Cancer stem cells—allies of the tumor, enemies of the patient

March 6 2018

Scientists of the UEx Molecular Biology of Cancer Research Group want to identify which proteins within the cells are involved in retaining the undifferentiated characteristics of the tumour, which would allow it to be attacked more successfully Credit: UEx

The scientists of the UEx Molecular Biology of Cancer Research Group seek to uncover the physiological mechanisms of cancer stem cells, which are responsible for the progression of the tumour. Thus, they are working on identifying new cell proteins that control cellular differentiation. Cancer stem cells possess the capacity to adopt highly undifferentiated states, characteristic of pluripotent cells, which may contribute to the progression and maintenance of tumour cell types in the same way that a healthy stem cell can give rise to different cell phenotypes. "These cancer stem cells are more resistant to the attack of chemotherapeutic agents. They are capable of regenerating the tumour and helping the tumour cells to spread to other organs," explains Pedro Fernández Salguero, lead researcher on the project.

The deregulation of cellular differentiation plays a very important role from an oncological point of view, because it fosters the development of more undifferentiated and aggressive tumours with worse prognosis. "Therefore, we want to identify which proteins within the cells are involved in retaining the undifferentiated characteristics of the tumour, which would allow it to be attacked more successfully. We also want to identify those leading to differentiated characteristics that reduce tumour development," adds Fernández Salguero.

One specific protein might contribute to keeping the tumour in a more highly undifferentiated state that could affect its metastatic capacity and its response to therapy. The researchers observed that a certain cell protein, the dioxin receptor (Ahr), participates in this process of cellular differentiation. "We have studied lines of cancer stem cells derived from patients and analysed tumour markers of potential clinical interest in animal models. The results obtained from both models have been validated in biopsies from patients with hepatocellular carcinoma and melanoma at the Infanta Cristina Hospital, in Badajoz (Spain)."

In this validation, the investigators found different values for this protein

within the tumour and in the non-cancerous tissue from the same patients. They also found that the protein changes its expression in advanced stages, compared with stages prior to the development of the tumour (hepatic cirrhosis or hepatitis, in the case of hepatocellular carcinoma).

Thus, the results point to a therapeutic value for this protein (Ahr) because controlling it might repress the pluripotency of the cancer stem cell and reduce the malignity of the tumour. Naturally occurring molecules have been identified that modulate the activity of this protein in specific ways. In addition, the dioxin receptor might also facilitate the development of tools for the prognosis and evolution of the types of cancer in the study, hepatocellular carcinoma and melanoma.

Hepatocellular carcinoma is a primary liver cancer distinct from hepatic metastases originated by other tumours. It is highly aggressive and generally has poor prognosis. Further, its incidence is rising—this tumour usually appears as a consequence of an alcoholic liver cirrhosis or an infection by hepatitis B or C. Currently, those suffering from liver cancer have few therapeutic opportunities; one of the few options is a liver transplant. Tools for molecular prognosis and therapeutic targets are very scarce, and the current survival rate for patients with advanced hepatocellular carcinoma is below 10 percent. As a consequence, it is necessary to identify new molecules and therapeutic options complementing the use of surgical resection and the transplant.

More information: Ángel C. Roman et al, The aryl hydrocarbon receptor in the crossroad of signalling networks with therapeutic value, *Pharmacology & Therapeutics* (2017). DOI: 10.1016/j.pharmthera.2017.12.003