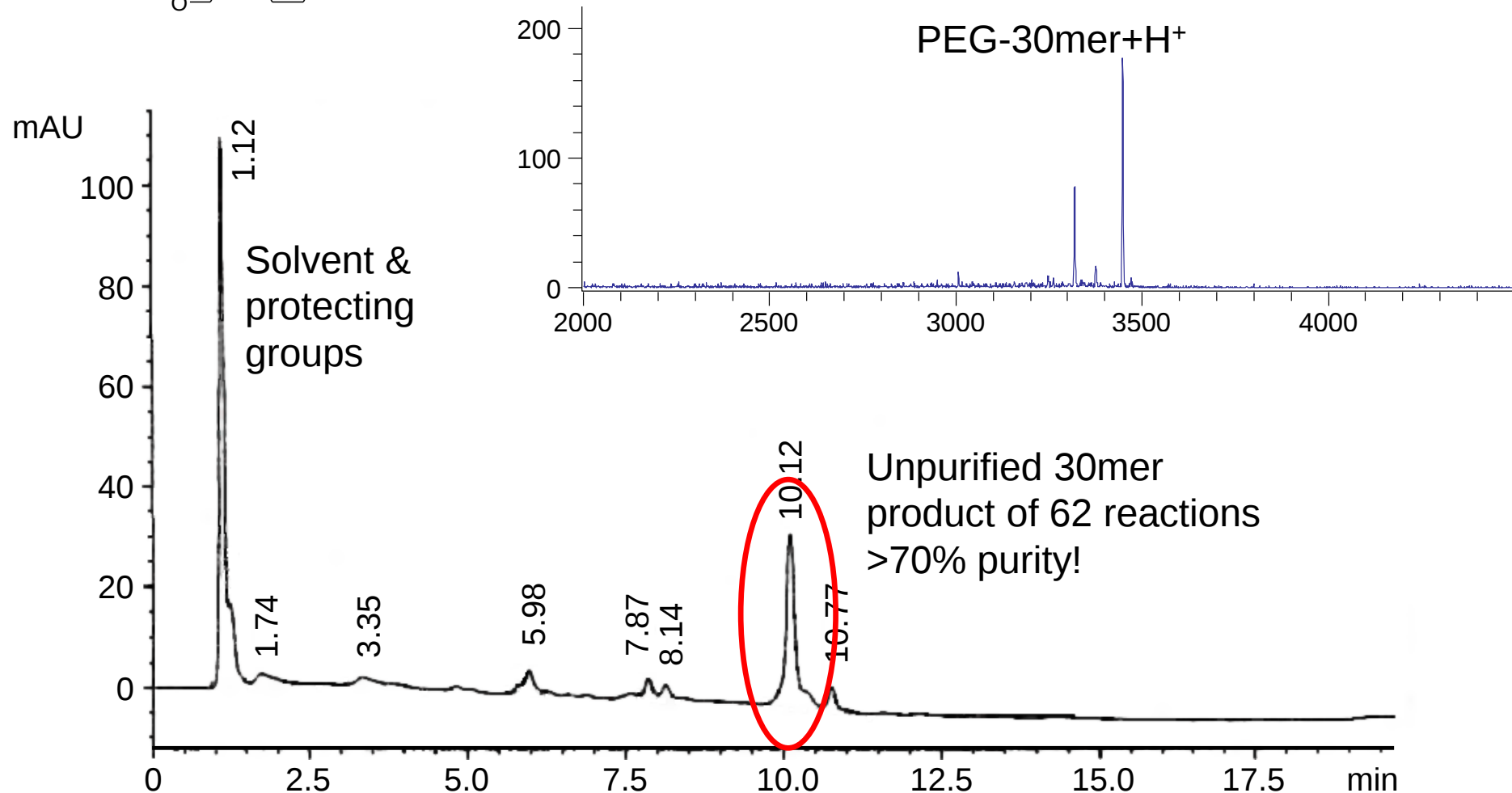
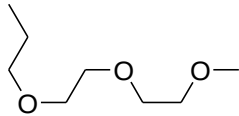


- Overall yields: 80% and 70%



PEGylated GLP-1 Peptide

HAQGTFTSDVSSYLEGQAAKEFIAWLVKGR





Acknowledgements



Graduate Students:

Paris Hamilton (PEGylated peptides)
Kirstin Sockwell (Actinide chemistry)
Megan Sibley (Ln/An separations)



Undergraduate Students:

Alexandra North, Rebecca Pontius, Victoria Haberman,
Jessica Cannon, Brion Riley, Spencer Temples, Matthew Churitch

Collaborators:

Brian Powell (EEES), Susan Chapman (Biology), Charles Schwartz (GGC)