CRISPR System for Gene Editing

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Invention

The invention relates to a 'Clustered Regularly Interspersed Short Palindromic Repeat (CRISPR) CRISPR associated (Cas)' (CRISPR-Cas) system targeting a genome sequence in a eukaryotic cell, i.e. a system useful for making modifications within the cell genome.

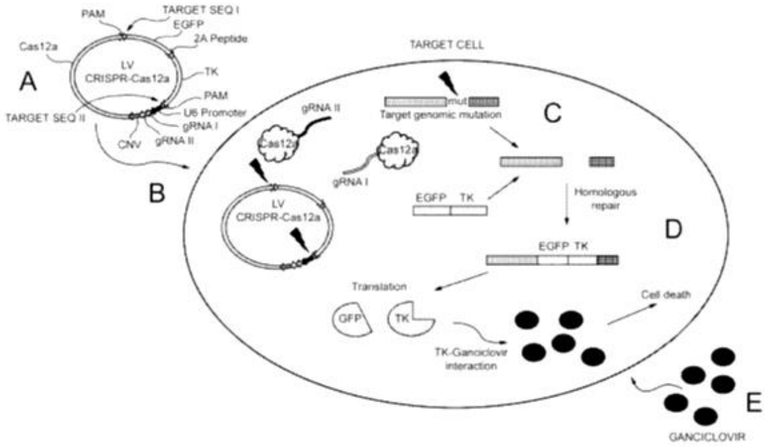
CRISPR technology is able to produce cuts in the DNA double strand by using an RNA molecule, called guide RNA (sgRNA), which guides an endonuclease enzyme, in this case the Cpf1 enzyme, to a specific target site on the genome.

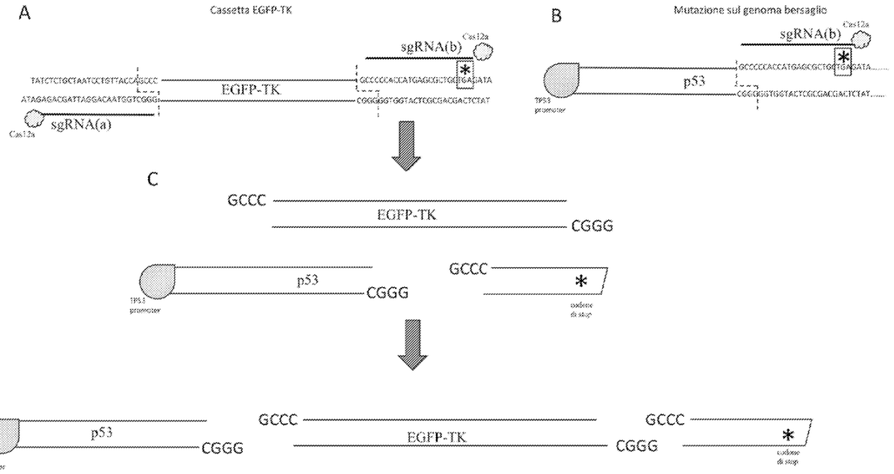
In this context, the present CRISPR technology exploits the host DNA repair system for the in-frame insertion of a suicide gene (e.g. thymidine kinase) into the genome of cells with specific cancerous mutations. Once transduced in the target (cancerous) cell and the suicide gene inserted in the correct locus, administration of a specific inducer (e.g. ganciclovir) triggers the death of the taget cell.

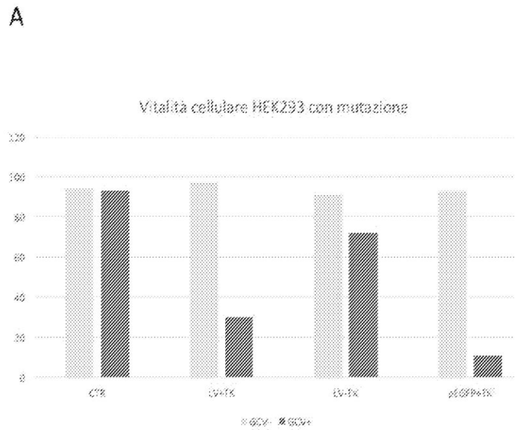
The suicide gene is further engineered at its 5' end to replace any nonsense mutations at the desired insertion locus and thus allow for the correct site-specific expression of the suicide protein.

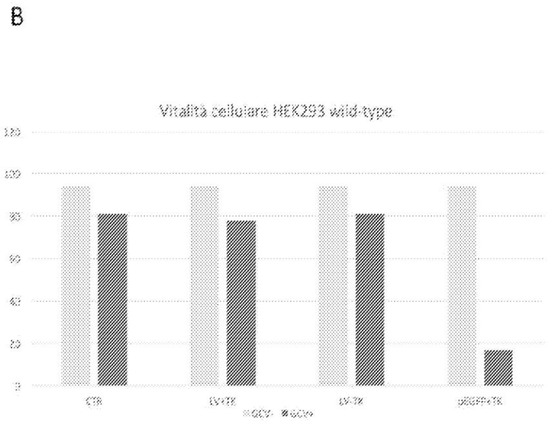
The system is also carried by (slow)viral vectors suitably modified to increase transduction specificity in the target cells; furthermore, the system is capable of self-inactivation through the action of the Cas enzyme on its own DNA sequence.

Drawings & pictures





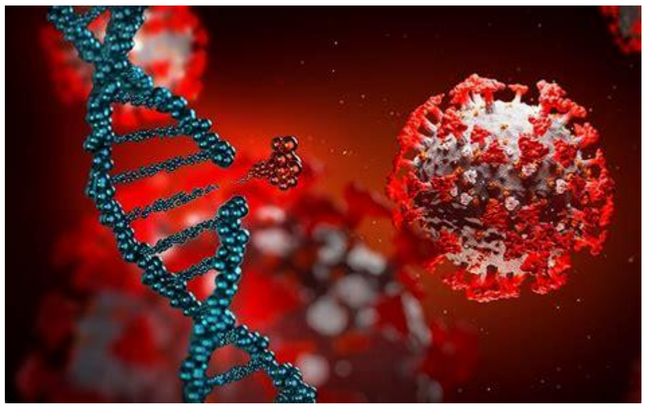




Industrial applications

The technology may be of interest to biotechnology and pharmaceutical companies having (or wishing to expand to) Advanced Therapy Medicinal Products (ATMPs) in their pipeline, as well as in hospitals, health care facilities or health service facilities working in personalised medicine.

In particular, the invention applies to difficult-to-treat neoplasms (e.g. B-cell chronic lymphatic leukaemia, or B-CLL). In this case, the insertion of the suicide gene will result in the ablation of the leukaemic clone without affecting other non-leukaemic cells and by exploiting the presence of specific mutations in the *p53* gene.



Possible developments

Currently evaluated at a TRL of 3, the technology can be further developed within specific technology maturation projects aimed at raising the level and allowing its introduction into the industrial network.

The group is looking for industrial partners operating in the pharmaceutical sector interested in collaborating on the aforementioned technological maturation of the invention.

The University of Siena is open to negotiate specific agreements for the exploitation, licence or option of the patented invention.

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