Researchers describe JNK protein's key role in tissue regeneration

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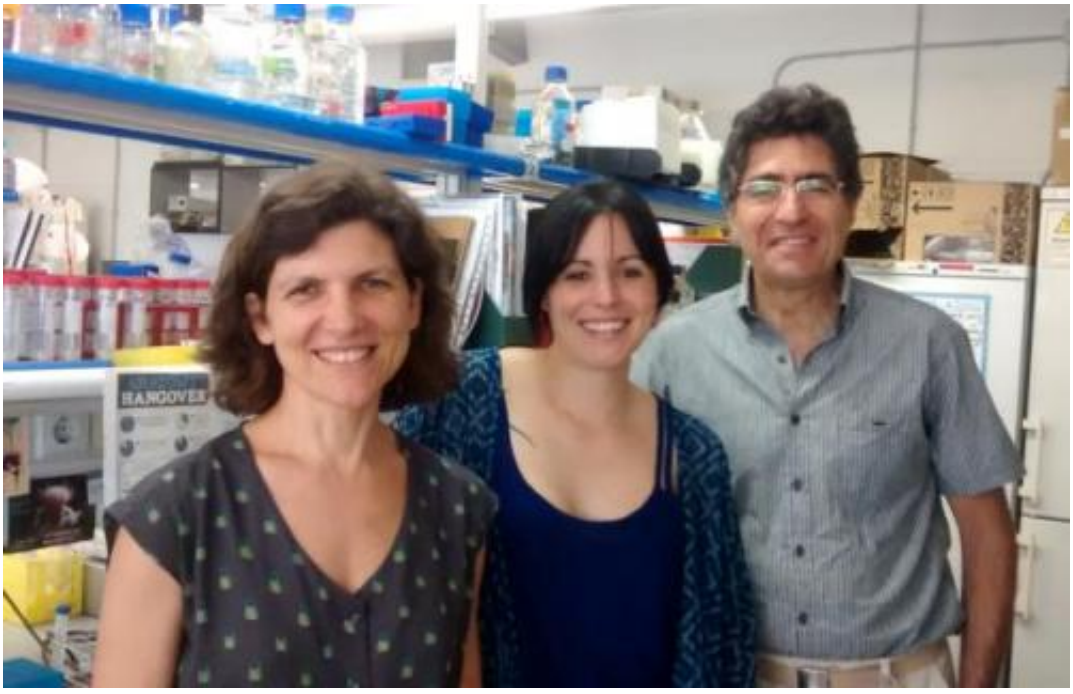

From left to right, researchers Teresa Adell, María Almuedo-Castillo and Emili Saló at the University of Barcelona.

Researchers from the Department of Genetics of the University of Barcelona (UB) and the Institute of Biomedicine of UB (IBUB) have proved the major role that JNK protein plays in tissue regeneration in adult organisms. The study, published in the journal *PLOS Genetics*, used planarians —a type of worm able to regenerate any part of its body— to address the question. The study was coordinated by Emili Saló and

Teresa Adell, professors from the Department of Genetics of UB. Besides, it is part of the PhD thesis developed by Maria Almuedo Castillo, researcher at UB. Experts from the Max Planck Institute for Molecular Biomedicine (Münster) and the University of Münster (Germany) also participated in the study.

Freshwater planarian flatworm are a popular model system in regeneration and stem cell research because they are able to regenerate any part of their body, even the head, in two weeks. This amazing plasticity relies on the presence of a population of adult pluripotent stem cell, the neoblasts, which are able to become any type of cell. However, the mechanisms that trigger regeneration remain little known.

JNK: a protein well preserved throughout evolution

UB researchers focused the study on the function of JNK protein, a well-preserved kinase in metazoan evolution. To date, it was known that JNK was involved in the control of cell proliferation and death, but little was known about the role it plays in tissue and organ regeneration.

In the study, JNK functions were blocked through RNA interference in order to observe organism's differences when JNK is activated and deactivated. Teresa Adell, author of the paper, explains that "in any organism, after a wound or an amputation, cell proliferation must be activated in order to generate new cells, as well as cell death, to integrate well new and old tissues". "We —adds the expert— have just discovered that JNK is crucial to control both processes at the same time: the temporal control of the cell cycle progression of stem cells and the activation of apoptosis". "We consider that the control that a single protein exerts of both mechanisms at the same time is key to coordinate both responses, so regeneration is developed in a controlled way", concludes Adell.

New factor to create tissues in vitro

JNK is also crucial for planarians' ability to adapt their size in accordance with nutritional supply. Planarians get smaller when there is no food, and they return to their original size when feeding is reinstated. The study proves that JNK acts as a hub in the maintenance of body proportion and the adjustment of the size of organs. "Against tissue loss, JNK modulates gene expression, induces the elimination of unnecessary cells and controls cell division that stem cells need", highlights Maria Almuedo.

This ability to regulate both cell death and stem cell division gives new insights into regenerative medicine, a field in which one of the greatest challenges is to generate and maintain tissues and organs in vitro to transplant them later. These tissues are generated from human pluripotent stem cells and one of the difficulties of the process is to achieve them to be functional and proportioned Planarians' regeneration and remodelling is a model that enables to solve this problem.

"Our study proves that JNK plays a key role in maintaining a balance between cell apoptosis and proliferation in organisms based on pluripotent stem cells like planarians", underlines Emili Saló, professor and head of the Department of Genetics of UB. "Therefore —he concludes—, the regulation of JNK activity will be another factor to bear in mind to optimize stem cell cultures and maintain functional organs in vitro".

JNK deregulation and cancer

JNK loss of function favours the deregulation of cell death and proliferation, a process that has been related to tumour development. The new study points out that the relationship between JNK and cancer

is more complex than it was though. "Our results demonstrate that JNK activity inhibition in planarians does not induce tumours. This result points out that JNK's role as carcinogenic agent is not enough to develop a tumour; on the contrary, tumours emerge from an alteration of several signalling pathways that occurs simultaneously", explains Teresa Adell. To study the relationship between JNK and other signalling pathways in tumour process is one of the future research lines of UB research group.

More information: "JNK Controls the Onset of Mitosis in Planarian Stem Cells and Triggers Apoptotic Cell Death Required for Regeneration and Remodeling," María Almuedo-Castillo, Xenia Crespo, Florian Seebeck, Kerstin Bartscherer, Emili Salò, Teresa Adell. *PLOS GENETICS*, Published: June 12, 2014, DOI: 10.1371/journal.pgen.1004400

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