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Timothy A. Chan

A multidisciplinary team of Memorial Sloan Kettering investigators has shown for the first time that the gene that causes the inherited form of Parkinson's disease also plays a role in many types of cancer, including colon and lung cancers and glioblastoma, the most common form of brain cancer. The study, published in the December issue of *Nature Genetics*, was led by physician-scientist Timothy A. Chan, a radiation oncologist and member of the Human Oncology and Pathogenesis Program and the Brain Tumor Center. [PubMed Abstract]

The gene, called *PARK2*, encodes a protein that acts as a tumor suppressor. Tumor suppressors prevent the formation of cancerous cells. When these suppressors are mutated and unable to function, tumors can develop. In familial (inherited) Parkinson's disease, mutation of *PARK2* leads to inappropriate activation of the cell-division cycle in neurons. But because neurons are cells that are unable to divide, the cells die, leading to Parkinson's disease. When *PARK2* is mutated in cell types that can divide, levels of a protein

called cyclin E rise and cause the cells to multiply out of control, sometimes leading to cancer.

The researchers found the mutation when studying an area of chromosome 6 that was known to play a role in many cancer types. “We used microarrays to study cells from several different tumor types,” Dr. Chan explained. “When we mapped and sequenced the most likely candidate gene in the area, we were surprised to find that it was *PARK2*, which was already known for its role in Parkinson’s. Research is beginning to show that similar genetic mutations can have very different effects, depending on the type of cell in which they occur.”

Future research will focus on developing mouse models to study the mutation in cancer progression and in trying to determine additional genetic mutations that *PARK2*-deficient tumors need to develop into cancer. Investigators are also looking at whether people with the inherited forms of Parkinson’s disease have a higher cancer risk.