Reversing cancer cells to normal cells

April 29 2007

A Northwestern University scientist describes new research that used an innovative experimental approach to provide unique insights into how scientists can change human metastatic melanoma cells back to normal-like skin cells -- by exposing the tumor cells to the embryonic microenvironment of human embryonic stem cells, the zebra fish and the chick embryo.

In earlier work, Northwestern University scientist Mary J.C. Hendrix and colleagues discovered that aggressive melanoma cells (but not normal skin cells nor less aggressive melanoma cells) contain specific proteins similar to those found in embryonic stem cells. This groundbreaking work led to the first molecular classification of malignant melanoma and may help to explain how, by becoming more like unspecialized stem cells, the aggressive melanoma cell gained enhanced abilities to migrate, invade and metastasize while virtually undetected by the immune system.

Now, in the American Association of Anatomists' plenary lecture and symposium, at Experimental Biology 2007 in Washington, DC, Dr. Hendrix describes new research that used an innovative experimental approach to provide unique insights into how scientists can change human metastatic melanoma cells back to normal-like skin cells - by exposing the tumor cells to the embryonic microenvironment of human embryonic stem cells, the zebra fish and the chick embryo.

Dr. Hendrix's plenary lecture on April 29 is a highlight of the scientific program of the American Association of Anatomists. Her presentation is titled "the convergence of embryonic and cancer signaling pathways: role

in tumor cell plasticity." Plasticity refers to the ability of the tumor cell, like the embryonic cell, to express or change into multiple, different types of cells.

First, a quick primer on the shared characteristics of aggressive tumor cells and embryonic stem cells: Embryonic stem cells are pluripotent, meaning they are able to differentiate into any of the more than 200 cell types in the adult body. Which type of cell they become depends on the signals they receive from their microenvironment. Similarly, during cancer progression, malignant cells receive and release signals from their own microenvironment, cues that promote tumor growth and metastasis.

In order to better understand what signals the melanoma cells are sending and receiving, Dr. Hendrix and her colleagues used the microenvironment of the zebrafish to study whether the tumor cells could communicate with the zebrafish stem cells and affect their early development. The zebrafish is a widely-used organism for genetic and developmental studies because of its prolific reproduction, rapid development, and transparent embryo that develops outside the body (making it especially easy to simply watch development), and the fact it develops organs and tissues comparable to those in humans, such as heart, kidney, pancreas, bones and cartilage.)

Using the zebrafish model, and the extraordinary technologic advances made in microscopy and molecular biology in recent years, the team was able to show that the aggressive melanoma cells secrete Nodal, a critical component underling the two-way communication between tumor cells and the embryonic microenvironment. Nodal is an embryonic factor (also called a morphogen) responsible for maintaining the pluripotency of human embryonic stem cells: their ability to develop or "morph" into one of a variety of body cells. When aggressive melanoma and other tumor cells (recent findings also report Nodal expression in breast cancer and testicular cancer) regain the ability to express a potent embryonic

morphogen like Nodal, the presence of the Nodal and the signals it sends and receives appear to play a key role in tumor cell plasticity and progression.

Most noteworthy, Dr. Hendrix's team's also has shown that inhibition of Nodal signaling leads to a reduction in melanoma cell invasiveness and ability to create new tumors. In fact, with inhibition of Nodal, the metastatic melanoma cells are reverted to a more benign skin cell without the ability to form tumors.

Findings from the zebrafish study were further confirmed in the human embryonic stem cell model and the chick embryo model - where inhibiting Nodal signaling led to the reversal of the melanoma cells to a more normal cell type.

This is a promising area of research, says Dr. Hendrix. The discovery of a new signalizing pathway in melanoma and other tumor cell types and the ability to inhibit Nodal and thus reverse the melanoma cell back toward a normal skin cell provide a previously unknown target for regulating tumor progression and metastasis.

Dr. Hendrix's distinguished lecture is part of a session titled the cell microenvironment in development and cancer.

Source: Northwestern University

provided for information purposes only.