

## ENGINEERING DNA POLYMERASES FOR APPLICATION IN DNB-BASED SEQUENCING TECHNOLOGY

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DNA polymerases serve as the core engine to afford sequence information in sequencing technologies that have revolutionized modern biological research. For application in the DNB-based sequencing platform, an assemblage of DNA polymerases was engineered to catalyze the requisite biochemical reaction. In the process, naturally occurring polymerases were tapped into through deep-learning algorithms for constraints between individual protein residues to narrow down the protein sequence space and to annotate protein sequences in light of their catalytic properties. And the constraints were subsequently applied in designing potential polymerase candidates with the guidance of the sequence annotations. Additionally, ancestral protein sequences were estimated to expand the candidate repertoire. Furthermore, the candidates were subjected to *in silico* screening before examined by an HTS methodology based on fluorescence signal. Finally, the resulting proteins were expressed and purified for testing in the DNB-based sequencing platform. Our sequencing data suggested that these proteins behave better than their existing counterparts.