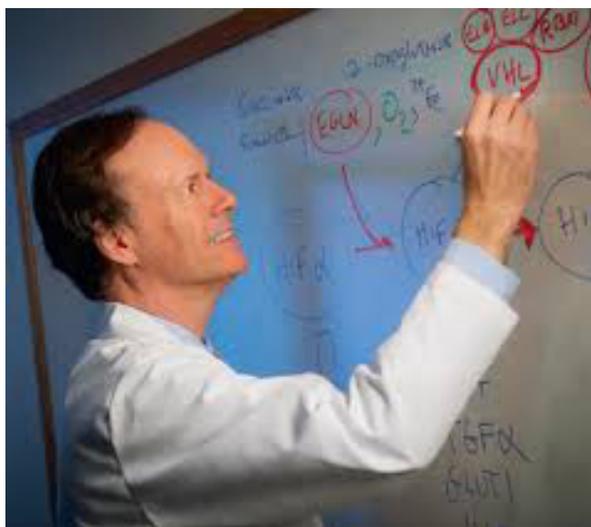


VHL ALLIANCE

Curing Cancer through VHL



“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

Appropriations FY2022 Request:

Include language to create support of von Hippel-Lindau (VHL) research through the DoD PRCRP

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.

“Until a cure is found, **HOPE** is my daily medicine”

Julie Flynn
1974-2018



Von Hippel-Lindau (VHL) Facts

VHL is a genetic form of cancer. VHL patients battle a series of tumors in up to 10 parts of the body throughout their lives. Tumors can develop in the brain, spine, retina, kidney, pancreas, adrenal gland, inner ear, reproductive tract, liver, and lung. Lack of timely intervention can lead to high rates of medical disability and mortality.

The incidence of VHL is approximately 1:36,000, the same occurrence rate as glioblastoma, which took the lives of both Senator Ted Kennedy and Senator John McCain. Twenty percent of patients are first in family due to a spontaneous mutation.

VHL tumor development and growth are unpredictable. This and the fact that VHL's presentation is different in every person, making annual testing necessary (blood work and radiological screening, including MRI, CT scans, etc.). Currently the only form of treatment is surgical intervention. VHL patients face countless surgeries in their lifetime, sometimes starting as early as 3 years of age.

Identifying a cure or therapeutic agent would decrease the need for surveillance and multiple surgeries, lower the risk of post-surgery complications, and improve patient outcome and quality of life, thus reducing the cost of patients' health care and allowing patients to remain in the work force.

In addition, the biochemical pathway involved in VHL overlaps with the pathways of many cancers. Therefore, a treatment for VHL will likely be valuable for other forms of cancer such as brain, bladder, breast, colon, ovarian, kidney, and pancreatic. Research is essential to discovering an effective cure.

RESEARCH IS THE ONLY PATH FORWARD
#CURINGCANCERTHROUGHVHL

FY2022 REQUEST SUMMARY:

Language to be included in the Defense 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 leads to abnormal cell or cancer growth. This fact was acknowledged by the choice of the 2019 Nobel Prize of Medicine. Nearly a dozen medications currently used to treat various forms of cancer are direct results of VHL research. The Committee strongly encourages the DoD PRCRP 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, 2023.”