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Improved illumina sequencing by polymerase engineering

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The sequencing-by-synthesis (SBS) chemistry commercialized by Illumina has been a key enabler of massively parallel nextgeneration sequencing, which in turn has dramatically reduced the cost of sequencing human genomes and resulted in personalized medicine initiatives and population sequencing efforts throughout much of the world. The capacity of engineered archaeal family B DNA polymerases (pols) to incorporate modified nucleotides has been exploited by researchers throughout academia and biotechnology, including Illumina's SBS chemistry. Nucleotides with a 3'-reversible terminator and fluorophores attached via the base serve as the basis for base calling in Illumina NGS platforms. Pols deployed on the first Genome Analyzer[™] instruments had poor incorporation efficiency of these modified nucleotides. Through our engineering efforts, we have facilitated a significant reduction in chemistry time while improving sequencing data quality and enabling over 300 bp read lengths. The critical goal of our research is to engineer pols with enhanced selectivity, fidelity, and incorporation efficiency of modified nucleotides to enable faster sequencing turnaround time and boost adoption of NGS technologies in the clinic.

Biography

Seth McDonald received his PhD in Biochemistry from the University of Utah where he studied the structure and biological implications of the interaction of the essential Spn1 and Spt6 transcription factors in Saccharomyces cerevisiae. In his Post-doc at Colorado State University, continuing his use of x-ray crystallography and enzyme kinetics, he engineered fast and accurate RNA polymerases from small RNA viruses that effectively restrict viral genome variations within the given population required for infection and survival. At Illumina, he has made significant contributions to the structural and functional understanding of how polymerases incorporate nucleotides modified on the base and sugar. He is the assay development and structural biology lead in the protein engineering group where he continues to contribute to the ongoing enzyme engineering projects within Illumina.

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