

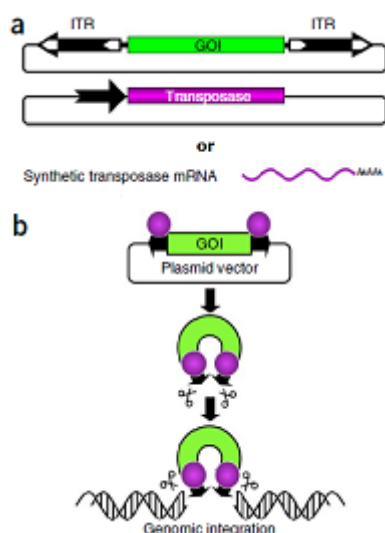
## Technology Offer

# Stable Gene Transfer with Hyperactive Sleeping Beauty Transposase SB100X

Reference Number TO 03-00251

## Challenge

DNA transposons represent natural gene delivery vehicles that integrate into the host genome via a cut-and-paste mechanism. Their stable insertion thereby provides the basis for long-term expression of transgenes in cells and organisms. Common viral gene transfer vectors give rise to safety concerns and are involved with considerable costs and complexity regarding GMP production. Therefore, the Sleeping Beauty (SB) transposon system has emerged as an attractive and simple alternative in gene therapy and is currently being used in eight clinical trials. Since successful gene transfer strongly depends on transposase activity the creation of hyperactive transposase variants significantly enhanced the efficiency of this promising technology.



a) Bi-component SB-transposon system. b) The gene of interest is excised and integrated by the transposase.

## Technology

Hyperactive transposase SB100X has been engineered with ~100-fold enhancement in efficiency when compared to first-generation transposases. It shows an impressive capability to mediate gene transfer and sustained gene expression in primary human cells comparable to viral transduction efficiencies. In contrast to retroviral vectors which have a potential safety risk due to the preference to integrate into transcription units, the SB vector system facilitates random genomic integration. By virtue of this beneficial integration pattern, SB is regarded to be the safest transposon system currently used in gene therapy. The use of SB100X allows for reducing the transposase amount without compromising high transposition rates. As an example, T-cell modification with a CD19-specific CAR requires 10-times lower amounts of plasmid DNA coding for SB100X than the less active SB11 which is currently used in gene therapy clinical trials for this application. SB100X mediates efficient transgenesis in various difficult-to-transfect cell lines (e.g. human embryonic stem cells or iPSC) and represents a powerful tool for gene delivery and insertional mutagenesis purposes. In addition, SB100X achieves sufficient germline transgenesis in mice, rats, rabbits and pigs to open new avenues for genetic engineering in animal models.

## Commercial Opportunity

In-licensing of IP and know-how, collaboration in future product development.

## Patent Situation

### Priority claiming patent application in 2007

Granted patents: European Patent EP2160461; US Patent 9,228,180; Japanese Patent JP5726522; Australian patent AU2008271523

### Pending patent applications:

US patent application 14/957,877; Canadian patent application CA2692501

## Further Reading

Nature Genetics 41 (6): 753-761 (2009-06); Expert Opinion on Biological Therapy 12 (2): 139-153 (2012-02); Human Gene Therapy Methods 25 (4): 241-252 (2014-08); Nature Protocols 9 (4): 810-827 (2014-04); Crit Rev Biochem Mol Biol. 2017 May 18;1. "Going non-viral: the Sleeping Beauty transposon system breaks on through to the clinical side".