



VHL 101:

## Introduction to VHL: Terminology and Concepts

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## Agenda

- Introduction to Language and Concepts
  - Understanding the cause
  - Possible Effects
  - Prevention
  - Research toward a cure
- Teamwork for Health



## Who We Are

Families and Health Care Professionals working together

## Our Mission

to improve diagnosis, treatment, and quality of life for individuals and families affected by von Hippel-Lindau



## Effects and Treatments

- Who gets which effects?
- Why?
- What to do?
- How to get more than your local doctor knows?
- Important to learn from ALL families, ALL experience, ALL research, worldwide
- Examples:
  - hB in pituitary
  - ELST



## Before 1993, we were alone

- Each patient knew only his own family
- Most of the articles were case studies of one patient
- We needed to see the whole picture



Blind Men Study the Elephant; artist: Liu Zhangde; granite; Wuhan; 1985.



## What Causes VHL?

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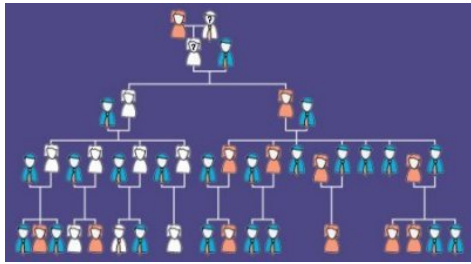
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-- ©1994, Sprint Communications Company



## Family Tree



Source: National Cancer Institute



## Pedigree

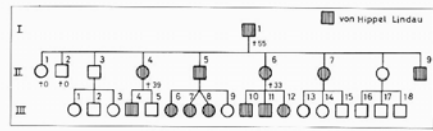
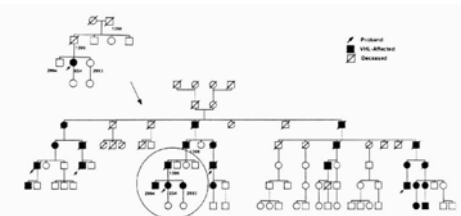


Figure 1. Pedigree of the family. American Journal of Medicine, 99:159, August 1994.



## Founder Effect



A proband, or index person, is the presenting patient. For example, patient #54 gave the family history shown at the top. Genealogical studies starting out from the individual patients resulted in the determination that all these people were related. Females are represented as circles, males as represented as squares.

Source: French VHL Study Group

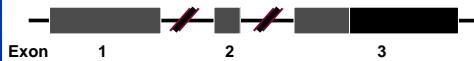


## Understanding the Cause

- Collecting data on genotypes
  - 1996, Hawaii, agreement to collect genotype data
  - and to begin to understand genotype/phenotype relationship
  - leading us to better understanding of the chemical cause and effect of pheo, kidney cancer, etc.
  - In 2010 we will ask researchers to focus on translation



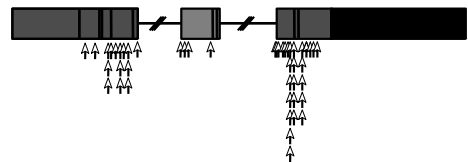
## Human VHL Gene



Source: National Cancer Institute



## Inherited Mutations



as published by Chen F, Kishida T, Yao M, et al. Germ line mutations in the von Hippel-Lindau disease tumor suppressor gene: correlations with phenotype. Human Mutation (1995) 5:66-75.

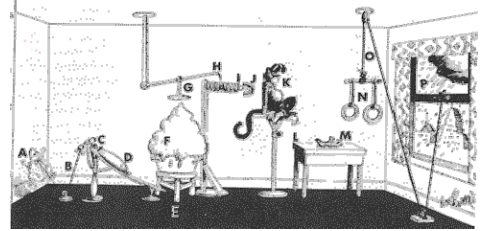


### How Does it Work?

If there is too little pVHL... **Black box** ...a tumor grows.



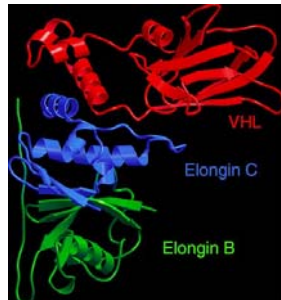
### Rube Goldberg's View



How to close the window if it rains when you're out.



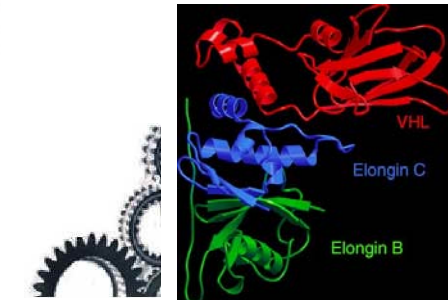
### Structure of the Gene



Source: Dana Farber Cancer Research Institute, Boston



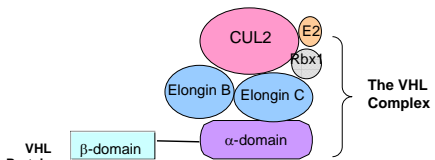
### Structure of the Gene



Source: Dana Farber Cancer Research Institute, Boston

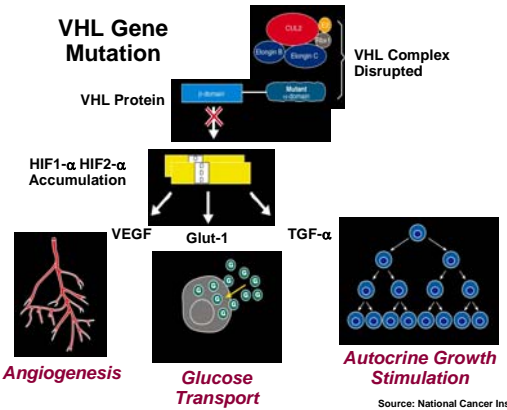


### pVHL Forms a Complex (Subassembly) with Elongins C and B and Cul-2



Source: National Cancer Institute  
*Science* 269:1995, *PNAS* 94:1997

### VHL Gene Mutation



Source: National Cancer Institute



## Prevention

- How can we prevent tumors from developing?
- Can you fix a car with a paper clip?
- How do we learn enough about the underlying mechanisms to know where to put the paper clip?



## Managing VHL

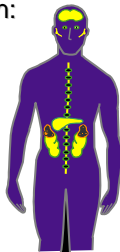
- Keep strong
- Monitor for early detection
- Get appropriate treatment
- Keep that glass half full



## Von Hippel-Lindau (VHL)

Tumors may develop in:

- Eyes
- Brain or Spine
- Inner Ears
- Both Kidneys
- Pancreas
- Adrenal Glands



## Of Dandelions and Cancer



## Strategy: Pick 'em while they're yellow



## In 1994 . . .

- They had just found the gene
- We had no Handbook
- We knew very little
- Our doctors usually knew less
- Those of us in families had our theories . . .





### The Board Decided

- We wanted a cure
- Research will get us there
- Meanwhile there are
  - Lots of people
  - Lots of tumors
- We needed to work not only on research but also on education and better treatments for now.



### Educating and Supporting Families

- Handbook
- Hotline support, e-mail
- Chapters in 36 states
- 18 countries, 6 continents!
- Online support group at Inspire
- Local and regional meetings
- Radio: Powerful Patient

See <http://vhl.org/support>



### Supporting our Doctors

- Awareness to speed diagnosis
- Handbook
- Medical Advisory Board
- Clinical Care Centers
- Biennial Medical Symposia
  - Connecting research teams
- International Chain of Information



### Fostering Research

- Funding research grants
- Banking Tissue
- Collecting research data
- Collecting anecdotes and promoting interest in a hot question (e.g. ELST, APMO)
- Biennial medical symposia



### The Take-Away Message

- Everyone has two copies of the VHL gene (two alleles)
- People with the condition VHL have one copy that doesn't work right.
- BUT the second copy does work and provides sufficient pVHL to suppress tumors.
- You can change the odds by keeping that second copy strong.



VHL Family Alliance

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## Questions?

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## Teamwork for Health

Families and Health Care Professionals  
working together  
to improve diagnosis, treatment, and  
quality of life  
for individuals and families  
affected with von Hippel-Lindau

**VHL Family Alliance**