Directed evolution of novel affinity proteins for biomedical applications

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During biological evolution, iterated mutation and natural selection provide solutions for challenges that organisms face in the natural world. However, the traits that result from natural selection only occasionally overlap with features of biomolecules that are sought by humans for engineering applications and/or therapeutic purposes. In order to guide molecular evolution and access useful artificial properties more frequently, directed evolution in the laboratory has been used to mimic natural evolution. Here, a diverse library of genes is translated into a corresponding library of proteins and screened/selected for functional variants in a manner that maintains the correspondence between genotype (genes) and a desired phenotype (proteins and their functions). These functional mutant genes are replicated and serve as starting points for subsequent rounds of diversification and screening. Over many generations, these beneficial mutations accumulate, resulting in a successively improved phenotype for specific biological events. Here, we aim to enhance protein receptor-ligand interactions[1] using directed evolution for biomedical applications.

In this project, the PhD candidate will use a novel mammalian cell protein engineering platform[2] and combine it with mechanical experiments to evolve new classes of binding proteins for biopharmaceutical applications. The proposed directed evolution strategy uses two key pieces of technology that will be contributed by each of the two working groups. The Nash Lab works in the areas of molecular mechanics[3], and molecular biophysics. The Reddy Lab has developed mammalian cell protein display[2] and engineering platform using immunogenomic editing technology. These complementary methods will be combined to investigate new classes of binding molecules.

References

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