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Engineering Tn5 transposase enzyme to improve DNA sequencing library preparation

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Statement of the Problem: Next generation sequencing has opened new doors into genomics. Recent advances in sequencing technology have enabled researchers to sequence genomes with unprecedented accuracy and speed. However, preparing DNA sequencing libraries still remains as a challenging step. Transposase-based library preparation offers a simple, fast, scalable, and flexible solution. However, when compared to other (ligation-based) library preparation methods, transposases show some insertion bias that affects the final DNA sequencing library.

Methodology: We applied various machine learning algorithms to random mutagenesis libraries of transposases to efficiently design new mutant transposases with less insertion bias.

Findings: We present the discovery of a mutant transposase (Tn5-059) with low GC insertion bias and AT dropout. Libraries prepared by this mutant have good uniformity of genome coverage as well. Tn5-059 also shows low sensitivity to the amount of input DNA. In addition, this enzyme shows efficient performance in DNA sequencing libraries for open chromatin profiling.

Conclusion & Significance: DNA input tolerance together with superior coverage uniformity are two important factors to be considered in DNA sequencing library preparation. Tn5-059 successfully delivers on both of these aspects, which leads to less sequencing volume and lower sequencing cost. We discuss the importance of choosing a correct assay as well as the importance of filtering data based on the biology behind the assay.

Biography

Amirali Kia has completed his Bachelor's and Master's working on the application of various artificial intelligence algorithms in computational fluid mechanics. He then started his PhD at Stanford University where his focus was on high performance computing and developing fast algorithms with applications in computational biology. He started his career at Illumina by joining Protein Engineering group to apply machine learning algorithms to enzyme engineering. He is now a senior manager at Illumina in the Computational and Applied Biology Department, leading Deep Learning group. The focus of his team is to bring new AI algorithms to genomics and Illumina's internal technology.

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