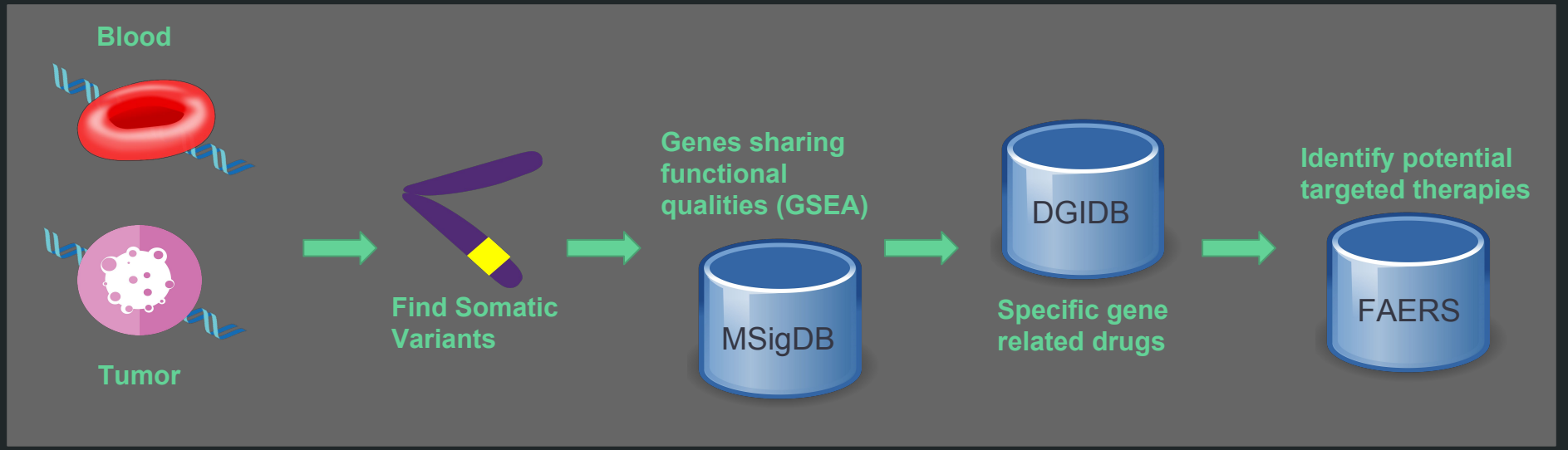
Drug candidates towards personal medicine

Kidney Bean
SVAI P1RCC
May 20, 2018

Bill has a rare form of cancer.

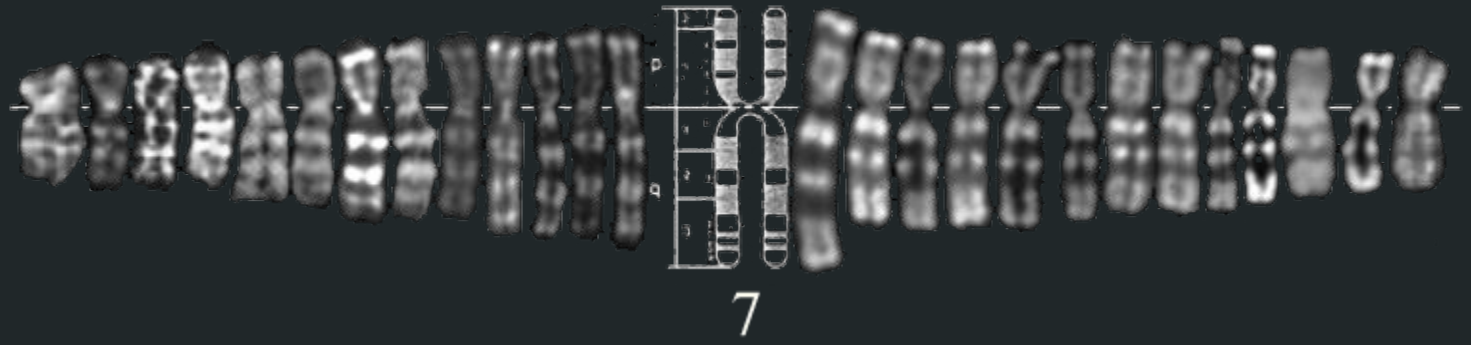
We identified candidate drugs that may target his specific somatic mutations.

Pipeline

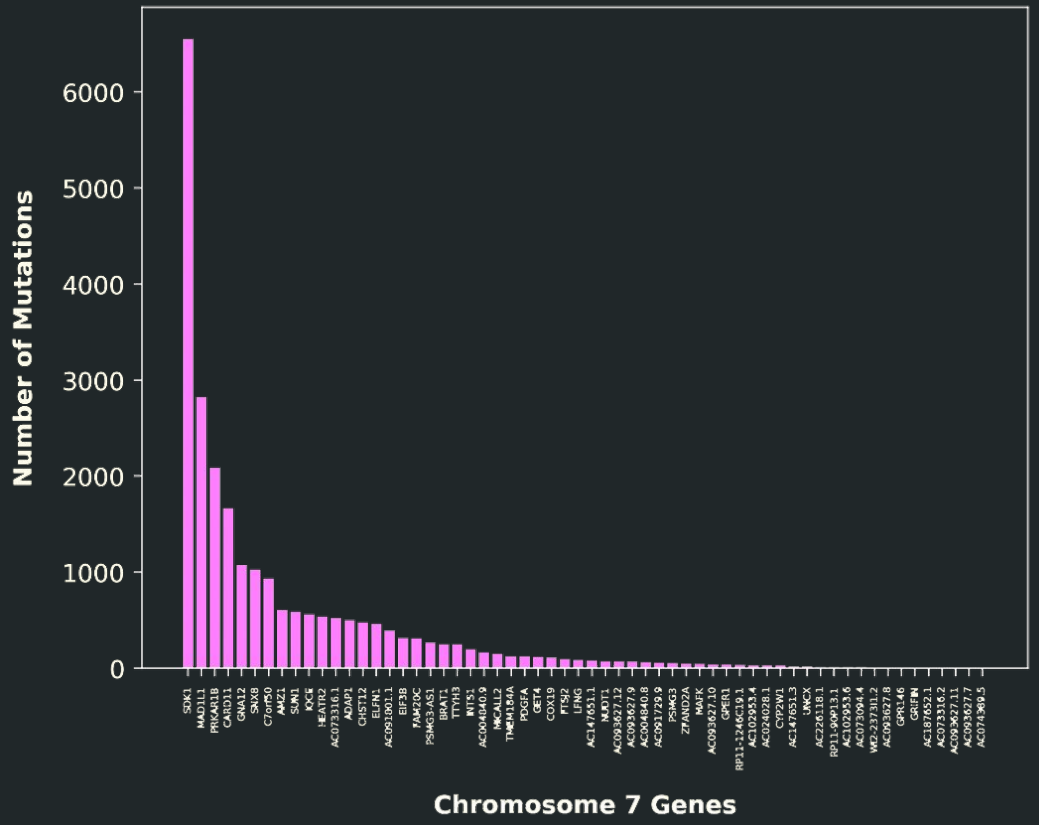

Blood
Tumor
Find Somatic Variants
Genes sharing functional qualities (GSEA)
MSigDB
DGIDB
Specific gene related drugs
Identify potential targeted therapies
FAERS

Filtered and identified P1RCC Variants from chromosome 7

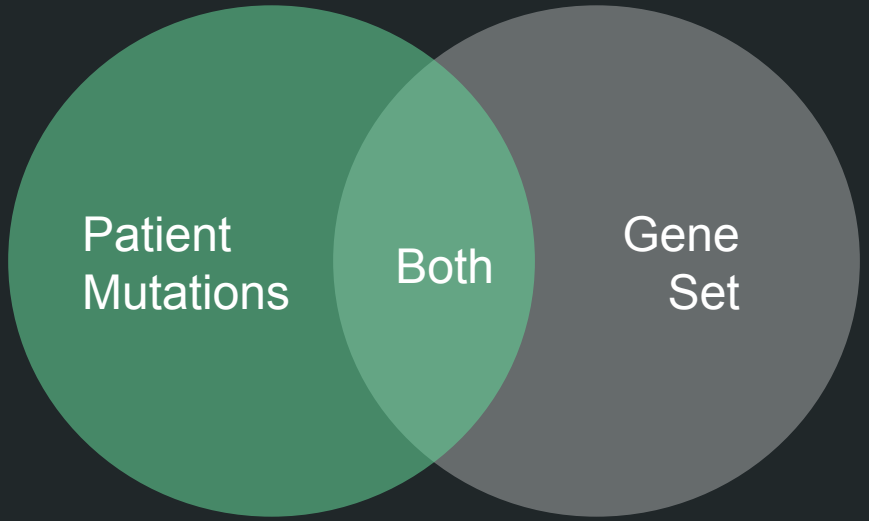
- Chromosome 7 implicated in many cases of P1RCC



Map Somatic Variants (SNVs only)



GSEA - Fisher Exact Test



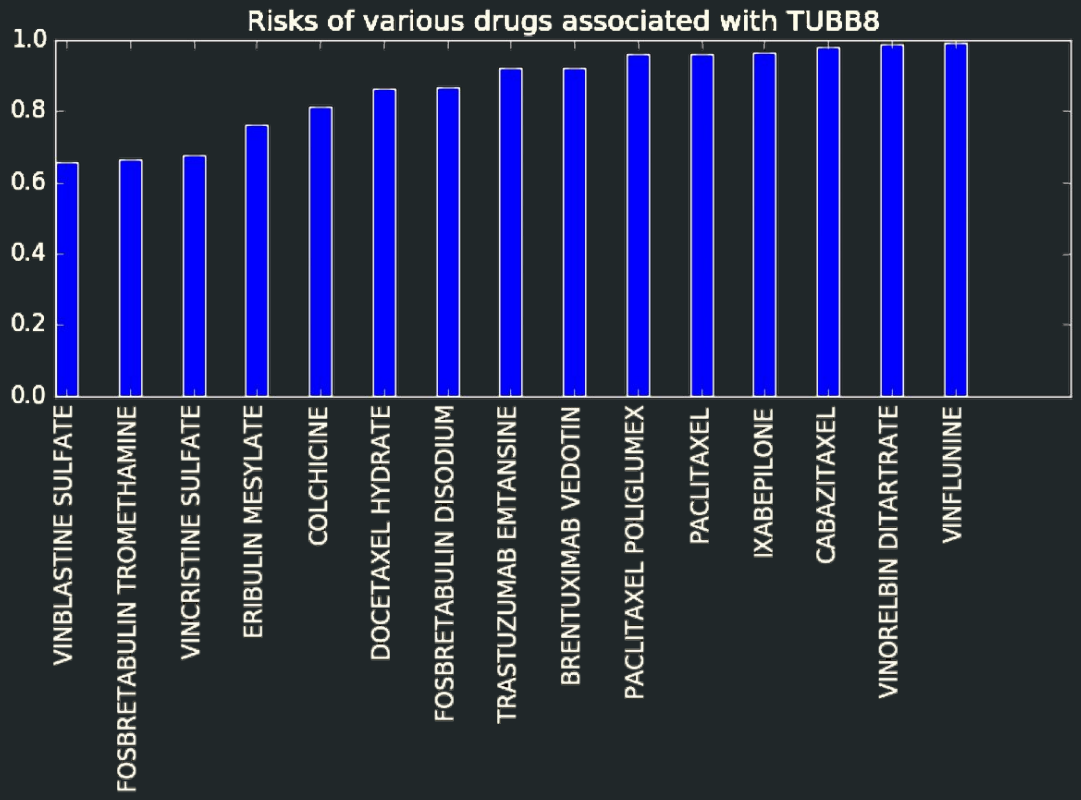
Contingency Matrix

Subject ✓ Gene Set ✓	Subject ✓ Gene Set ✗
Subject ✗ Gene Set ✓	Subject ✗ Gene Set ✗

Map tumor-relevant genes to drug-gene

e.g. TUBB8 target drug candidates

y=p(serious|event)



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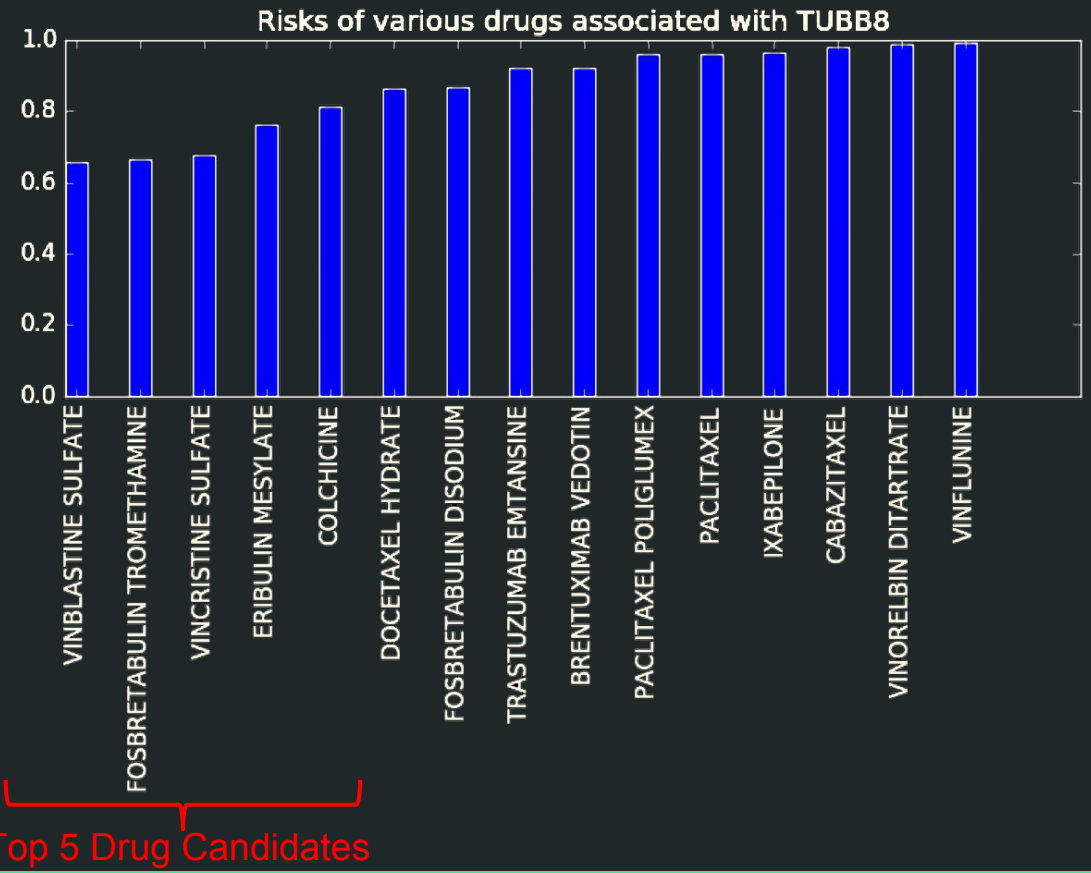

Top Drug Candidates

- Vinblastine Sulfate (Velban)
  - *Used to treat fibromatos and germ cell tumors for cancers:*
  - *Hodgkin lymphoma, non-Hodgkin's lymphoma, testicular, breast, lung (Non-small cell lung cancer), head and neck, and bladder cancers, melanoma, fibromatosis and germ cell tumor, certain blood disorders and histiocytosis*
- Fosbretabulin tromethamine
  - *Damages vasculature of cancer tumors by arresting mitosis of endothelial cells*
- Vincristine Sulfate
  - *Acute leukemia, Hodgkin's and non- Hodgkin's lymphoma, neuroblastoma, rhabdomyosarcoma, Ewing's sarcoma, Wilms' tumor, multiple myeloma, chronic leukemias, thyroid cancer, brain tumors.*
  - *It is also used to treat some blood disorders.*

Top Drug Candidates

- Eribulin Mesylate
  - *(also called HALAVEN) is a prescription medicine used to treat adults with breast cancer that has spread to other parts of the body, and who have already received other types of anti cancer medicine.*
  - *Risks low white blood count (neutropenia)*
- Colchicine
  - *Used to treat gout*
  - *Also used for similar pain treatments of pain in the abdomen, chest, or joints*
  - *Risk: potentially change in heartbeat (QT prolongation)*

What’s Next

1. More in-depth data research: what databases exist?
2. Identify upstream genes via e.g. KEGG
3. Improve risk analysis and priority variant calling

SV.AI Kidney Bean

Appendix

Recommendation Engine to identify targeted therapies by leveraging the relationship between a gene and existing drugs

Pipeline

1. Identify somatic variants by comparing blood and tumor sequence data
2. Filter data to focus only on variants that are likely to be significant in p1RCC (chromosome 7, FILTER='PASS', etc)
3. Map somatic variant positions to gene
4. Run Gene Set Enrichment Analysis (GSEA) to identify correlation to specific functional pathways (e.g. tumorigenesis, angiogenesis)
5. Map genes significant to tumor development to drug-gene interaction databases to identify potential targeted therapies
6. Rank therapies by safety risk
7. Propose top 5 off-label, under-investigated therapies for Bill

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