Developments of Small Molecules Binding to DNA and Studies of Their Biological Effects

Dr. Yang, URP 2024

1. Synthesis of the Dimeric Ligand Binders to d(CCG) Repeats

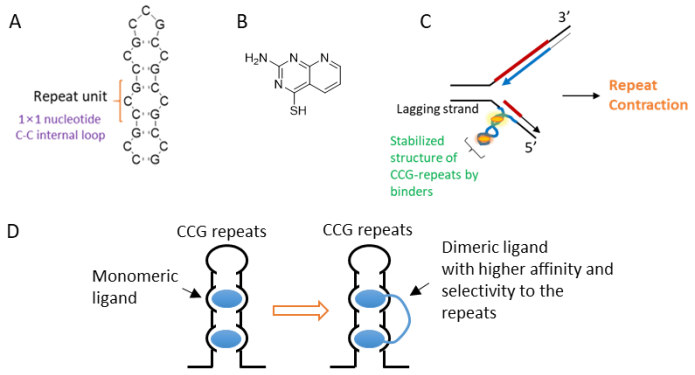

Fig 1. A. Secondary structure of d(CCG) repeats. B. Discovered d(CCG) binder. C: Proposed binder-induced repeat contraction. D: Design of dimeric ligand binder with higher affinity and selectivity to d(CCG) repeats.

More than 40 neurodegenerative diseases are caused by simple repeat expansions. Fragile X-related disorders are caused by the expanded CGG/CCG repeats in the X chromosome. Previously, my group discovered selective d(CCG) repeats binders which can potentially contract the expanded repeats. In the coming summer, to improve the affinity and selectivity, the dimeric ligand binders will be designed and synthesized. In addition, the proposed binder-induced repeat contraction will be tested by using a single-stranded plasmid model.

2. Mechanistic Study of the Observed Anti-Bacterial Activity by Photoactivated Double-Stranded DNA Cleavers

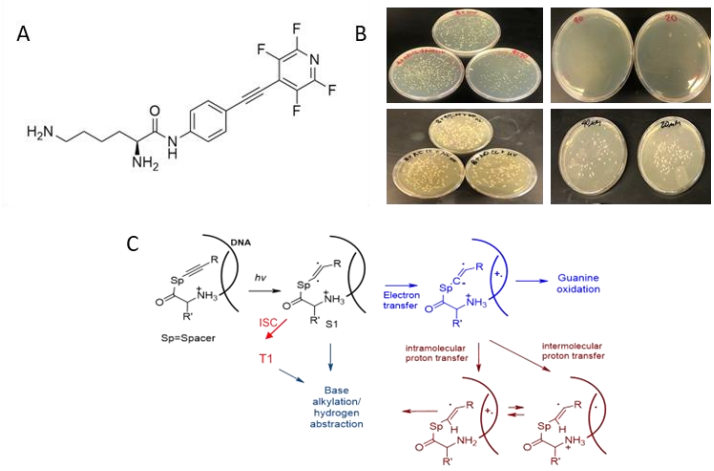

Fig 2. A. Structure of C-Lysine conjugate. B: Bacterial culture images (Top: *S. aureus*, Bottom: *E. Coli*, Left: Controls, Right: C-Lysine treated. C. Proposed possible mechanisms for DNA cleavage by C-lysine. conjugates.

C-Lysine conjugate, an effective photoactivated double-stranded DNA cleaver, was tested for its potential antibacterial activity, and promising results were observed: 0.5 μM and 7.5 μM of IC_{50}s against the gram-positive strain (*S. aureus*) and the gram-negative strain (*E. coli*), respectively. In the coming summer, we will continue the mechanistic studies for the observed anti-bacterial activity and for the antibacterial activity difference between the gram-positive and gram-negative strains. In addition, we will study the pH-dependent activity of the compound at the cell level, which can be applied to cancer treatment.

<u>The student will be expected to enroll in CHEM 4997R in Spring 2024 to prepare for the summer research project.</u>