NANOTRANSDUCER-BASED GENOME EDITING SYSTEM

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Invention

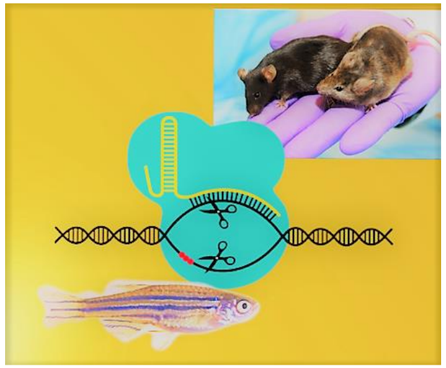
The invention concerns a system based on a nano-transducer able to **modify a target DNA sequence in a cell in order to delete harmful mutations underlying genetic diseases**.

The main novel aspect of NANO-GENE is the **nano-transducer consisting of a hybrid system**, comprising a **nanoparticle** covalently linked to a **gRNA/dCas9** (a mutated Cas9 that binds DNA to the target site via g-RNA but unable to cut DNA).

The nanoparticle is designed to absorb energy at a specific wavelength and convert it into heat. Activation of the nanotransducer by laser irradiation causes localized temperature increase only at the gene locus recognized by the ribonucleoprotein. The local temperature increase can cause DNA melting (if it exceeds 100 °C) or activation of a thermophilic nuclease (if it reaches 65 °C).

The new genomic editing tool NANO-GENE overcomes the limitations of CRISPR/Cas9 systems, since it replaces the nuclease activity of Cas9 with a nanotransducer, whose activation is constrained by the occurrence of a number of conditions. These conditions are also influenced by the operator irradiating the target site. This process, being activated only upon the occurrence of that conditions, is a **system of extreme reliability and specificity**.

Drawings
& pictures



Industrial applications

Medicine; Gene therapy; DNA aberrations; Cancer; Rare genetic diseases.

The invention aims to develop a highly specific therapeutic approach for the treatment of diseases triggered by specific DNA gene aberrations.

The technology represents one of the most innovative biotechnological systems in the field of CRISP/Cas9, as it provides a novel nanotransducer-based genome editing engineering concept.
In the field of programmable biology, the technology allows to recognize and perform cutting only at on-target sites and exclude activity on off-targets. This makes the system much more reliable and specific than known techniques.

The superiority of NANO-GENE technology over current methodologies lies in its multi-function integration:

- **temporal** - editing occurs only when the laser is on,
- **spatial** - editing occurs only where the laser is focused, and
- **fidelity** - editing occurs only when the nanotransducer is on-target.

Possible developments

Studies to optimize the technology were performed in nonmammalian zebrafish embryos. The tests demonstrated **high specificity** on the gene of interest and independence from intrinsic Cas9 activity. The system exhibits **reduced toxicity** compared with common CRISPR/Cas9 and compatibility with a multi-gene treatments, with minimization of undesirable effects such as nonspecific genome cutting.

The technology will soon be validated in a mouse model of melanoma. The technology could provide a new therapeutic tool for melanoma treatment and new biotechnological solutions for precise and targeted genome editing of living cells, overcoming the limitations of approaches in use to date.

The inventors are collaborating with various academic and corporate partners under the I-GENE project, funded by the EC in the FET-OPEN program.

You can contact us to learn more about the status of the ongoing studies and collaborate with the team on the implementation of the system.

Take a look on www.youtube.com/watch?v=LIrkvNaz27k

and on the web site of the project: https://i-geneproject.eu/

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