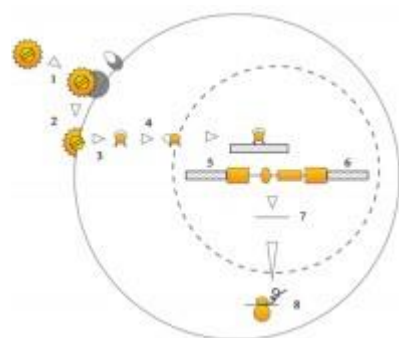


Integrative lentiviral vectors or LentiFlash®?

Depending on your application, Flash Therapeutics provides (through Vectalys' manufacturing platform) **integrative lentiviral particles & LentiFlash®**, an innovative non-integrative lentiviral particle.

1. Integrative lentiviral vectors



**STABLE
EXPRESSION**

**DNA
DELIVERY**

**LONG-TERM
EXPRESSION**

**INTEGRATION
INTO THE HOST
GENOME**

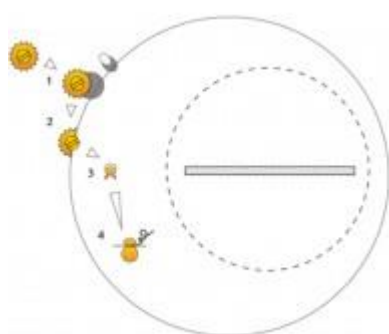
Applications:

- ▶ Gene overexpression
- ▶ Cell engineering
- ▶ CAR-T cells
- ▶ Immunodeficiency...

Benefits compared to DNA transfection:

- ▶ 100% transduction efficiency in primary and stem cells
- ▶ Preserve original cell phenotype
- ▶ Do not affect cell viability and proliferation
- ▶ For both dividing and non-dividing cells

2. LentiFlash®: RNA delivery lentiviral particle (non-integrative)



**TRANSIENT
EXPRESSION**

**RNA
DELIVERY**

**SHORT-TERM
EXPRESSION**

**NO
INTEGRATION**

Applications:

- ▶ Gene editing
- ▶ Cell differentiation
- ▶ Cell reprogramming
- ▶ Immunotherapy

Benefits of LentiFlash®, a game-changing class of RNA carriers:

- ▶ 100% transduction efficiency in primary and stem cells
- ▶ No genomic traces
- ▶ mRNA transfer without cytotoxicity
- ▶ Preserve original cell phenotype
- ▶ For both dividing and non-dividing cells

3. FAQs

Why should I use LentiFlash® instead of transfection reagents?

Transfection reagents are commonly used to transiently transfer RNA in cells of interest. However, these reagents may impact the cell viability, lead to high cell toxicity and can modify the cell phenotype (when used on difficult to transfect cells). LentiFlash®, an RNA delivery particle derived from lentiviral vectors, resolves these main drawbacks.

Why is the use of LentiFlash® recommended for gene editing?

Gene editing using CRISPR-Cas9 system is widely used nowadays, but it has been shown that a stable expression of CRISPR-Cas9 into cells of interest may lead to off-target activity which results in unexpected genome modifications. For this reason, we advise scientists to use LentiFlash® for gene editing experiments (for transient RNA delivery).

Are LentiFlash® engineered cells considered to be Genetically Modified Organism (GMO)?

Non-viral systems such as electroporation are largely used especially for RNA delivery. Derived cells engineered with such tools are not considered as GMO and ensure a high level of safety. This last point is crucial and encourages industry to test and promote these gene transfer technologies. Once researchers have validated a gene delivery process from cell transduction to disease effect with a viral tool, they try to switch to a non-viral system for regulatory and cost reasons, despite those tools' efficiency and toxicity issues. A strong advantage of the non-integrative delivery of genetic material into cells mediated by LentiFlash® is that this approach does not result in the production of genetically modified organisms (GMO). It means that even if the biologic drug is a GMO itself, the resulting modified cells are free of any trace or signature from non-human or viral sequences. The transient expression is expected to trigger a cellular process which will remove a genetic sequence or will commit cells into a specific pathway.