ENGINEERING GENE EDITORS FOR IN VIVO THERAPEUTICS

Wei Leong Chew, Genome Institute of Singapore
chewwl@gis.a-star.edu.sg

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Engineering gene editors enables new biotechnological and therapeutic applications. We utilise an understanding of the cellular genomic repair pathways to engineer a C-to-G base editor capable of mediating a precise C:G to G:C transversion in the mammalian genome, enabling a transversion chemistry not realized by earlier base editors. To further develop these base editors for in vivo applications, we leverage split Cas9 proteins and engineered adeno-associated viruses (AAVs). Engineering these AAVs on their capsid surfaces tailor them for improved specificity towards target organs. These delivery vectors are further assessed using a new single-cell library-on-library assay, which evaluates efficiency and specificity of individual delivery vector variants across multiple cell types in heterogeneous tissues. The strategic engineering of both therapeutic cargo and delivery vector brings us closer to realizing precision genome surgery in vivo.