MedicalXpress

An immunosuppressive drug could delay the onset of neurodegenerative diseases

October 15 2012

Rapamycin, a drug used to prevent rejection in transplants, could delay the onset of neurodegenerative diseases such as Alzheimer's and Parkinson's. This is the main conclusion of a study published in the *Nature* in which has collaborated the researcher Isidro Ferrer, head of the group of Neuropathology at the Bellvitge Biomedical Research Institute (IDIBELL) and the Bellvitge University Hospital and Full Professor of Pathological Anatomy at the University of Barcelona. The research was led by researchers from the International School for Advanced Studies (SISSA) in Trieste (Italy).

The collaboration of the research group led by Dr. Ferrer with SISSA researchers began five years ago when they observed that Parkinson's patients showed a deficit in UCHL1 protein. At that time, researchers didn't know what mechanism produced this deficit. To discover it a European project was launched. It was coordinated by the Italian researchers and participated by other European research groups, including the group led by Dr. Ferrer. The project, called Dopaminet, focused on how dopaminergic neurons (brain cells whose neurotransmitter is dopamine) are involved in Parkinson's disease.

Contrary to most common hypothesis that a DNA fragment encodes a protein through a messenger RNA molecule, the researchers found that it also works in reverse. They found a balance between the protein and its mirror protein, which is configured in reverse, and they are mutually controlled. If the protein mirror is located in the nucleus of the cell, it does not interact with the protein, while if it is in the cytoplasm, then

both of them interact.

In the case of Parkinson's disease the protein UCHL1 appears reduced and also its mirror protein is localized in the nucleus, and in the cytoplasm. Thus, the researchers sought a method to extract the mirror protein from the nucleus and made it interact with the original UCHL1 protein. The authors found that rapamycin was able to extract them from the nucleus. The drug allows the two proteins, the UCHL1 and its mirror, hold together in the cytoplasm, which would correct the mistakes that occur in Parkinson's disease.

This in vitro research has allowed describing a new unknown mechanism. It is necessary that the UCHL1 mirror protein should accumulate in the nucleus and escape from the cytoplasm and join the UCLH1 protein. The combination of both makes the system work.

"The rapamycin can not cure Parkinson's disease, but it may delay the onset of neurodegenerative diseases such as Alzheimer's and Parkinson's itself. Rapamycin can protect and delay the beginning of these diseases. It can complete the treatment, but it should be combined with other existing treatments", explains Isidro Ferrer.

Anyway, it is still far its application in patients. The next step is to validate these results in animal models and study the effects of rapamycin in combination with other drugs.

More information: Claudia Carrieri, Laura Cimatti, Marta Biagioli, Anne Beugnet, Silvia Zucchelli, Stefania Fedele, Elisa Pesce,Isidre Ferrer, Licio Collavin, Claudio Santoro, Alistair R. R. Forrest, Piero Carninci, Stefano Biffo, Elia Stupka & Stefano Gustincich. Long non-coding antisense RNA controls Uchl1 translation through an embedded SINEB2 repeat. *Nature*. DOI: 10.1038/nature11508

Provided by IDIBELL-Bellvitge Biomedical Research Institute