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# Improved gene therapy is a promising candidate for cystic fibrosis treatment

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An improved gene therapy treatment can cure mice with cystic fibrosis (CF). Cell cultures from CF patients, too, respond well to the treatment. Those are the encouraging results of a study presented by the Laboratory for Molecular Virology and Gene Therapy at KU Leuven, Belgium.

Cystic fibrosis or mucoviscidosis is a genetic disorder that makes the mucus in the body thick and sticky, which in turn causes clogging in, for instance, the airways and the gastrointestinal tract. The symptoms can be treated, but there is no cure for the disorder.

Cystic fibrosis is caused by mutations in the CFTR gene. This gene contains the production code for a protein that functions as a channel through which chloride ions and water flow out of cells. In the cells of CF patients, these chloride channels are dysfunctional or even absent, so that thick mucus starts building up.

"A few years ago, a new drug was launched that can repair dysfunctional chloride channels", Professor Zeger Debyser explains. "Unfortunately, this medicine only works in a minority of CF patients. As for the impact of gene therapy, previous studies suggested that the treatment is safe, but largely ineffective for cystic fibrosis patients. However, as gene therapy has recently proven successful for disorders such as haemophilia and congenital blindness, we wanted to re-examine its potential for cystic fibrosis".

That is why lead authors Dragana Vidovi and Marianne Carlon examined

an improved gene therapy treatment based on inserting the genetic material for chloride channels—coded by the CFTR gene—into the genome of a recombinant AAV viral vector , which is derived from the relatively innocent AAV virus. The researchers then used this vector to 'smuggle' a healthy copy of the CFTR gene into the affected cells.

Both in mice with cystic fibrosis and in gut cell cultures from CF patients, this approach yielded positive results. "We administered the rAAV to the mice via their airways. Most of the CF mice recovered. In the patient-derived cell cultures, chloride and fluid transport were restored".

There is still a long way to go before gene therapy can be used to treat cystic fibrosis patients, Debyser clarifies: "We must not give CF patients false hope. Developing a treatment based on gene therapy will take years of work. For one thing, our study did not involve actual human beings, only mice and patient-derived cell cultures. Furthermore, we still have to examine how long the therapy works. Repeated doses might be necessary. But gene therapy clearly is a promising candidate for further research towards a cure for cystic fibrosis".

This research was conducted in collaboration with the University Hospitals Leuven and the universities of Paris, Utrecht, and Rotterdam.

**More information:** Dragana Vidović et al. rAAV-CFTRΔR Rescues the Cystic Fibrosis Phenotype in Human Intestinal Organoids and CF Mice, *American Journal of Respiratory and Critical Care Medicine* (2015). DOI: 10.1164/rccm.201505-0914OC

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