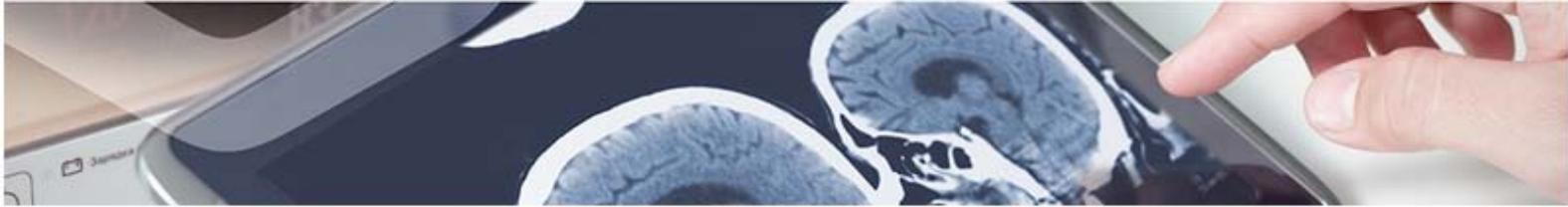


Laboratory reagents and materials

Insulator to prevent silencing and promote expression in Stem Cells

A research group from Andalusian Public Health System (APHS) has developed a new insulator that improves the expression pattern of vectors.



Description

Gene-transfer technologies aim to achieve a stable expression that does not affect the physiological expression of the target cell. Achieving this is essential both in basic science and in gene therapy. The only tools capable of achieving this stable expression in stem cells are retroviral vectors.

Retroviral vectors achieve stability of the expression by integrating themselves inside the genome of the genetically modified cell. This can have several undesirable effects:

1. Effect of the genome on the vector:
 - a. Silencing. The vectors stop expressing the transgene owing to epigenetic changes to the promoters/enhancers. Usually, the expression of the transgene in stem or primary cells is more prone to gene silencing than differentiated or immortalised cell lines.
 - b. Heterogeneity of the expression owing to the influence of enhancers present in the region of the genome where the vector has been integrated.
2. Effect of the vector on the cell (genotoxicity): Highly active enhancers or promoters present in the vector may influence the normal expression of genes near to the vector's integration site. In the worst of cases, these genes are oncogenes, their expression is activated and they may cause cell transformation.

To avoid the negative effects of this type of vector on heterochromatin and vice versa, the research group has developed an insulator that is included in the actual structure of the retrovirus. Specifically, the authors demonstrate the usefulness of lentiviral vectors.



Advantages

The main advantages of this new element integrated into lentiviral vectors are:

1. Improved expression pattern for different lentiviral vectors in stem cells.
 - a. Avoids gene silencing.
 - b. Reduces heterogeneity of expression depending on the integration site.
 - c. Increases expression levels.
 - d. Enhances regulation by doxycycline-regulated all-in-one vectors.

Owing to these characteristics, it could also improve the efficiency and safety of gene-therapy strategies that require the integration of genetic material in stem cell.



Intellectual Property

The technology is protected by a PCT patent application.



Aims

The research group is looking for a collaboration agreement for further development or a licence agreement.



Classification

Category: Laboratory reagents and materials
Technology: Gene therapy
Pathology: Various