Researchers discover novel mechanism of tumor cell invasion in melanoma

October 30 2013

(Medical Xpress)—The most devastating feature of cancer is that it often spreads throughout the human body and forms secondary tumors also known as metastases. One of the most aggressive metastatic cancers with no currently available curative therapy is melanoma, a type of skin cancer that originates from melanocytes, cells that normally make skin tan. Lifetime risk and mortality rates of metastatic melanoma have been steadily increasing for decades.

Formation of metastases largely depends on the ability of tumor cells to grow through surrounding healthy tissues, a process termed invasion. Cell invasion is controlled by a subset of G- proteins, a.k.a. guanosine nucleotide-binding proteins. These proteins could function only when bound to a special molecule, nucleotide guanosine triphosphate (GTP).

In a recent issue of *Cell Reports*, researchers from Roswell Park Cancer Institute (RPCI) and the University of Michigan, Ann Arbor, discovered a previously unrecognized mechanism by which tumor cells regulate activity of G-proteins and invasion. This mechanism is availability of GTP. Using cells from metastatic melanoma, researchers led by Mikhail A. Nikiforov, PhD, Professor of Oncology and Researcher in the Department of Cell Stress Biology at RPCI, discovered a gene, GMPR (guanosine monophoshate reductase) that mildly inhibits production of GTP in the cell.

Interestingly, this mild inhibition was sufficient to reduce activity of several G-proteins and, subsequently, invasion. Additionally, Dr.

Nikiforov's group demonstrated that invasion of melanoma cells could be regulated by the amounts of guanosine in cell culture media.

"If this is what is occurring in vivo, than we may be able to limit melanoma metastases by regulating guanosine amounts in human body," says the study's first author Joseph Wawrzyniak, a Ph.D. student and Research Affiliate in the Department of Cell Stress Biology at RPCI.

Moreover, the researchers discovered that amounts of GMPR were lower in samples of invasive than non-invasive human melanomas. Why is this important? Currently, there are no diagnostic and/or prognostic molecular markers for melanoma used in clinical settings. This could be exemplified by the fact that, according to Archives of Pathology & Laboratory Medicine, a false-negative diagnosis of melanoma was the single most common reason for filing a claim against pathologists between 1998 and 2003.

"Since GMPR expression differs between non-invasive and invasive melanomas at very early stages of the disease, this gene has a potential to be developed into diagnostic or prognostic marker," says Dr. Nikiforov. "Accordingly, because of support from National Cancer Institute, American Cancer Society and private donors such as the Tietgen Family Foundation, experiments aiming at identification of novel markers for melanoma are currently underway."

More information: www.cell.com/cell-reports/full … 2211-1247(13)00538-X

Provided by Roswell Park Cancer Institute

Citation: Researchers discover novel mechanism of tumor cell invasion in melanoma (2013,