Neurodegenerative diseases: UniTrento takes on the challenge

A research team has been using RNA strands as weapon and target for over 10 years, and invented a treatment approach that was patented in Europe and in the USA. More time and investments are needed to develop it into a therapeutic treatment, but this genetic mechanism, which works like a key in the lock, is very promising. It will provide a targeted approach to hereditary dementia, but applications may extend to other conditions associated with tau protein abnormalities, such as Huntington's disease, myotonic dystrophy and Alzheimer's disease. Support came from a local network for technology transfer involving Fondazione per la Valorizzazione della Ricerca Trentina and HIT Hub Innovazione Trentino.

Trento, 18 May 2020 – Only the right key fits into a lock. Only the right key opens the door. The same goes for RNA strands in the laboratories of the University of Trento: every strand covers only the corresponding fragment. In this way, RNA is both the weapon and the target at the same time in the fight against a number of neurodegenerative diseases. Treating these diseases has become a priority for public health globally, given the progressive increase in population ageing.

This genetic mechanism, which is part of international research on gene therapies, obtained a patent that is valid in Europe and in the United States.

The research work at the University of Trento is coordinated by Michela Denti, who in the last 10 years has been conducting studies on neurodegenerative diseases, focusing in particular on those with a genetic base. First things first: "I want to be clear with patients, their families and patient organizations. There is still a long way to go to get to a treatment, it will take further research, time and investments. So far, we have tested the effectiveness of the therapeutic approach on cells in a lab setting. We still have to go through the pre-clinical phase, which is a long, delicate and expensive phase, but is a fundamental requirement to reach the point where someone may show interest in our work and buy our patent to continue with clinical trials. We are continuing our research work with passion and determination because the mechanism we discovered is promising and we want it to become, in a few years, a new therapeutic treatment for rare and common conditions characterised by a progressive loss of neuronal functionality, for which there are no cures available today.

With her team, she explores RNA, that is ribonucleic acid that plays a fundamental role in the coding, regulation and expression of genes, at the Department of Cellular, Computational and Integrative Biology – Cibio of the University of Trento. RNA is the molecule that collects and transmits instructions for the production of proteins.
The discovery: an RNA-based molecular therapy for neurodegenerative diseases

The invention by Michela Denti, professor or applied biology, and by researchers Giuseppina Covello and Kavitha Siva, consists in an RNA-based molecular therapy for neurodegenerative diseases, the so-called tauopathies, caused by abnormalities in the tau protein (which is coded by the MAPT gene and associated to microtubule stability, and therefore to the proper functioning of some memory processes).

"We target tau messenger RNA that mutated in affected patients", she explained. "The RNA strand binds to the complementary strand, like the right key fits into a lock. So, it only targets the fragment of the strand that changed because of the mutation that causes the disease".

As regards the method, she added: "We develop RNA molecules (siRNAs, short interfering RNA or antisense oligonucleotides) which are based on short sequences of nucleotides (usually twenty or less) that can interfere with protein synthesis or with the processing of messenger RNA. We use them as therapeutic tools to treat genetic disorders with a high level of efficiency and precision. After 20 years of research, these approaches have become very successful in the past four years to treat rare and lethal genetic diseases, such as spinal muscular atrophy, acute liver porphyria and hereditary amyloidosis".

The molecules of the invention aim to offer a targeted approach to early-onset hereditary dementia, which occurs within 60 years of age (frontotemporal dementia and parkinsonism linked to chromosome 17), but applications may extend to other conditions associated with tau protein abnormalities; examples include Huntington's disease, myotonic dystrophy, but also Alzheimer's disease, a complex and multi factor disease which shares with frontotemporal dementia the accumulation of the tau protein in the brain.

Delivering this treatment is a major problem. "All researchers now are facing the same problem: how to make RNA therapeutics get to the target organ or tissue", said Michela Denti, who is a member of the expert panels (named Cost Actions) established at European level by the Cost European cooperation in science and technology to find solutions to the problem (Delivery of Antisense RNA Therapeutics).

Biomedical research: a local network for technology transfer

With a patented invention and looking forward to the testing phase, Denti remembers the support she received so far: "The University of Trento invested a lot in my research work and, through the Research support and technology transfer division, helped me participate in international funding competitions and in the patent filing process".

She also received advice on the potential of biomedical applications from Fondazione per la Valorizzazione della Ricerca Trentina, created by Fondazione Cassa di Risparmio di Trento e Rovereto, the Department of Cellular, Computational and Integrative Biology - Cibio of the University of Trento, and HIT - Hub Innovazione Trentino.

Finally, a few days ago, she learned that she could also benefit from services offered through the IP Booster project of the European Commission, designed to help develop intellectual property strategies to explore the potential market of the invention and evaluate competitors in the area of RNA-based therapeutics. Giuseppe Caputo of the Research support and
technology transfer division explained: "For the research project of Michela Denti, on which the University invested a lot in terms of patent protection, we took advantage, with support from HIT, of IP Booster, which provided four high value-added services related to the process to obtain the best legal protection for research results; the analysis of competitors and competition in the RNA therapeutics sector; an evaluation of the invention's potential and possible positioning on the market, to obtain the best possible placement; and advice and support in the negotiation of technology transfer agreements, which are essential for the economic exploitation of research results".

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