ProBioGen
Intelligent Biopharmaceutical Solutions

DirectedLuck® Transposase System

Highly Efficient Gene Delivery for Advanced Cell Line Development

Highly efficient gene delivery system based on epigenetic targeting combined with a carefully designed transposase and transposon. DirectedLuck® directs transposons specifically to integration sites with highest and stable transcriptional activity and thus enables higher titer and product quality for complex antibody formats. At the same time, it cuts down on effort and time to clinic.

Epigenetic targeting directs your transgenes to the most preferred genomic integration sites.

Typically, gene delivery technologies for cell line development rely on the integration of transgenes in a random fashion at spontaneous breaks. Best integration events occur as a matter of luck and lead clones are identified through extensive screens. Transposases mediate the integration of transgenes at multiple open genome loci and are known to facilitate cell line generation in many ways.

ProBioGen's transposase takes this principle, but is specifically designed to read and bind specific chromatin marks that signal the highest transcriptional activity.

Transgenes are directed to and are integrated into such highly active sites. This results in the highest transcription levels of your desired protein. The outcome is an unparalleled consistency of bulk pools with highest productivity that translates into superior producer clones with exceptional expression stability.

How does it work?

The transposase is equipped with a specific histone reader domain that identifies transcriptionally active sites in the specific host genome. As the histone code itself is universal, the DirectedLuck® transposase can be applied to a broad variety of host cells from different species and tissue origins.

Once associated with an active locus, the transposase precisely integrates a copy of the expression unit flanked by transposon ITRs, leaving the unwanted plasmid backbone behind. As a result, the cell line carries multiple transgene copies at most preferred loci.

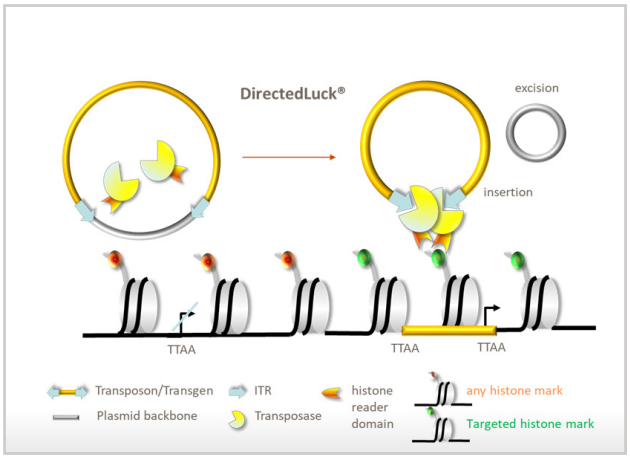

Fig. 1: Epigenetic Targeting at work

Time Saver!

Bulk pools recover much faster and express higher and more homogeneously. Screening for high-producing clones can be greatly reduced, allowing you to focus on product quality.

As bulk pools are highly representative for the clone to be selected later on, they can be used to manufacture early material for development work, TOX studies or even DS1 material, reducing overall timelines to the clinic. Increased productivity and reduced timelines have also an impact on cost of goods.

Features and Data

- Epigenetic targeting for highly efficient gene delivery
- Thoroughly designed transposase and transposon
- Moderate gene copy numbers and clean integration structures
- Hundreds of producer cell lines generated at ProBioGen or in licensee labs

Use Cases

- Drug discovery: fast bulk pools for a high number of candidate molecules
- Cut down time to clinic: DS1 manufacturing with stable high titer bulk pools feasible
- Short cut to viral vectors for cell and gene therapy: stable packaging cells and CAR-Ts
- Simple or complex biologics: generate superior cell lines

Advantages of DirectedLuck®

- Highest expression levels and exceptional stability
- Pools are highly representative of later clones
- Speeds up time to clinic
- Easy application in your lab, regardless of your host cell line
- Superior heterodimer rates for bi-specific mAbs
- Royalty and milestone-free for clients' projects at ProBioGen

Impact on Product Quality for Bi-specifics

Expression is strictly copy number dependent, offering great potential for improving product quality through transposon design. If you use different transposons for the transgenes, flexible and fast adjustment of plasmid ratios will modulate product purity in a predictable manner.

The DirectedLuck® technology is universally applicable, particularly suited for simultaneous insertion of multiple gene cassettes, easy to handle and robust. DirectedLuck can also be used to generate packaging and CAR-T cells for cell and gene therapy applications.

The DirectedLuck® technology is applied in service projects at ProBioGen and is also available under a license.

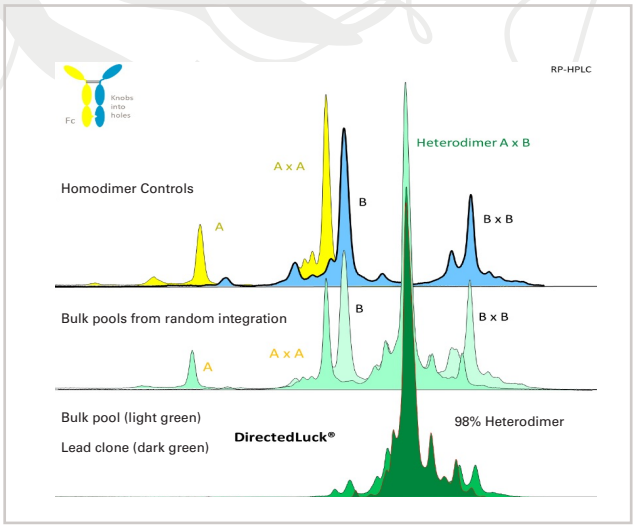

Fig. 2: Analysis of heterodimer content by RP-HPLC in pools and the lead clone for a 2chain-heterodimer molecule. Genes are placed on separate vectors. Note excess of unwanted byproducts (A or B) in pools generated by random integration.

Your integrated CDMO Partner for Biologics and Advanced Therapies

ProBioGen is a Berlin-based specialist in developing and manufacturing biopharmaceutical active ingredients, viral vectors and vaccines while applying proprietary technologies to improve product quality and features.

Combining both state-of-the-art development services, together with intelligent product-specific technologies yields biologics with optimized properties. Rapid and integrated cell line and process development, comprehensive analytical development and GMP-compliant manufacturing are performed by a highly skilled and experienced team.

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