



SB-INNOCENT - SLEEPING BEAUTY TRANSPOSASE WITH ENHANCED BIOSAFETY

Keywords: Sleeping Beauty, transposase, biosafety, gene and cell therapy, T-cells, improved integration profile, safe harbor, reduced genotoxicity

INVENTION NOVELTY

The present invention provides Sleeping Beauty (SB) transposase variants with enhanced biosafety and an improved integration profile for safe harbors while maintaining integration efficiency, thus enabling safer gene and T-cell therapies.

VALUE PROPOSITION

The novel SB-Innocent variant provides a substantially improved genomic integration profile, with higher frequencies of insertions in genomic safe harbors and reduced activity in oncogenic or gene-dense chromatin yet preserving robust transposition efficiency and transgene expression. This enables safer generation of CAR-T, TCR-T and NK cell products, as well as in vivo gene therapy approaches in hematopoietic, hepatic, muscular or neural tissues, by using a fully non-viral system that is scalable, cost-efficient and easier to manufacture than viral vectors. By administering SB-Innocent as a plasmid, minicircle, mRNA or protein, the system circumvents the complexity and pre-existing immunity associated with viral capsids.

TECHNOLOGY DESCRIPTION

The SB-Innocent variant provides a substantially improved integration pattern, achieving 7-10-fold enrichment in safer territories. It maintains SB100X-like transposition activity and stable transgene expression, while simultaneously avoiding oncogenic TADs or gene-dense chromatin and regulatory regions. On a molecular level SB-Innocent avoids rigid non-B DNA structures (e.g. perfect palindromes, G-quadruplexes) that are associated with replication stress, favouring structurally relaxed regions instead. In comparison to SB100X and established safety mutants such as K248R SB-Innocent shows the best overall combination of increased safe-harbor enrichment, reduced integration into high-risk regions and largely preserved transposition activity.

DEVELOPMENT STATUS

Characteristics of SB-Innocent have been studied in various cell types (T-cells, HeLa and HEK cells) and are currently further validated.

COMMERCIAL OPPORTUNITY

The SB-Innocent transposase and further improved SB-transposase variants are available for in-licensing.

PATENT SITUATION

EP25206906.7 claiming SB-Innocent has been filed in Oktober 2025.

FURTHER READING

Manuscript in preparation.

