DNA Nanobiotechnology

We aim to perform combinatorial biosynthesis of peptides by constructing a DNA-programmable, biocatalytic peptide synthesizer that we call the NONRIBOSOME. DNA has been used to arrange enzymes in catalytic cascades where proximity enhances catalytic throughput. This effect is particularly pronounced in enzymatic assembly lines such as nonribosomal peptide synthetases, where intermediates of the peptide formation reaction are covalently tethered to the protein (Huang et al., 2020). We have split apart a nonribosomal enzyme and reassembled the functional complex on a DNA strand. By using DNA as a template, we aim to program NRPS modules for the synthesis of novel peptides which may, compared to nonribosomal natural products, have better activity, fewer side effects, or avoid antimicrobial resistance.

