Advancing Safety in Genome Editing

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The SIMPLE-seq project aims to develop an innovative and user-friendly in vitro method for evaluating the off-target activity of base editors (BEs). This technology addresses a critical gap in the safety assessment of modern genome editing techniques. Building on a method originally developed for CRISPR-Cas9 nucleases, SIMPLE-seq is specifically adapted to the unique mechanisms of base editors. While CRISPR-Cas9 induces double-strand breaks in DNA, base editors create only single-strand breaks. Through innovative enzymatic modifications, these breaks are converted in a way that allows precise analysis using high-throughput sequencing. This enables accurate mapping of unintended DNA alterations.

SIMPLE-seq will first be validated in benchmark studies with established base editors and subsequently applied in clinically relevant scenarios, such as genome editing of CD7, CD52, and TRBC1/2 in T cells. The aim is to comprehensively assess the safety and specificity of base editors, making their clinical applications safer and more predictable. SIMPLE-seq represents a reliable, cost-effective, and scalable method with broad applications in both research and industry. Led by Dr. Carla Fuster García and Prof. Dr. Toni Cathomen at the University of Freiburg, the project team is committed to establishing SIMPLE-seq as the new gold standard for the safety assessment of base editors.