CNIO SCIENTISTS DEVELOP A NOVEL MULTIMODAL TREATMENT AGAINST PANCREATIC CANCER STEM CELLS

Madrid, November 4th, 2011 - Scientists working with Prof. Christopher Heeschen in the Clinical Research Programme at the Spanish National Cancer Research Centre (CNIO) have been successful in their search for novel therapies against pancreatic cancer stem cells as the root of a devastating disease. Pancreatic cancer remains one of mankind's deadliest diseases and its incidence is still rising.

Investigations spearheaded by Dr. Enza Lonardo in the Stem Cells & Cancer Group provide conclusive evidence for the re-activation of a developmental pathway in cancer stem cells reminiscent of those found in embryonic stem cells. The team was able to identify Nodal and Activin as two critical components determining the two-way communication between cancer stem cells and an embryonic-like microenvironment, which strongly increases their plasticity and aggressiveness. Nodal and Activin are embryonic factors (also called morphogens) responsible for maintaining the pluripotency of human embryonic stem cells.

Intriguingly, the Nodal/Activin pathway is not only a driving factor in pancreatic cancer stem cells, but also in pancreatic stellate cells, which are abundantly present in the stroma surrounding pancreatic cancer cells, and may serve as a supportive niche for cancer stem cells. Preclinical studies performed by the investigators show that the cancer stem cell compartment can be severely altered by inhibition of this pathway resulting in chemo-sensitisation of the cancer stem cells. Importantly, long-term survival could be achieved when combined with targeting of the stroma (promoted by another developmental pathway called hedgehog) and chemotherapy for eliminating the differentiated cancer cells.

Therefore, these data for the first time demonstrate that cancer stem cells critically rely on the activity of an embryonic pathway. The Nodal/Activin pathway represents a previously unknown target for stalling tumour progression and metastasis. If combined with efficient depletion of the stroma in order to destroy the tumour microenvironment and to allow better accessibility of the cancer (stem) cells by administered drugs, Nodal/Activin inhibitors are capable of dramatically improving the outcome of mice in clinically most relevant models.
Therefore, Dr. Heeschen’s group (www.heeschen-lab.org) is now focusing their efforts on the clinical translation of this promising new treatment modality.

The mentioned study was very recently published in the November issue of Cell Stem Cell, the world’s leading journal in stem cell research.

You may access the full article by visiting the following web page: http://www.cell.com/cell-stem-cell/home