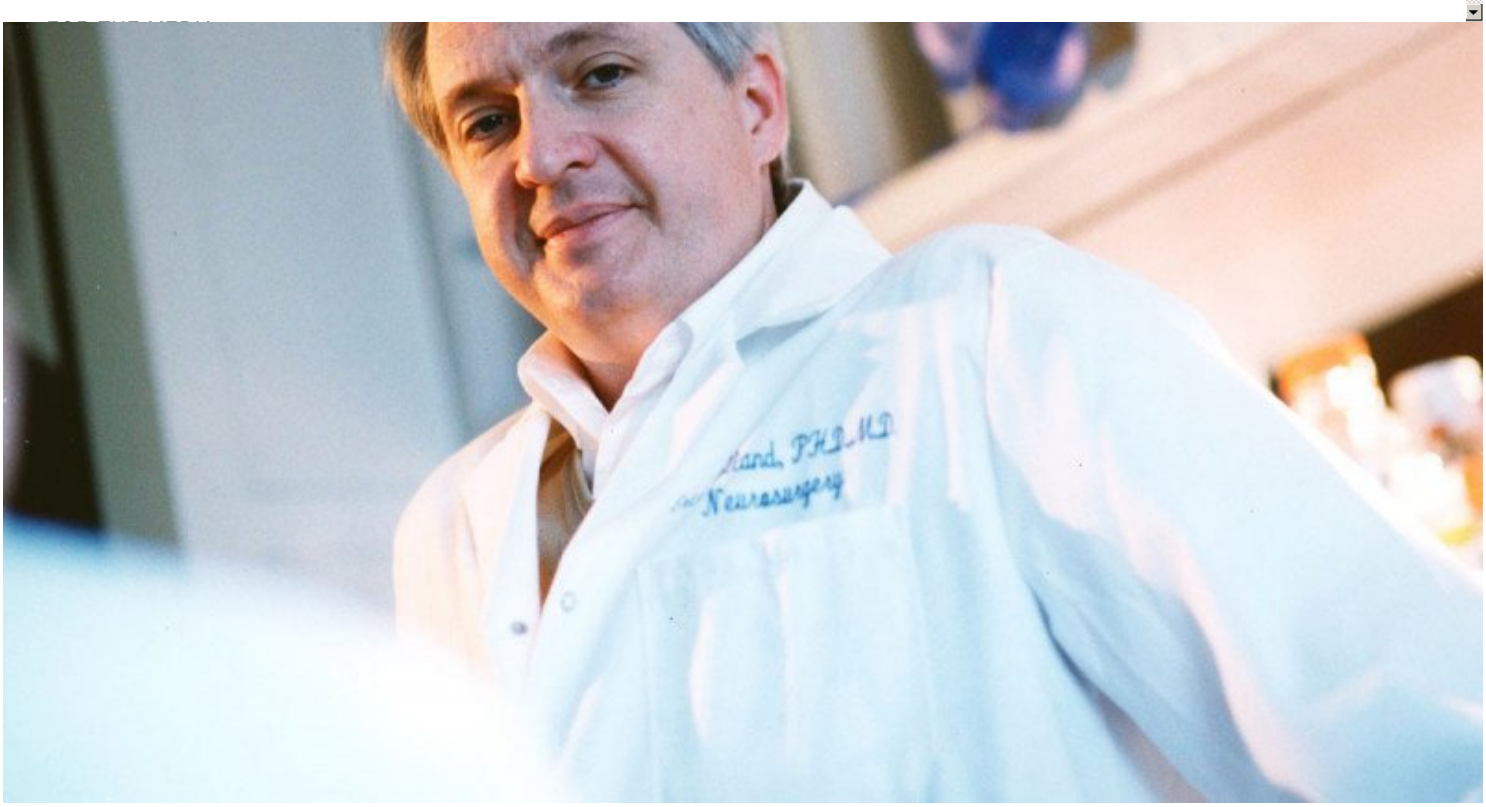

Discovery Shows that Activating Rearrangements in Receptor Genes are More Common than Previously Thought Media Advisory

A multi-institutional team led by investigators from Memorial Sloan Kettering Cancer Center has published a study that provides new insight into genetic changes that make some forms of glioblastoma, the most common type of primary brain cancer, more aggressive than others and explains why they may not respond to certain therapies. The research was led by senior author Eric C. Holland, MD, PhD, — an MSKCC surgeon, researcher and the Director of the Brain Tumor Center — and was published in the October 1 issue of the journal *Genes & Development*.

Glioblastoma has several subtypes, which are characterized by different genetic changes found in the tumor cells. One common subtype is characterized by cells with increased signaling from a protein called platelet-derived growth factor receptor (PDGFR). In this study, which involved screening patients' tumor samples for PDGFR mutations, the researchers were surprised to find that almost half of all glioblastomas with excess copies of the *PDGFR* gene also had rearrangements in the gene itself, creating proteins that are continually turned on. These rearrangements were either shortened forms of the protein or involved the fusion of the protein to another receptor. Fusion genes have not been found in brain tumors previously but are well studied in certain types of leukemia, and more recently have been found in some solid tumors as well.

Much of the team's work was made possible by data coming from The Cancer Genome Atlas (TCGA), an effort funded by the National Institutes of Health to understand the molecular basis of cancer. Glioblastoma is one of three forms of cancer that has been studied in detail as part of TCGA's initial pilot phase, along with ovarian cancer and lung cancer.

The presence of the rearrangements in the *PDGFR* gene suggest that these specific tumors have evolved to be dependent on signaling through this receptor, a target for several drugs under development. According to the researchers, the recent study suggests that more effort needs to be put into identifying exactly which subtype of glioblastoma a patient has in order for therapies to be targeted appropriately.