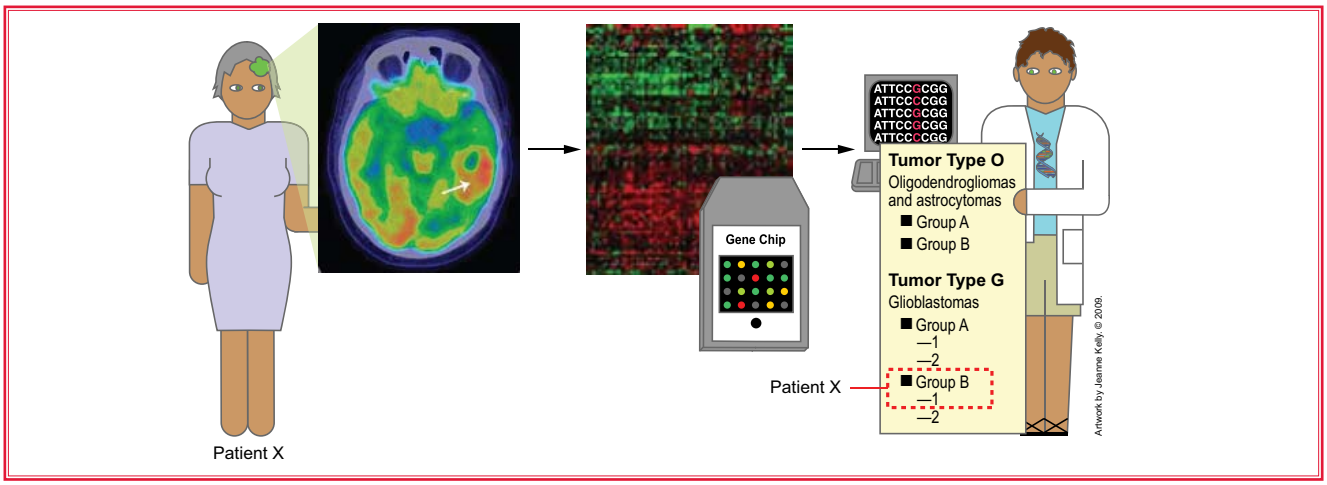
Brain Cancers: Not All Made the Same

Primary brain tumors are an increasingly significant cause of cancer-related mortality in the United States. Gliomas, in particular, have attracted more attention in recent decades because there are several reports suggesting an increasing trend in incidence rates, and the prognosis for patients with high-grade gliomas is still very poor. Of the approximately 17,000 Americans diagnosed each year with malignant gliomas, about 50 percent survive one year after diagnosis, and 25 percent survive after two years. Because the disease is nonetheless relatively rare, progress in understanding the disease has been slow. Oftentimes, two glioma patients whose tumors look the same in an MRI or under a microscope experience completely different outcomes despite being given the exact same treatment. In fact, these seemingly alike tumors actually have distinct genomic profiles and molecular abnormalities. But from standard pathology, we could never discern the difference.



(Image: J. Kelly)

Howard Fine, M.D., and colleagues analyzed genomic profiles from patients diagnosed with malignant glial cells using computer-generated groupings to subclassify the brain tumors into two major groups: O type tumors, which were predominantly oligodendrogliomas and astrocytomas, and G type tumors, which were mostly glioblastomas. They further divided the G tumors into two additional levels of subclassification.

"To understand how best to treat our patients, we really have to get past the 200-year-old tradition of just looking at a microscope and saying, 'Oh it kind of looks like that tumor, or it kind of looks like this tumor,'" said Howard Fine, M.D., Chief of the Neuro-Oncology Branch at CCR. To that end, Dr. Fine and colleagues undertook a large-scale analysis to classify different types of glioblastomas based on the simultaneous expression of genes within the tumor cells. Their findings were published in the March 2009 issue of *Cancer Research*.

In the first gene expression profiling study to look at the whole family of gliomas rather than just a subset of gliomas, Dr. Fine and colleagues used a series of statistical and mathematical models to analyze the results from arrays containing 20,000 to 25,000 genes at one time. The researchers were able to identify two major types of gliomas: an oligodendroglioma-rich group, further divided into two subgroups, and a glioblastoma-rich group, divided into four subgroups. These subgroups have many of the same molecular pathways and genetic mutations, so they are more biologically similar and, therefore, should represent patient groups that are more likely to respond to similar treatments.

These subgroups have been correlated with histological and clinical features, but they still need to be validated by data from more patients to determine the extent to which they are meaningful for diagnosis and prognosis. The researchers will need to determine if their analysis method helps to select therapies that are more effective for patients in that particular subgroup "For me," said Dr. Fine, "as a translational scientist, and first and foremost a physician who's taken care of 20,000 patients with gliomas in the past 20 years, what I really care about is: Will the subgroups allow us to improve the outcomes of our patients? That's ultimately the only validation that really matters."

To learn more about Dr. Fine's research, please visit his CCR Web site at http://ccr.cancer.gov/staff/staff.asp?profileid=5635.