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Molecular Genetics of Brain Tumors

Over the last several years we have learned a lot about brain tumors. There are proteins inside of tumor cells that give us information about the type of tumor, how it may behave, or how it may respond to treatment. Some of these tests are routine, while others require more detailed testing. On many occasions, the results are interesting but the significance or impact of the finding is unclear. On a few occasions it may actually influence the type of treatment you may receive. There are still many things we do not know, and the results of all of the testing must be considered with caution. Here are some of the proteins and genes we are beginning to understand in brain tumors:

- **IDH** (Isocitrate Dehydrogenase): IDH is a gene present in all cells in our body. The protein it produces affects many things that normally happen inside of our cells. In some tumors it is mutated (abnormal). As a result of this mutation, the function of the protein is changed. IDH mutations are frequently found in grade II and III astrocytomas and oligodendrogliomas and rarely in glioblastoma. Tumors that have this abnormality often behave less aggressively than those that do not. The presence of the mutation generally does not influence how we treat the tumor although there are exceptions. We routinely test tumors for this mutation but it may take as long as 1 to 2 weeks to receive the result. Having this mutation might be better than not having the mutation.
- **1p/19q**: 1p and 19q are sections of two different *chromosomes* (the part of our cells that contains genetic information) that are often “deleted” or missing from cells in grade II and III oligodendrogliomas. When these deletions are present in tumors, the tumors tend to behave less aggressively and may be more responsive to treatment. We routinely test for the deletions of 1p and 19q when we suspect the tumor is an oligodendroglioma.

- **MGMT** (Methylguanine Methyltransferase): This is another protein present in all cells of our body. It is a protein that repairs damaged DNA and therefore protects our normal tissue from damage. There is a switch (called methylation) that controls whether a cell produces MGMT. In some tumors the switch is on (hypomethylated), while in others it is off (hypermethylated). As a result, some tumors have higher levels of the protein, while others have lower levels. Whether the gene is on or off may predict how aggressive the tumor is or how it responds to certain medicines (chemotherapy). There may be some circumstances where it will influence how we treat tumors but this is still debated. We routinely test for astrocytomas and oligodendrogliomas for MGMT but it may take 2-3 weeks to receive the results.

There are many other proteins and genes that are abnormal in gliomas that we do not routinely test for as they do not impact how we treat the tumor. At your request we can send your tumor tissue that has been already removed to a commercial lab. However, this is often not covered by insurance or there may be a significant copay. Also, there needs to be enough tissue to do the test. If you are interested we will be happy to discuss further.

Despite the presence or absence of these abnormal genes and proteins, it is still very difficult to predict how any individual's tumors will behave or respond to a treatment. There is a lot more to learn about these and other abnormalities present in tumors cells.