Gene therapy

HIGHLY INDUCIBLE TET-ON VECTOR SYSTEM

A research group from the Andalusian Public Health System (SSPA) has developed a TetR(Tetracycline repressor)-based all-in-one lentiviral system.

Oficina de TRANSFERENCIA DE TECNOLOGÍA
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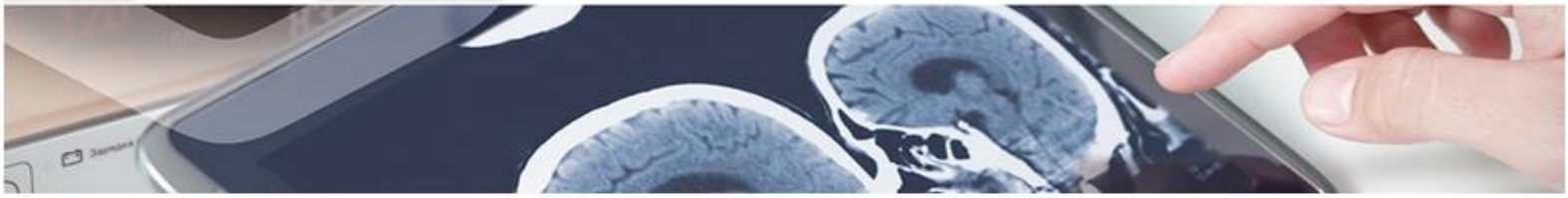

Description

Inducible gene expression systems based on antibiotic or hormones are a potent research tools and are constantly developed for their use in basic research and/or clinical application. Among the existing inducible transcriptional gene regulatory systems, the rtTA (reverse tetracycline controlled trans-activator)-regulatable system is the most widely exploited tool for controlling gene expression. However, all these tetracycline-inducible system require a tetracycline-dependant-transactivator to activate the regulated promoter. The requirement of a transactivator for transcriptional activity has several undesired consequences.

The research group has developed a TetR-based all-in–one lentiviral system that efficiently generates doxycycline-responsive cell lines without the requirements of cloning and/or antibiotic selection. This vector called CEST, is the result of the combination of all the elements required for Tet-ON regulation into a single lentiviral vector. CEST contain the doxycycline-responsive cassette (CMV-TetO) driving the expression of the transgene and the SFFV (Spleen-Focus-Forming-Virus) promoter expressing high amounts of the TetR protein. This vector efficiently produced doxycycline-regulated inmortalized and primary cell lines such as 293T and human Mesenchymal Stem Cells (hMSCs).

Advantanges

The regulatable gene expression system has numerous advantages properties that make it particularly suitable for application to gene therapy and basic research. For example, the system provides an “on”/”off” switch for gene expression that allows for regulated dossing of a gene product in cell lines or in a subject. This vector efficiently generates immortalized and primary human doxcycline-responsive cell lines.

CEST vector do not cause toxic effects. The research group have analyzed the potential alteration of TetR overexpression in hMSC, an important target for cell-gene therapy applications. They did not find any alteration on the phenotype or in the cell cycle status on hMSCs that were transduced at high MOI (multiplicity of infection) with the CEST vector and that were highly-responsive to doxycycline.

Intellectual Property

The technology is protected by an European and EEUU patent application.

Aims

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

Classification

Technology: Gene therapy
Pathology: Several

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