Fundación Centro Nacional de Investigaciones Oncológicas Carlos III

A STUDY LED BY CNIO VALIDATES A NEW ANTI-CANCER THERAPY BASED ON CELL DIVISION

- **The study confirms the therapeutic potential of inhibiting Aurora-A, a protein involved in cell division processes, in cancer treatment**

- **The absence of the Aurora-A protein in mice reduced the progression of skin and breast tumours**

- **The team proposes new biomarkers, such as the study of the nuclear volume in cells, to evaluate the efficiency of drugs that inhibit Aurora-A in clinical practice**

Madrid (Spain), November 15, 2013. Aurora-A is a protein involved in the cell division process that is highly expressed or synthesised in a large number of human cancers, especially in those associated with a bad prognosis. Several pharmaceutical companies have recently developed these protein inhibitors, although the therapeutic and physiological effects that blocking Aurora-A might have on adult tissues are still unknown.

A study led by Ignacio Pérez de Castro, a researcher in the Spanish National Cancer Research Centre's (CNIO) Cell Division and Cancer Group, and its Group Leader, Marcos Malumbres, describes the cellular consequences of genetically deleting Aurora-A, an important target for the development of new anti-cancer agents, in mouse models. The work, which was carried out in collaboration with researchers Terry Van Dyke and Dale Cowley, from North Carolina University in the US, is published today in *Cancer Research*, the most cited cancer journal.

AURORA-A, AGEING AND CANCER

Aurora-A is a protein involved in the regulation of the cell cycle, a process by which cells reproduce and form tissues. Although these elementary functions had been widely studied in several model organisms and mouse embryos, their role in tissues and adult organisms remained unknown.

Using genetically engineered Aurora-A deficient mice, the authors of the study have discovered that the absence of this protein causes an increase in the number of cells with a high DNA content; this is a consequence of an aberrant distribution of the genetic material upon division.

“This phenomenon causes defects in cell proliferation, as well as an increase in the number of dead and senescent cells, which triggers premature ageing in the animals studied”, says Ignacio Pérez de Castro. The researcher adds that: “In those mice, we also see an increase in DNA damage and, most importantly, a reduction in the progression of skin and breast tumours”.

The study helps to solve two of the great limitations pharmaceutical companies find themselves up against when they carry out clinical trials with Aurora protein inhibitors. Firstly, the compounds used in clinical trials are not completely specific and are not capable of adequately discriminating between the three members of the Aurora family: Aurora-A, B or C. Mice generated by CNIO confirm the therapeutic value of the first member of this family of proteins.

“Secondly, clinical studies with these inhibitors have surveillance problems as a result of the lack of markers that allow monitoring their effects on the cells”, says Marcos Malumbres. The researchers propose studying the volume of the cell nucleus, a consequence of a change in DNA content, as a new tool for evaluating the efficiency of these new anti-cancer drugs.

Given that Aurora-A inhibition damages DNA, Malumbres’s team says that the use of Aurora-A inhibiting drugs could sensitise tumours to anti-cancer agents that are currently in clinical use and attack cells causing high levels of DNA damage.

Reference article:
***Requirements for Aurora-A in tissue regeneration and tumor development in adult mammals*. Ignacio Pérez de Castro, Cristina Aguirre-Portolés, Gonzalo Fernández-Miranda, Marta Cañamero, Dale O. Cowley, Terry van Dyke, Marcos Malumbres. *Cancer Research* (2013). DOI: 10.1158/0008-5472.CAN-13-0586**

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