ENGINEERING A HYPERACTIVE TCBUSTER TRANSPOSASE FOR EFFICIENT GENE DELIVERY FOR CELL THERAPY APPLICATIONS

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We present a novel engineered transposase to address the challenges associated with current therapeutic approaches to cell therapies including chimeric antigen receptor (CAR) T cells for hematological malignancies. While CAR-T cells have shown remarkable clinical efficacy, their widespread use is hindered by the high costs and limitations of viral vectors, including constrained cargo size capacities and a higher risk of insertional mutagenesis. To overcome these issues, we have developed a non-viral transposase-based editing platform centered around our novel hyperactive TcBuster (TcB-M™) transposase.

TcB-M™ represents a departure from previous engineering efforts used to enhance transposases like PiggyBac and Sleeping Beauty. Leveraging a unique high-throughput screening platform in combination with DNA shuffling combinatorial libraries, we screened a mutant library of over three million variants, significantly exceeding the scale of previous transposon development efforts. This breakthrough has enabled us to create the hyperactive transposase TcB-M™ with significantly improves integration rates while reducing the need for plasmid DNA transposon and maintaining a safer integration profile than viral methods. TcB-M™'s flexibility with cargo size allows us to use large multicistronic plasmids for delivering multiple genes into various cell types, including primary T-cells, NK cells, and induced pluripotent stem cells (iPSCs).

Our TcB-M platform is a proven non-viral gene editing technology capable of delivering large or challenging therapeutic cargos across various cell types. By overcoming the hurdles associated with viral-mediated editing, TcB-M™ accelerates the production of crucial therapeutics and offers a versatile and cost-effective solution for advancing CAR-T and other cell-based therapies to market.