

What does this all mean?

Synopsis of the Symposium:

Day One: Basic Science

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Take home message #1: epigenetics turns VHL gene off

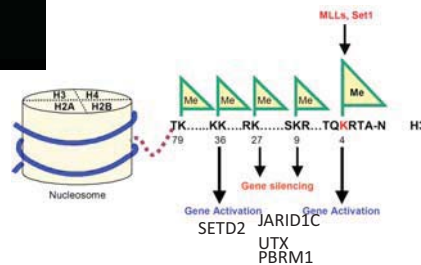
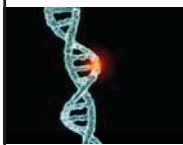
VHL mutation



VHL methylation



What is histone and why should I care?

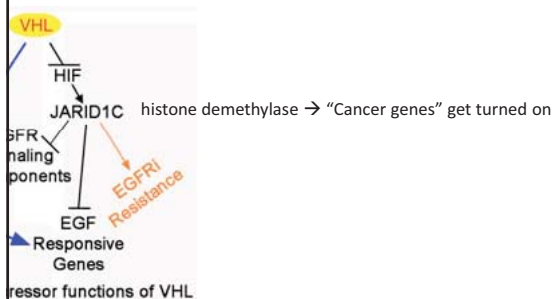


Take home message #1: what else happens...

Kimryn Rathmell

- VHL RCC: 2 types
- Type ccA: many histone modifier mutations
 - Good prognosis, SETD2, 71 tumors with known VHL mutations
- Type ccB: no histone cha

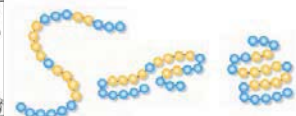
Take home message #1: JARID1C



Take home message #2: getting VHL with certain types of VHL to work anyway (TRiC)



Slow it down so VHL gets more time to be folded



Unfolded or misfolded proteins
Aggregation-prone
Protease-sensitive
Bind chaperones
Non functional

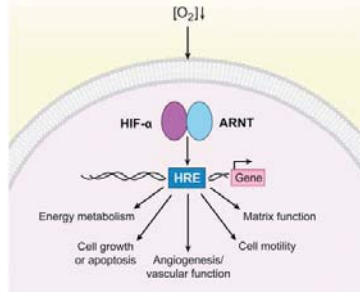
Globular soluble protein
Stable and soluble
Protease resistant
No chaperone binding
Functional

Modern proteasome inhibitor:
Carfilzomib ✕



Dr Jonasch is setting up a new clinical trial

Take home message #3: HIF1a vs HIF2a



HIF1a actually helps keep the tumor in check

HIF2a seems to be the bad guy

Simon MC et al, 2008, Annu. Rev. Physiol. 70:51-71

Drug Developments

- Dr. Giacca
- Performed screen of 130,000 drugs on VHL cells -> 5 looked good. They block movement in the cell. Development still needs to be done.