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# Cancer stem cell subpopulation drives metastasis of human pancreatic cancer

September 12 2007

Scientists have identified a distinct subpopulation of cancer stem cells (CSCs) that is responsible for metastasis of a deadly human pancreatic cancer. The research, published by Cell Press in the September issue of the journal Cell Stem Cell, provides insight into the role of CSCs in cancer initiation, progression, and metastasis and suggests new directions for development of more effective therapeutics.

Pancreatic adenocarcinoma ranks as the fourth leading cause of cancer death and is relatively incurable due to early metastatic spread and high resistance to radiation and chemotherapy. In order to better understand the pathology of this deadly cancer, scientists have recently begun to explore the role of CSCs in pancreatic tumors. CSCs are thought to be a small population of tumor cells that have similar properties to normal stem cells in that they are self-replicating and capable of giving rise to populations of differentiated cells. Dr. Christopher Heeschen from the Department of Surgery at Ludwig-Maximilians-University in Munich, Germany led a study to examine the role of CSCs in pancreatic cancer.

The researchers discovered that human pancreatic cancer tissue contains tumorigenic and chemotherapy resistant stem cells defined by expression of CD133, a surface marker expressed by a variety of normal and malignant stem cells. They identified a distinct subset of cells expressing both CD133 and the chemokine receptor CXCR4, which plays a key role in blood cell migration, in the invasive front of the tumor. Implantation of isolated CD133+/CXCR4+ cells into mice resulted in metastatic tumor development, identifying them as CSCs. Cancer

metastasis was abolished by inhibiting CXCR4 or by transplanting CD133+/CXCR4- cells instead, underlining the importance of CXCR4 for the invasive cell behavior. Clinical studies revealed that tumor samples with a high number of CXCR4+ cells were more migratory and came from patients that suffered from more advanced metastatic disease. This important correlation may provide more accurate individual prognoses, allowing for improved selection of therapeutic agents.

These findings demonstrate for the first time that a specific CD133+/CXCR4+ cancer stem cell population present at the tumor-host interface is critically involved in pancreatic tumor metastasis. “The further molecular characterization of the pancreatic CSCs identified in the present study will be crucial for the development of new therapeutic strategies to eliminate these tumorigenic and metastatic cells. This may eventually provide a more effective treatment for our patients suffering from this deadly disease. In this respect, the demonstrated possibility of expanding pancreatic CSCs in vitro will dramatically help us in the evaluation of drug efficacy,” offers Dr. Heeschen.

Source: Cell Press