Autism and epilepsy: Trento working on new treatment options

Marta Biagioli of Cibio will receive 120,000 dollars in research funding over three years from two American foundations for an innovative idea based on the use of a non-codifying RNA class that for decades has been regarded as a by-product of cellular metabolism. These molecules stimulate the production of proteins in a number of neurological diseases associated with protein deficiency.

Trento, 27 January 2017 – (e.b.) For decades scientists have thought that these were useless molecules, produced by cells for unknown reasons. Only recently have they discovered their role, and now they are the cornerstone of a new therapeutic approach for neurological diseases like autism and epilepsy. The research work of Marta Biagioli, head of the NeuroEpigenetics Laboratory at Cibio – Centre for Integrative Biology at the University of Trento [http://web.unitn.it/en/Cibio/37591/neuroepigenetics-laboratory], is going in this direction.

«We do know – explained Marta Biagioli – that the information for the correct functioning of living organisms is contained in DNA, which is a long chain of encoded data that uses a four letter alphabet to “create words”. These “words” are amino acids, which combine with each other to form proteins, the functional bricks of the cells. RNA is a molecule that acts as a bridge, a link, that transforms the information contained in DNA into proteins. While the protein coding function of RNA is well known, scientists have long discussed the role of non-coding RNA, to the point that it was considered mainly useless. We now know that non-coding RNA has important regulatory functions together with other protein-coding RNAs and in many other cell processes».

For her idea, Marta Biagioli received funding from two different American foundations financing research on neurological diseases: a 50,000 dollar “Innovator Award” from the Citizens United for Research in Epilepsy [http://www.cureepilepsy.org/research/2016grantees.asp], and a 70,000 dollar “Young Investigator Award”, that she received for 2016-2017 from the Brain and Behavioral Research Foundation [https://bbrfoundation.org/yi]. Marta Biagioli, 44, a molecular biologist from Tuscany with a background in human genetics at Harvard Medical School in Boston, joined Cibio in November 2014 and, with her team, investigates autism spectrum disorders and epilepsy, which can be caused by insufficient protein production. The novelty of this approach lies in using artificial non-
coding RNAs to stimulate the targeted and controlled production of these particular proteins.

Biagioli was a member of the research team that, for the first time, in 2012, demonstrated the usefulness of a subgroup of non-coding RNA. The principal investigator in that study was Stefano Gustincich, professor at SISSA in Trieste and now also Director of the Department of Neurosciences at the Italian Institute of Technology (IIT) in Genoa.

“We learned – continued Biagioli – that some specific molecules of non-coding RNA can combine with corresponding protein-coding molecules and facilitate their inclusion in “assembly lines” (polysomes), which are fundamental for the production of proteins. This functioning mechanism was patented [United States Patent number 9,353,370 (granted: May 2016)] and called “SINEUP”]. TransSINE Technologies, the spin-off company co-founded by Gustincich, aims to develop SINEUPs for biotechnological and therapeutic purposes and provides us with the technology we need”.

How does SINEUP work in practice, and when can it be an efficient therapeutic approach?

“A number of neurological disorders, like autism spectrum disorders and epilepsy, can be caused by a protein deficiency. Despite the recent progress achieved in biology and genetics, disorders caused by an insufficient production of a given protein are currently incurable. SINEUP represents a new therapeutic approach. By creating artificial non-coding RNA molecules that combine with RNA normally present in cells we can selectively increase the production of a given protein, the specific protein that is missing in patients with certain diseases”.

“This idea – continued Biagioli – has its origin in a close group of researchers who have started to work together to investigate the therapeutic potential of this new class of non-coding RNAs in autism and epilepsy”.

Biagioli’s research team takes advantage of the technological skills of Stefano Gustincich’s team, and of the experience of Silvia Zucchelli, researcher at the University of Piemonte Orientale and member of TransSINE Technologies, who has long been working with Gustincich and is studying the molecular mechanisms that regulate the functioning of SINEUP. The group collaborates and exchanges information with two other laboratories at Cibio, respectively led by Simona Casarosa and Yuri Bozzi, who have considerable experience in studying the functioning of the central nervous system.