# Cibio Use CRISPR to Knock Out Cystic Fibrosis

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*This is the research team @Cibio with Giulia Maule and the p.i. Anna Cereseto. Credit: Photo by Alessio Coser @UniTrento.*

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The fight against cystic fibrosis continues, this time targeting in particular some of the mutations that cause it. This time, scientists relied on genome editing. A research team of the Cibio Department of the University of Trento was able to prove the efficacy of Crispr-Cas, the molecular scissors it has been working on for some time, in solving once and for all the problem that causes the disease.

The approach adopted by the team of the University of Trento, led by Anna Cereseto, opens new perspectives in the treatment of cystic fibrosis, a genetic disease for which no cure is currently available. The research work was carried out in collaboration with KU Leuven, in Belgium. The research project (“A new gene therapy approach: repairing splicing mutations in the Cftr gene through genome editing”) benefited from two years funding amounting to 90,000 euro from the Italian foundation for research on cystic fibrosis (Fondazione ricerca fibrosi cistica), with the participation of the Cystic fibrosis association of Trentino (Associazione trentina fibrosi cistica). The results of the study were published today in *Nature Communications*, an open access journal.

The disease is caused by a mutation of the gene that produces Cftr (the cystic fibrosis transmembrane conductance regulator), whose malfunctioning affects multiple organs, especially the lungs. The UniTrento/KU Leuven research team adapted the Crispr-Cas system, the molecular scissors that are revolutionising biomedicine, to permanently edit at least two types of the mutation that cause cystic fibrosis. In particular, the technique is called "SpliceFix" because it fixes the gene and restores the protein production mechanism at the same time.

Giulia Maule, doctoral student in Biomolecular sciences at the University of Trento and first author of the article, explained: "We have devised a genome editing strategy based on Crispr-Cas to permanently remove two different mutations that cause the disease. Crispr-Cas works like a genomic scalpel to cut out the mutated elements with extreme accuracy. We demonstrated that our repair strategy works on patient-derived organoids and with a high level of precision: it targets only the mutated sequences, leaving non-mutated DNA untouched".

The young researcher underlines a novel aspect of the study: "Instead of animal models, we have used organoids that we developed from the patients' cells, a choice that allowed us to verify the efficacy of the molecular strategy in a context that is very similar to that of the patients with cystic fibrosis".

Cystic fibrosis is also called the invisible disease because it doesn't show on the outside, and yet it takes a huge toll on the lives of the people it affects. Most of all, they have lung and digestive problems. The disease is inherited from parents. In Italy, about one in 25 people is a carrier. This means that a couple of carriers has one chance in four to have a child with the disease. There are about 6,000 people with cystic fibrosis in Italy, and 200 new cases every year.

Reference: Maule et al. 2019. Allele specific repair of splicing mutations in cystic fibrosis through AsCas12a genome editing. Nature Communications. DOI: https://doi.org/10.1038/s41467-019-11454-9.