

Developments of Dimeric Ligand Binders to d(CCG) Repeat of FXS and to r(AUUCU) Repeat of SCA10 and Studies of Their Potential Therapeutic Effects

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Nucleotide repeat expansion causes various human neurodegenerative diseases, and most of them have no available treatment currently. Selective binders to the secondary structure of repeat expansion can be a possible therapeutic method. For example, binders for d(CCG) repeat of Fragile X Syndrome (FXS) may lead to the repeat contraction (Fig. 1A) and binders to r(AUUCU) repeat of Spinocerebellar ataxia type 10 (SCA10) can restore the sequestered proteins (Fig. 1B).

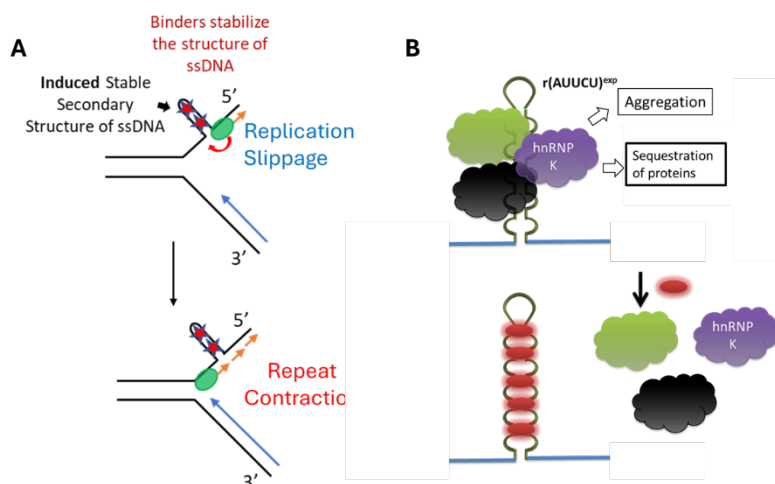


Fig 1. A: Proposed binder-induced repeat contraction for FXS treatment. B: Potential treatment for SCA10.

Previously, my group discovered the selective d(CCG) and r(AUUCU) repeat binders from screening chemical libraries. In the coming summer, to improve the affinity and selectivity of the selected binders to the target repeats (Fig. 2A), we will synthesize various dimeric ligand binders using several methods, as shown in Fig. 2B&2C. We will also test the binding affinity and selectivity of the synthesized dimeric ligand

binders.

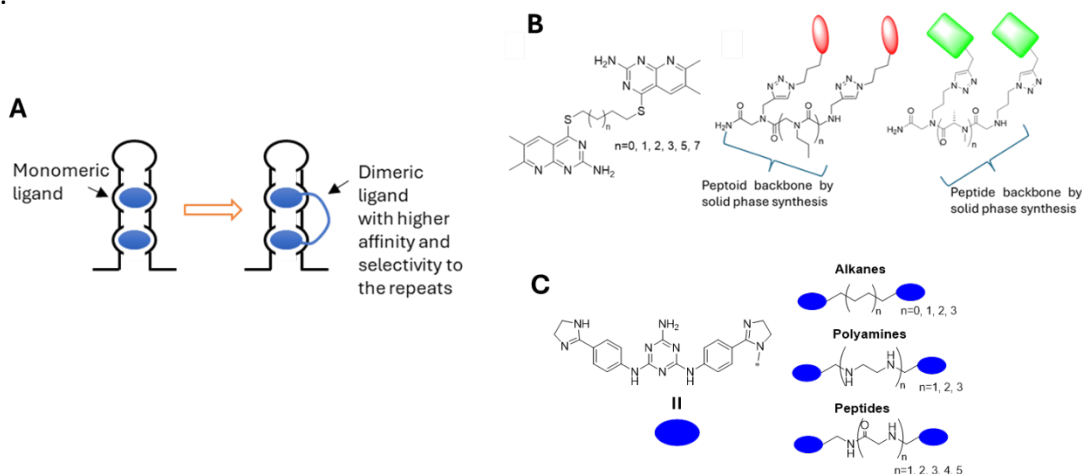


Fig 2. A: Strategy of dimeric ligand binders. B: Designed dimeric ligand binders for FXS treatment. C: Designed dimeric ligand binders for SCA10 treatment.

The student will be expected to enroll in CHEM 4997R in Spring 2026 to prepare for the summer research project.