MedicalXpress

CNIO researchers propose a new therapeutic target that prevents cell division

October 8 2013

Cell division is an essential process for the development of an organism. This process, however, can cause tumour growth when it stops working properly. Tumour cells accumulate alterations in their genetic material, and this makes them divide in an uncontrolled fashion, thus encouraging growth of the tumour. Over the past few years, knowledge of the regulation of this process has led to the discovery of new therapeutic strategies based on blocking cell division or mitosis.

The Cell Division & Cancer Group, led by Spanish National Cancer Research Centre (CNIO) researcher Marcos Malumbres, has managed to decode a new mechanism that regulates cell division, in which the key molecule involved, Greatwall ? also known as Mastl? could be a new therapeutic target for oncology treatments. The study is published today in the scientific journal *Proceedings of the National Academy of Sciences* (*PNAS*).

Greatwall: a key player of the cell division puzzle

The control of cell division or mitosis depends on many proteins, amongst them, Aurora and Polo. Currently, many pharmaceutical companies have shown interest in these molecules, for which inhibitors have already been developed, some of which are currently undergoing clinical trials in oncology.

Greatwall, the protein Malumbres's group has focused their work on, is

also a protein that regulates cell division. Until now, almost all of the studies on this protein were carried out on the Drosophila melanogaster fly or on other invertebrate bodies. CNIO's Cell Division & Cancer Group, in collaboration with researchers from the National Centre for Scientific Research (CNRS) in Montpellier, France, has now generated the first genetic model of this protein in mammals, using the mouse as a model.

Thanks to this mouse model, the authors of the work have been able to see that cells lacking Greatwall are not capable of adequately dividing themselves: by eliminating Greatwall, cellular DNA does not form the right structure at the moment of cell division, the cell collapses and this prevents them from continuing to divide.

A new target for cancer therapy

As Mo?nica A?lvarez Ferna?ndez, one of the group's researchers and the first author of the article, says: "the next step now is to explore the potential therapeutic applications of this discovery".

One of the therapeutic advantages Greatwall offers, and one that differentiates it from other mitotic proteins, is that it acts by blocking the function of the PP2A phosphatase, a tumour suppressor frequently altered in human cancer. This implies that the inhibition of Greatwall could, at the same time, slow down cell division and reactivate tumour suppressor PP2A, a protein capable of inhibiting many of the oncogenic molecular pathways involved in cancer development.

The key now is to find out which tumours would benefit from using this strategy, as well as to develop compounds capable of inhibiting this protein. With regard to both of these aspects, CNIO's research group is already actively working with other groups and clinical units.

"Therapeutics development is currently in need of novel targets that attack tumours in a different way", says Malumbres, "and Greatwall offers new strategies amongst which can be found reactivating a very important tumour suppressor, something for which there are no direct therapies at the moment".

More information: Greatwall is essential to prevent mitotic collapse after nuclear envelope breakdown in mammals. A?lvarez-Ferna?ndez M, Sa?nchez-Marti?nez R, Sanz-Castillo B, Gan, PP, Sanz-Flores M, Trakala M., Ruiz-Torres, M, Lorca T, Castro A, Malumbres M. Proc. Natl. Acad. Sci. USA. (2013). DOI: 10.1073/pnas.1310745110

Provided by Centro Nacional de Investigaciones Oncologicas (CNIO)