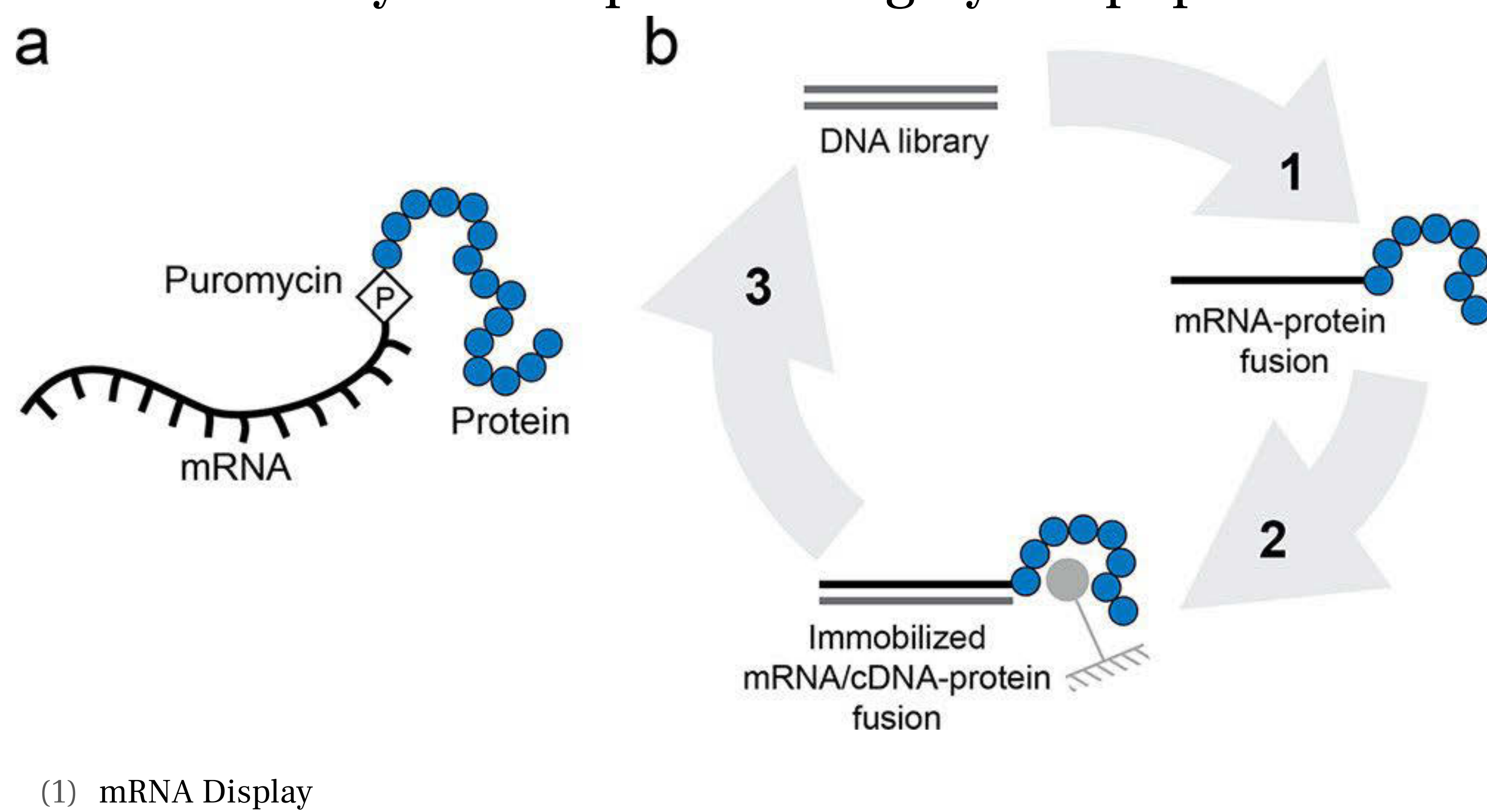


Abstract

- ★ We aim to unravel the underlying rules of cell permeation of cyclic peptides and develop novel high-throughput methods for screening their cell penetration
- ★ We aim to develop computational methods to predict the permeability of cyclic peptides based on their sequence

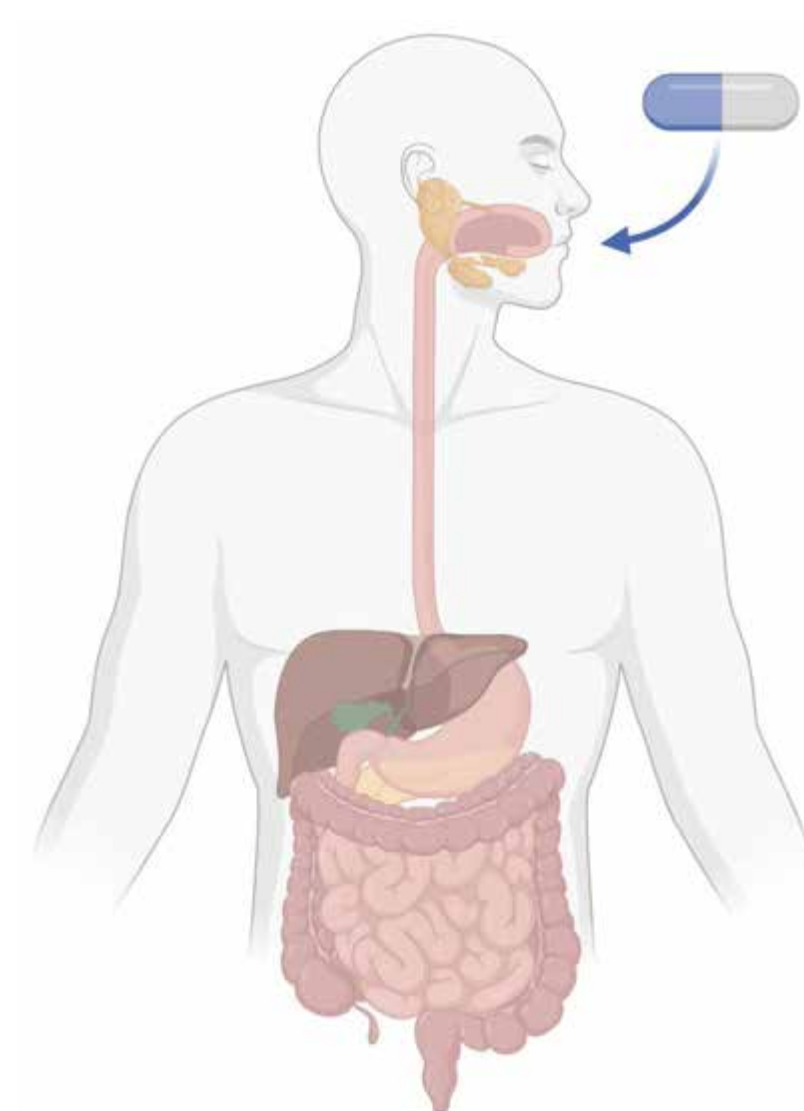
Research Question

- ★ How can we use mRNA display technology to develop a high-throughput permeability assay for the discovery of cell-penetrating cyclic peptides?



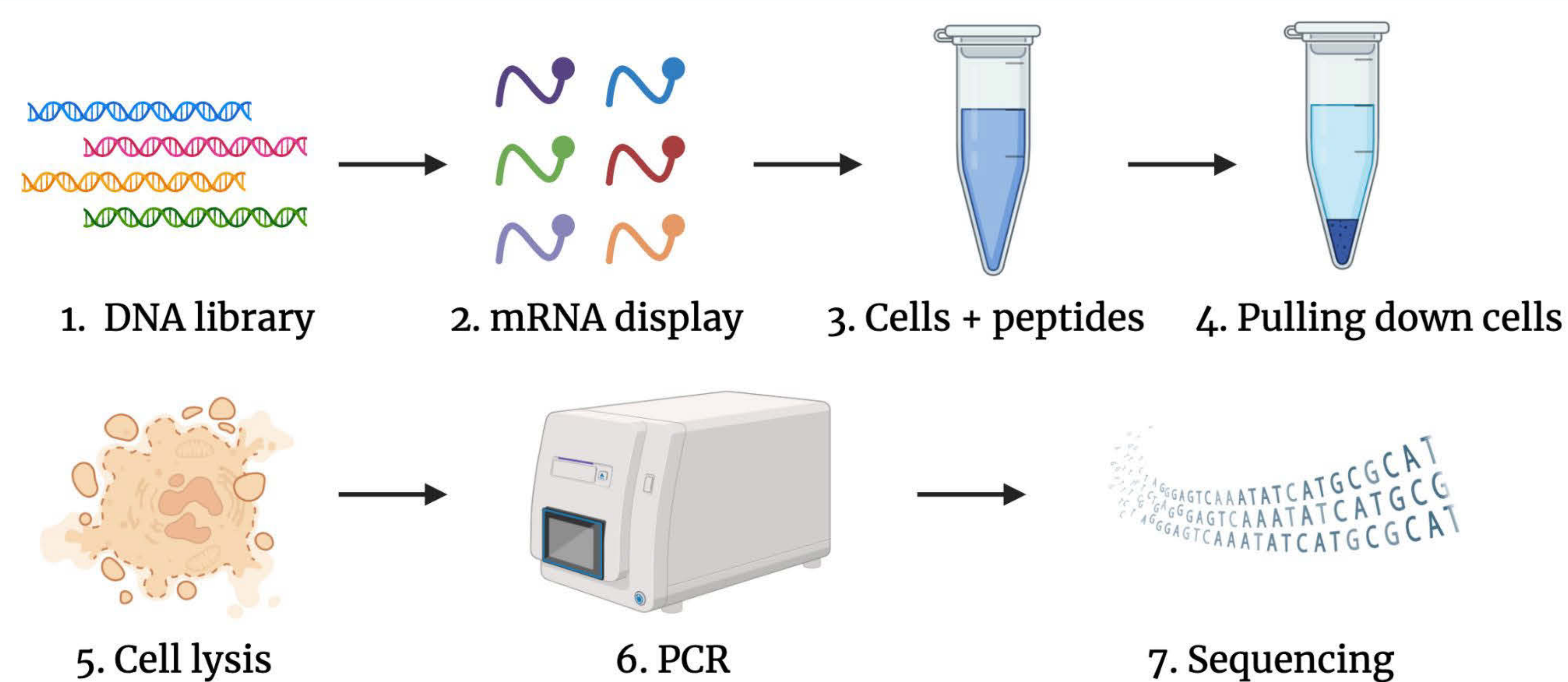
Introduction

- ★ Cell Penetrating Peptides (CPPs) are a promising tool in the delivery of therapeutic drugs to cells
- ★ Cyclic peptides have a large surface area and higher conformational rigidity and stability relative to their linear counterparts that potentiate them to have a higher affinity and specificity for any target of interest
- ★ Cyclic CPPs have higher resistance to degradation, unlike their linear counterparts
- ★ A high-throughput assay of cyclic CPPs could increase the efficiency of the discovery of the features of CPPs and screen their permeation
- ★ Understanding the core features of cell-penetrating peptides will allow for great advancements in therapeutics and the development of less invasive oral bioavailable treatments



(2) Diagram of Oral Bioavailability

Methodology and Roadmap

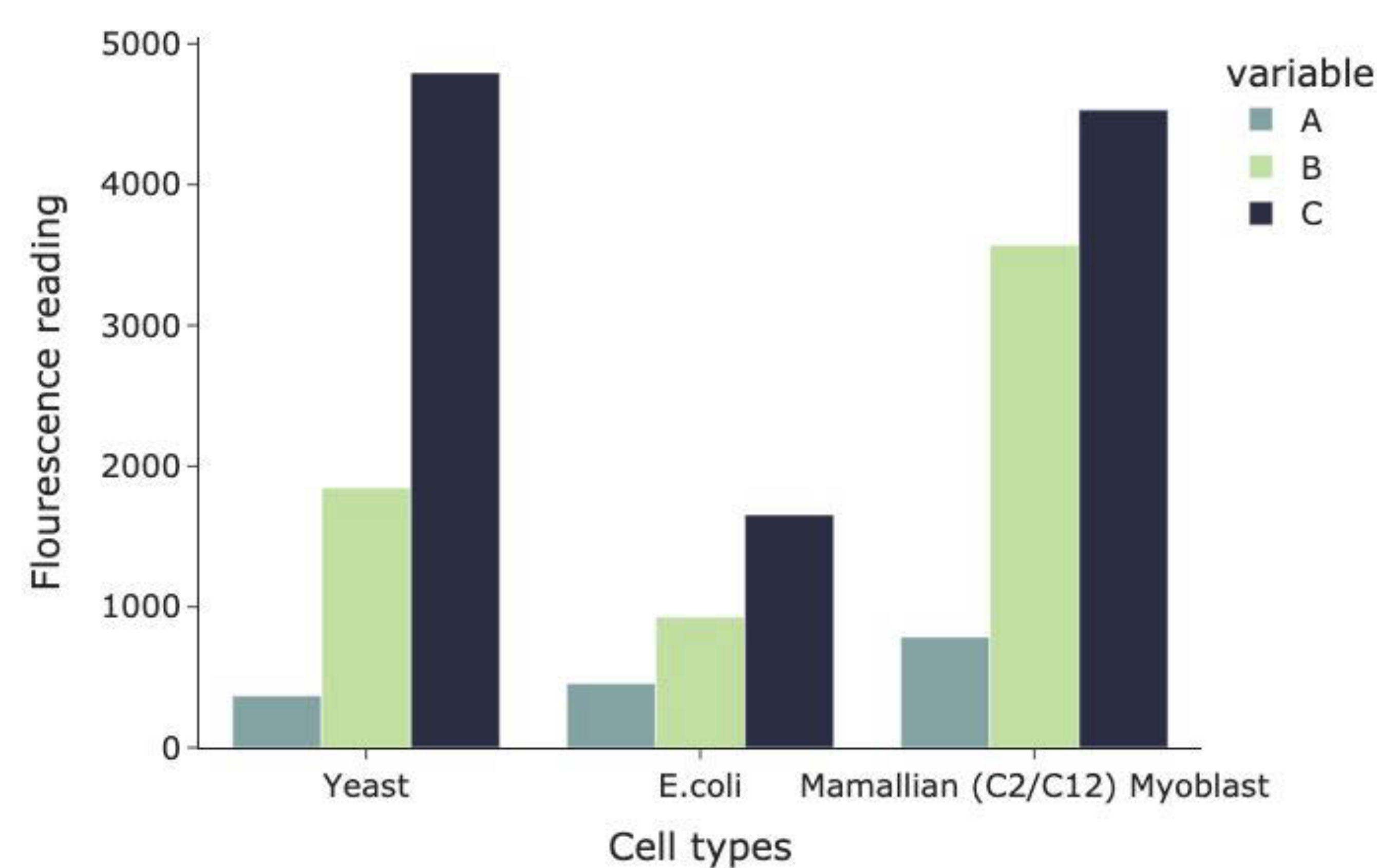


(3) Roadmap

- ★ By amplifying the DNA from within the cell and within the buffer we can determine which peptides stayed in the buffer and which penetrated through to the cell. Preferentially, the peptides are selectively permeable and prefer to permeate diseased cells. Then the peptides can be used as vehicles for the drug to deliver the therapeutic to its target within the cell.

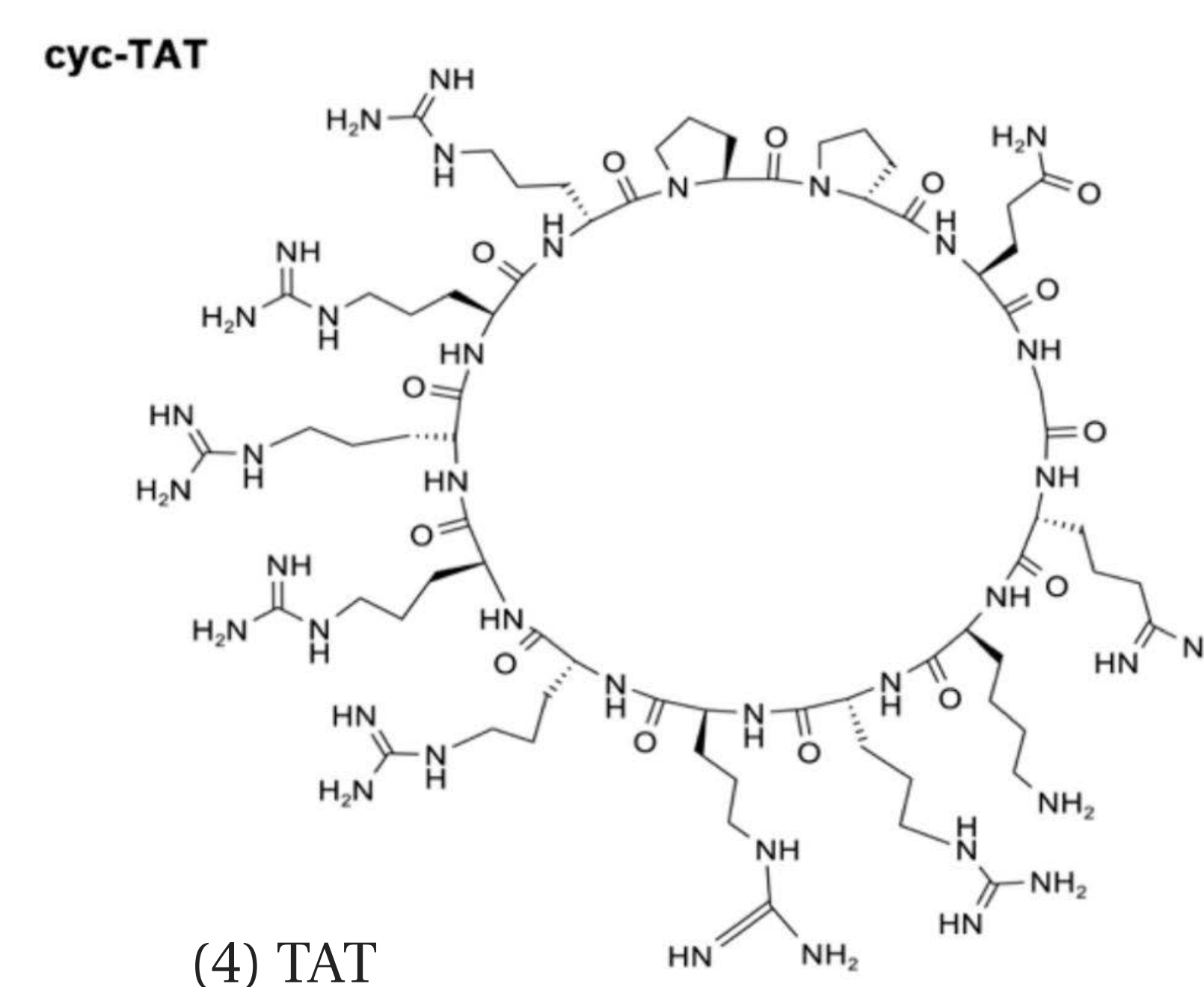
Results

Fluorescence Reading Across Cell Types



Future Directions

- ★ TAT was the first cyclized CPP. High-throughput assay would increase the ability to discover and create more CPPs such as this one



References

- (1) *ACS Synth. Biol.* 2020, 9, 2, 181-190
- (2) Created with biorender.com
- (3) Created with biorender.com
- (4) Zhang, H.; Zhang, Y.; Zhang, C.; Yu, H.; Ma, Y.; Li, Z.; Shi, N. Recent Advances of Cell-Penetrating Peptides and Their Application as Vectors for Delivery of Peptide and Protein-Based Cargo Molecules. *Pharmaceutics* 2023, 15, 2093. <https://doi.org/10.3390/pharmaceutics15082093>