Xeno Nucleic Acids (XNAs): In Vitro Selection, Functional transliteration, and In Vivo Replication by E. coli

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Abstract

Xeno Nucleic Acids are non-natural genetic polymers consisting of alternative sugar backbone structures that are different from the ribose and deoxyribose units found in RNA and DNA. Owing to the artificial sugars, XNAs are release resistant and therefore more compatible with physiological conditions, highlighting their great potential in the development of nucleic acid based medicine and biotechnology. Functional molecules of ligand binding XNA aptamers and catalytic XNA enzymes that outperform their DNA or RNA counterparts regarding both activity and biostability have been isolated by in vitro selections using engineered polymerases with XNA recognition activities. Nonetheless, limited by the availability of XNA polymerases, the development of functional XNA molecules is still limited in a small community of advanced laboratories. Towards the construct of XNA replication systems that can be commonly utilized by general labs that are interested in related studies, we have performed our research from three aspects: (1) the establishment of an in vitro functional XNA selection system by using naturally occurring DNA polymerases, (2) the characterization of an interesting phenomenon of catalytic activity takeover between two XNA polymers, 2'-fluoro-2'-deoxy arabino nucleic acid (FANA) and α-L-threose nucleic acid (TNA), and (3) the demonstration of efficient and faithful in vivo replication of FANA containing mosaic templates by the replication machinery of E. coli. Our studies not only expand the biological toolkit that can be readily used for routine XNA operation in research labs, but also reinforce the notion that XNAs, governing by diversified artificial sugar backbones will effectively extend the structural space of nucleic acids beyond that of canonical DNA and RNA. The further exploration of XNA biophysical properties and biological functions will inspire the development of nucleic acid based biomedicine and biotechnology.

Biography

Yajun Wang received her Ph.D in Chemistry in May 2016 from the University of British Columbia, BC, Canada, where she focused her research on enhancing the catalytic efficiency of catalytic DNA molecules (DNAzymes) by expanding the functionalities of DNA to mimick the catalytic mechanism of protein enzymes. Following her Ph.D training, Wang moved to the University of California, Irvine in June 2016 for her postdoctoral research. Sponsored by the Simons Foundation on the Collaboration of Origin of Life, Wang worked on the development of chemical and biochemical tools that support the study of the chemophysical properties of Xeno Nucleic Acids, and established

XNA SELEX systems for the in vitro selection of functional XNA molecules. She then started her independent career as a professor in the Institute of Basic Medicine and Cancer (IBMC), Chinese Academy of Sciences, At IBMC, her team has focused at the interface of chemical and synthetic biology to (1) develop artificial nucleic acids with ligand binding (aptamers) and catalytic activities (nucleic acid enzymes), and (2) exploring novel application scenarios for XNA as activity-enhancing decorating residues in ASO, siRNA, and mRNA vaccines, aiming to create artificial nucleic acid based agents gaining both bio-stability and diversified functionalities for biotechnology and medicine. Her research has been published on Nature Chemistry, Nature Communications, Journal of American Chemical Society, Nucleic Acid Research, Chemical Science, etc.