“When you are studying about von Hippel-Lindau disease you are not just studying about [the] .... disease. ... you are also now touching other diseases as well where we can use the VHL gene to understand what is happening.”

William G. Kaelin, Jr., MD
2019 Nobel Laureate in Medicine

Cancer has a major effect on society. Approximately 40% of all people will be diagnosed with cancer at some point during their lifetimes. The significant impact of cancer in today’s world was acknowledged by the Nobel Prize Committee when they selected Dr. William G Kaelin, Jr, Sir Peter J. Ratcliffe, and Dr. Gregg L. Semenza as the 2019 Nobel Laureates for Medicine.

Together, these esteemed researchers provided an understanding of how cells can sense and adapt to changing oxygen levels and how this results in cancer, such as brain, bladder, breast, colon, ovarian, kidney, and pancreatic. It all begins with one gene, the VHL gene.

Cells perceive a lack of oxygen (hypoxia) through a defect in the tumor suppressor gene (VHL). This protects the transcription factor, Hypoxia-Inducible Factor (HIF), from binding to the VHL protein and allowing HIF to accumulate in the cell. This, in turn, causes an overexpression of various cellular growth factors and alters the ways cells utilize glucose and generate energy. These changes lead to an over production of blood vessels which ultimately results in the creation of tumors. Understanding how to overcome the HIF accumulation and the cell’s perception of hypoxia is key to preventing tumor development and growth.

Thanks to research on the VHL gene, the FDA has approved 8 drugs for the treatment of breast cancer and kidney cancer, the fastest growing form of cancer in the United States. (Kidney cancer risk factors include tobacco use and obesity). These approved drugs target the regulation of cellular growth factors (the downstream) consequence of elevated HIF levels. A HIF inhibitor is currently in clinical trials for VHL and metastatic kidney cancer. This treatment will likely be effective in many other forms of cancer.
FY2021 REQUEST SUMMARY:
Language to be included in the Labor HHS appropriations report
“The Committee recognizes that finding a treatment and cure for von Hippel-Lindau (VHL) disease, in which the VHL tumor suppressor gene is damaged or nonexistent, is a key for treating and curing many other forms of cancer. The involvement of the VHL gene in how cells sense and adapt to oxygen availability lead to abnormal cell or cancer growth. This fact was acknowledged by the choice of the 2019 Nobel Prize of Medicine. Two of these awardees (Dr. William Kaelin, Jr. and Dr. Gregg Semenza) are NIH extramural grant recipients. Nearly a dozen medications currently used to treat various forms of cancer are direct results of VHL research. The Committee strongly encourages NIH to support additional internal research and extramural grants on von Hippel-Lindau disease, seeking both pharmacological and gene therapy treatments for VHL and other cancer patients. In addition, the Committee recommends a progress report be provided to Congress no later than March 1, 2022.”