Brain tumor treatment may increase number of cancer stem-like cells

5 March 2009

A new study suggests that the standard treatment for a common brain tumor increases the aggressiveness of surviving cancer cells, possibly leaving patients more vulnerable to tumor recurrence. The research, published by Cell Press in the March 6th issue of the journal *Cell Stem Cell*, provides valuable insight into the molecular mechanisms that enable cancer stem-like cells to escape cytotoxic treatment and repopulate the tumor.

Glioblastoma multiforme is the most prevalent and aggressive form of primary brain tumor and is notoriously resistant to standard therapies. Dr. Eric Holland, from Memorial Sloan-Kettering Cancer Center in New York, examined the role of ABCG2, a protein linked with drug resistance, in glioma cancer stem-like cells. "ABC proteins are transporters that participate in tumor resistance by actively transporting drugs across the cell membrane, serving to protect cells from chemotherapeutic agents," offers Dr. Holland.

Dr. Holland and colleagues employed a method that allowed visualization of ABC-mediated efflux of fluorescent dye to identify and isolate "side population" (SP) cells from mouse and human glioblastomas. "Because the SP phenotype in glioma cancer stem-like cells is mainly mediated by ABCG2, as shown by the almost complete abolition of this phenotype when ABCG2 activity is blocked, we subsequently studied the oncogenic potential of ABCG2," explains Dr. Holland.

The researchers confirmed that SP cells are highly tumorigenic, have the ability to self-renew, and are resistant to chemotherapy. These results verified that ABCG2 activity, although not by itself oncogenic, is a marker for glioma stem-like cells. Further, the researchers identified a detailed molecular mechanism that modulates the activity of ABCG2 and enhances the ability of cancer stem-like cells to expel drugs.

Importantly, Dr. Holland's group also found that the chemotherapeutic drug temozolomide, the standard treatment for gliomas, increased the number of glioma cells with stem-like characteristics. The researchers speculated that because temozolomide is not an ABCG2 substrate, the increase in the SP fraction likely resulted from enrichment of cells with stem-like properties. "In the process of increasing the number of cells in tumors with stem-like properties, temozolomide may render surviving cells even more resistant to subsequent treatment with drugs that are substrates for ABCG2," explains Dr. Holland.

Source: Cell Press