



Key Problems in Addressing the N+1 problem in Patient Care.

Daniel Quest

Note: The case study in this slide deck should not be considered clinical advice. The goal is to understand the informatics challenges!

Introduction

In 1900 David Hilbert in Paris at the International Congress of Mathematicians proposed 10 problems (later 23) that greatly influenced the progression of mathematics for the 20th century.



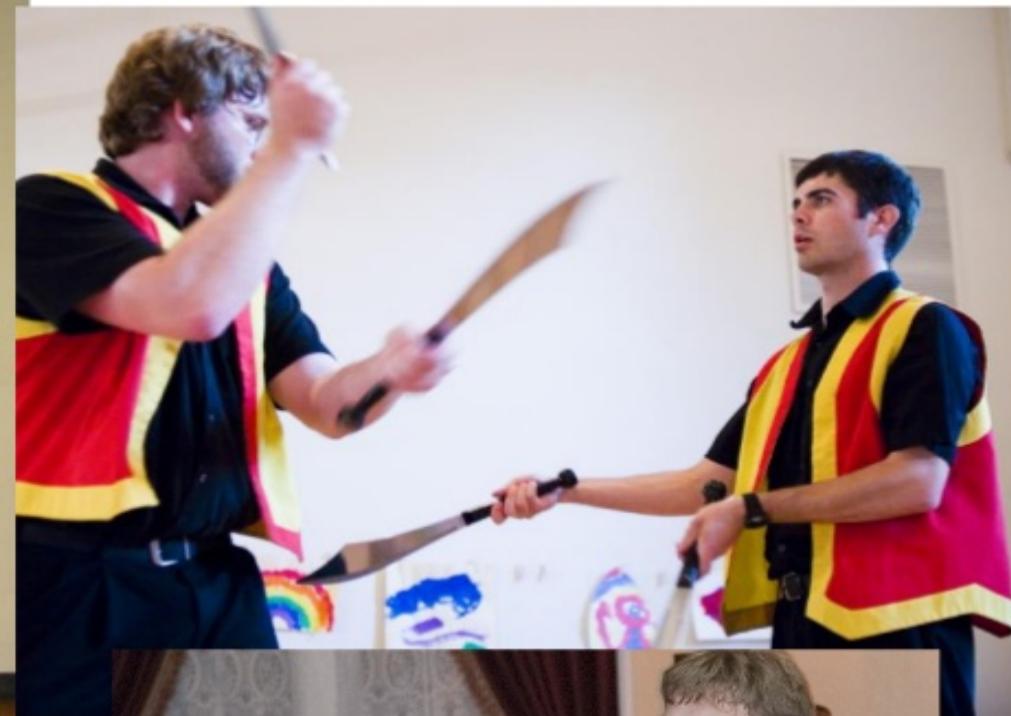
This is a similar journey – but in ‘genomic medicine’

Today I will present **9** problems:

AND SPARK IS AWESOME AT MOST OF THEM!









Madelyn Shumaker

Madelyn was 8 years old when diagnosed with DIPG (diffuse intrinsic pontine glioma), which is nearly always fatal and lacks an effective treatment. Nearly all die within two years. She underwent 'personalized medicine' in an attempt to target her cancer.



January 29, 2015:
Maddie goes to St. Jude Children's hospital for 6 weeks chemo/radiation as part of a DIPG clinical trial.

March 30, 2015:
Maddie returns home and starts school again. Maddie, has some slight hearing loss

April 15, 2015:
Maddie returns to St. Jude's for a follow up MRI. The results show the cancer virtually gone from the brainstem

June 12, 2015:
Maddie returns to St. Jude's for a follow up MRI. There is evidence of necrosis (cell death) in the brainstem.

October 29, 2015:
Maddie undergoes a revolutionary surgery at Sloan Kettering where they do a biopsy on the tumor for molecular and pathology analysis

November 14, 2015:
Maddie goes to Dr. Giselle Sholler Helen DeVos Children's Hospital in Grand Rapids, Mich for genome and transcriptome sequencing. The Tumor board recommends treatment based on the findings

January 26, 2015:
Maddie is diagnosed with DIPG

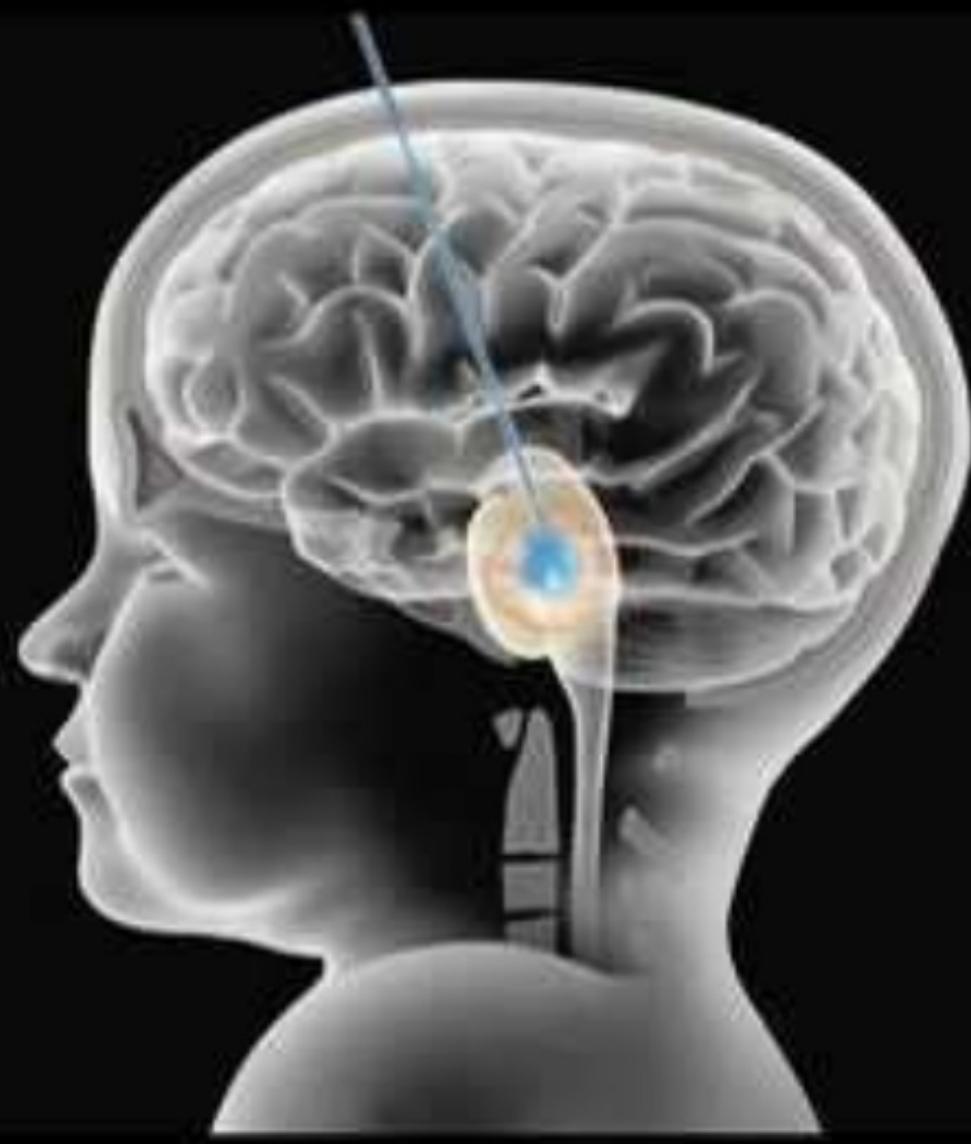
May 22, 2015:
Maddie undergoes a second round of chemo

October 20, 2015:
Maddie's symptoms worsen and become persistent, the cancer is recurrent

December 1, 2015:
Maddie begins to have adverse reactions to chemo

December 10, 2015:
Maddie passes away from DIPG



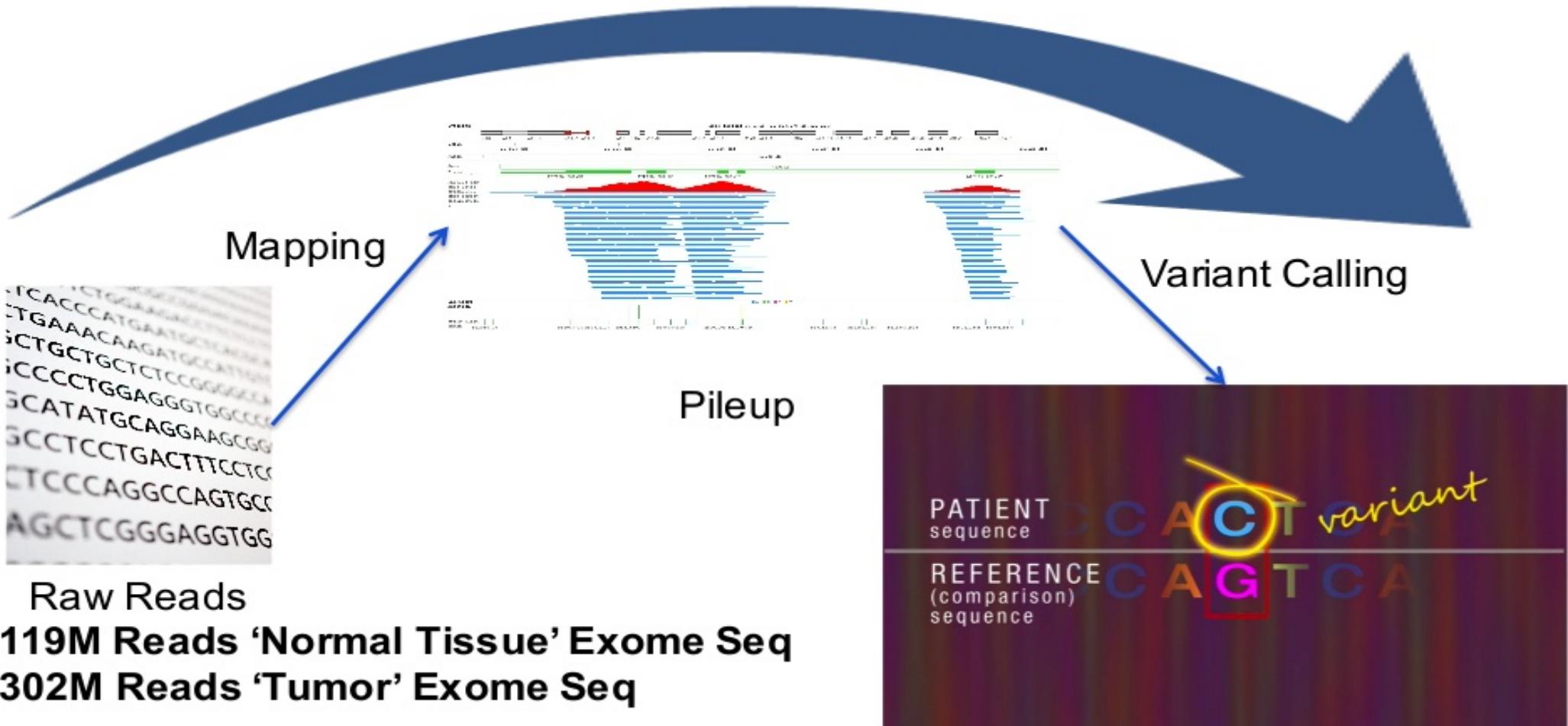


Data Types (Available to the Tumor Board)

- ▶ NGS Whole Exome (Somatic and Germline)
- ▶ RNAseq
- ▶ PDFs Describing Drug/Gene Interactions



Problem 1: Variant Calling



 <https://github.com/bigdatagenomics/> -
Variant Calling in Spark!

Genomic Variants
62,116 Variants 'Normal Tissue'
4361 Variants 'Tumor'

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Problem 2: Annotation



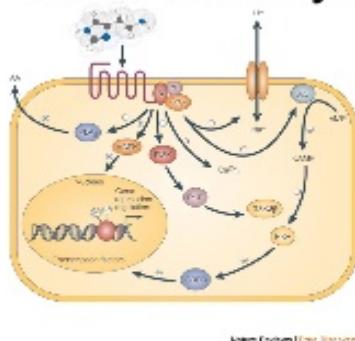
<http://bioinformaticstools.mayo.edu/research/bior/>

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Problem 2: Annotation

Information from data sources from other organizations and institutions that give important and actionable background.

Gene Functions and Pathways



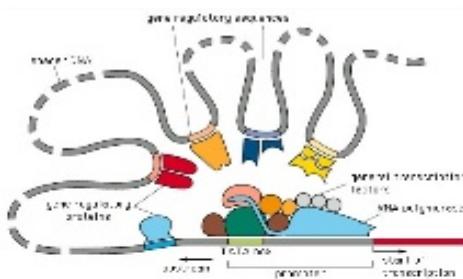
Our Data:

Genome, Transcriptome,
Epigenome, Microbiome,
Proteome



Oncogenes, tumor
suppressors, epigenetic
readers/writers, etc.

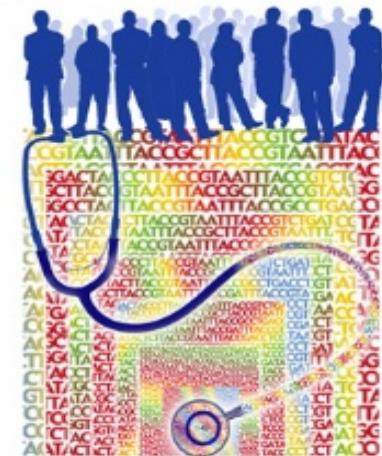
Gene regulation



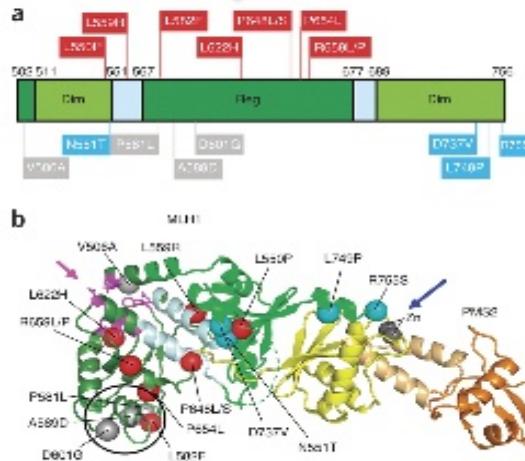
Mayo Clinical Knowledge



Population Variation



Functional Impact



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Drugs



Document Data Model

Original Data (normalized syntax)

Added Data
(normalized syntax + semantics)

CATALOG

Below is the corresponding Catalog structure for variant rs10399749.

```
{  
    "CHROM": "1",  
    "POS": "55299",  
    "ID": "rs10399749",  
    "REF": "C",  
    "ALT": "T",  
    "QUAL": ".",  
    "FILTER": ".",  
    "INFO": {  
        "RSPOS": 55299,  
        "GMAF": 0.2537,  
        "dbSNPBuildID": 119,  
        "SSR": 0,  
        "SAO": 0,  
        "VP": "050100000005030117000100",  
        "WGT": 1,  
        "VC": "SNV",  
        "SLO": true,  
        "ASP": true,  
        "G5A": true,  
        "G5": true,  
        "GNO": true,  
        "KGPhasel": true,  
        "KGPROD": true,  
        "OTHERKG": true,  
        "PH3": true  
    },  
    "_id": "rs10399749",  
    "_type": "variant",  
    "_landmark": "1",  
    "_refAllele": "C",  
    "_altAlleles": [  
        "T"  
    ],  
    "_minBP": 55299,  
    "_maxBP": 55299  
}
```

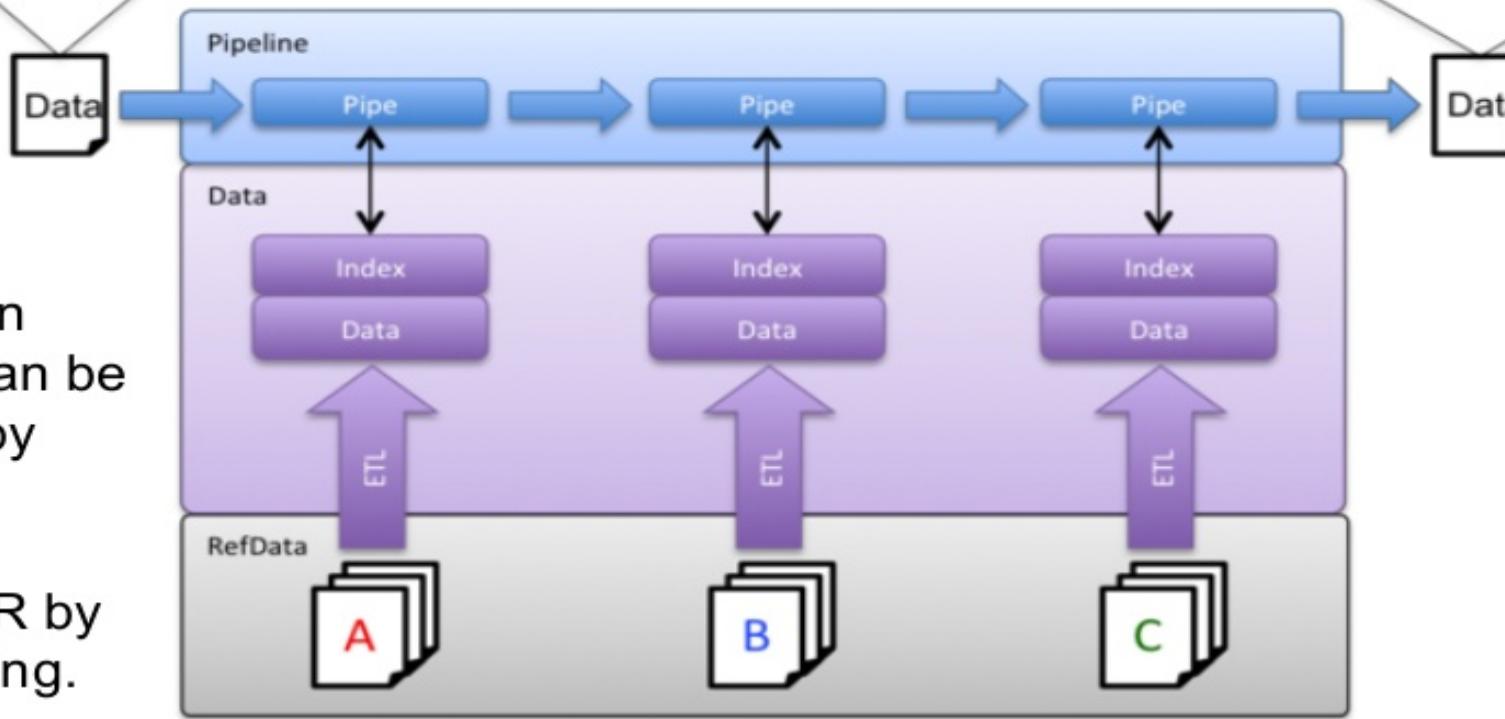


BioR Annotation Engine

CHROM	POS	ID	REF	ALT	QUAL	FILTER	INFO
chr2	48032098	.	A	T	.	PASS	DP=100
chr2	220462640	.	G	T	.	PASS	DP=100
chr4	54417522	.	A	G	.	PASS	DP=100
chr5	79950733	.	C	G	.	PASS	DP=100

CHROM	POS	ID	REF	ALT	QUAL	FILTER	INFO	A	B	C
chr2	48032098	.	A	T	.	PASS	DP=100	present	tolerated	0.001
chr2	220462640	.	G	T	.	PASS	DP=100	present	tolerated	0.239
chr4	54417522	.	A	G	.	PASS	DP=100	absent	tolerated	0.05
chr5	79950733	.	C	G	.	PASS	DP=100	present	damaging	1.000

>90% of annotation queries can be handled by genomic position search OR by ID matching.

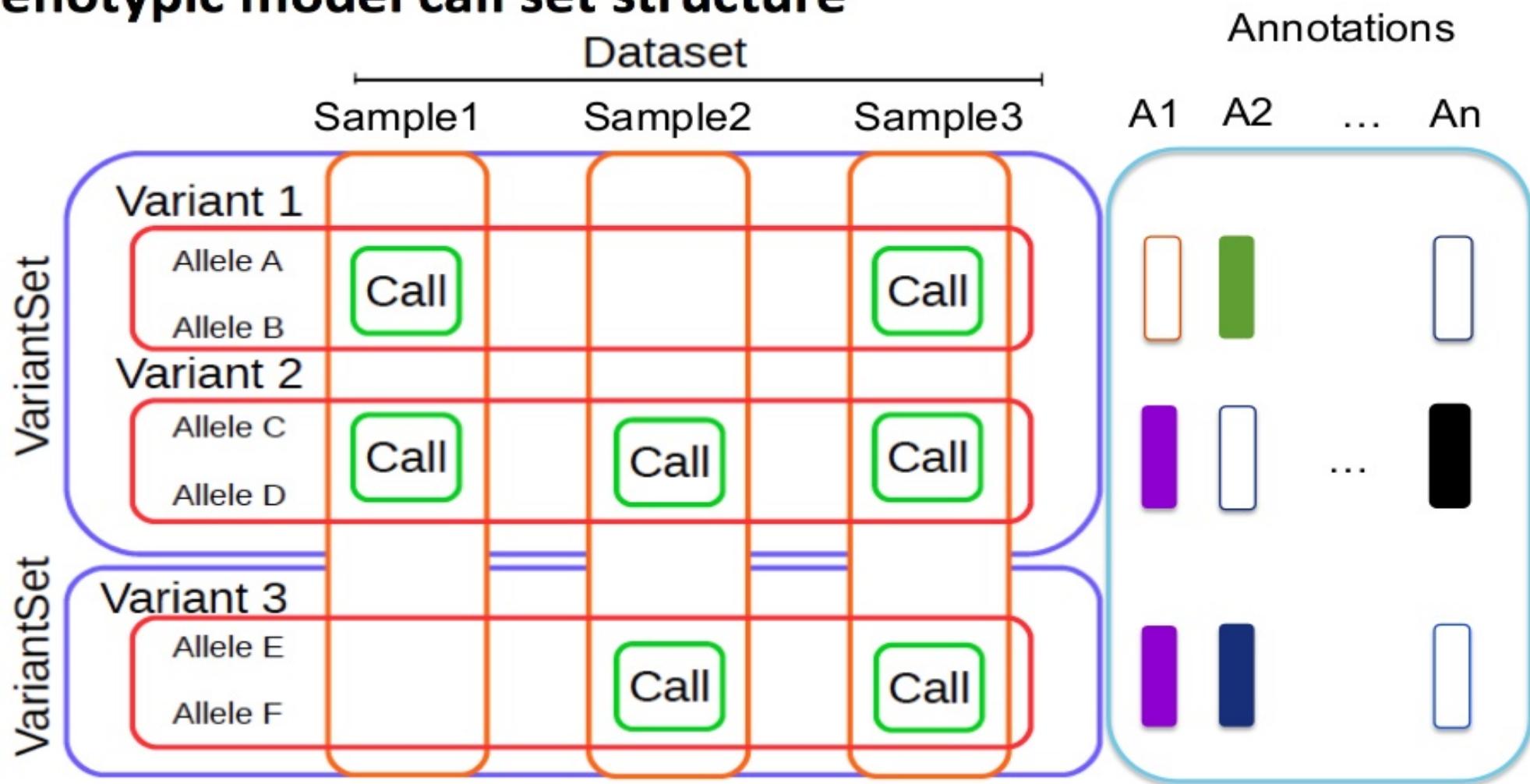


This is a Map-Reduce Problem! Spark to the rescue!



Problem 3: Variant Filtering

Genotypic model call set structure



Problem 3: Variant Filtering



Each case requires a different 'schema' because each disease is different.

Genetic Councilors at Mayo are Using VCF Miner in the Clinic to find the cause of disease



<http://bioinformaticstools.mayo.edu/research/vcf-miner/>

VCF-Miner Stats for Madelyn

#	Filter	Count
1	All Variants	61971 (whole exome – whole genome is usually ~3-5M)
2	Germline Mutations (Maddie relative to HG19)	54579
3	Somatic Mutations (tumor only)	7392
4	Variants in Cancer Genes (cosmic 595) && 3	202
5	SNPEFF Impact = HIGH MODERATE && 3	257
6	Polyphen = possibly damaging, probably damaging, unknown && 3	93
7	SIFT_TERM && 3	69
8	4 && 5	8
9	Variants Filtered by Annovar	83
10	Variants in final report to Tumor Board	7 (1 RARG, 6 PIK3CA)



Variants

[Columns](#)[Export](#)[Show Analysis](#)

25

records per page

Showing 1 to 8 of 8 entries

CHROM	POS	ID	REF	ALT	#_Samples	Samples	SNPEFF_Effect	SNPEFF_Gene_name
1	226252135	.	A	T	1	MGT9-209-08_EXO_T	NON_SYNONYMOUS_CODING	H3F3A
2	158630626	.	C	T	1	MGT9-209-08_EXO_T	NON_SYNONYMOUS_CODING	ACVR1
3	178936091	.	G	A	1	MGT9-209-08_EXO_T	NON_SYNONYMOUS_CODING	PIK3CA
4	1809110	.	CTG	C	1	MGT9-209-08_EXO_T	FRAME_SHIFT	FGFR3
4	54319247	.	CAG	C	1	MGT9-209-08_EXO_T	FRAME_SHIFT	FIP1L1
6	29911901	.	C	G	1	MGT9-209-08_EXO_T	NON_SYNONYMOUS_CODING	HLA-A
6	29911970	.	G	A	1	MGT9-209-08_EXO_T	NON_SYNONYMOUS_CODING	HLA-A
X	123224754	.	A	T	1	MGT9-209-08_EXO_T	NON_SYNONYMOUS_CODING	STAG2

[← Previous](#) [1](#) [Next →](#)

- In Clinical Report
- In Raw Report
- In DIPG Literature – not in report
- Novel found by VCF-Miner!

Missing in VCF-Miner ‘Damaging’ Analysis - **RARG** (there are two if we consider all somatic variants)



Problem 4 Clinical Oncology

Mutations in Genes Relevant to Cancer*

Gene name	Mut type	Location	Specific change	COSMIC	Gene description (NCBI)
ACVR1 (activin A receptor type I)	SNV	chr2:158630626, Pfam Domain: Transforming growth factor beta type I GS-motif	Missense, R206H, DNA allele ratio 0.46	150 coding mutations, 12 R206H	Activins are dimeric growth and differentiation factors which belong to the transforming growth factor-beta (TGF-beta) superfamily of structurally related signaling proteins. Activins signal through a heteromeric complex of receptor serine kinases which include at least two type I (I and IB) and two type II (II and IIB) receptors. These receptors are all transmembrane proteins, composed of a ligand-binding extracellular domain with cysteine-rich region, a transmembrane domain, and a cytoplasmic domain with predicted serine/threonine specificity. Type I receptors are essential for signaling; and type II receptors are required for binding ligands and for expression of type I receptors. Type I and II receptors form a stable complex after ligand binding, resulting in phosphorylation of type I receptors by type II receptors. This gene encodes activin A type I receptor which signals a particular transcriptional response in concert with activin type II receptors. Mutations in this gene are associated with fibrodysplasia ossificans progressive.
PIK3CA (phosphatidylinositol-4,5,-bisphosphate 3-kinase, catalytic subunit alpha)	SNV	chr3:178936091, Pfam Domain: Phosphoinositide 3-kinase family, accessory domain (PIK)	Missense, E545K, DNA allele ratio 0.14	8178 coding mutations, 1277 E545K	Phosphatidylinositol 3-kinase is composed of an 85 kDa regulatory subunit and a 110 kDa catalytic subunit. The protein encoded by this gene represents the catalytic subunit, which uses ATP to phosphorylate PtdIns, PtdIns4P and PtdIns(4,5)P2. This gene has been found to be oncogenic and has been implicated in cervical cancers.



Molecular Guided Report

Variant Type: Known Variants

Gene	AA Change	Genomic Event	Drug
			Indication
PIK3CA	E545K	SNV	sirolimus, temsirolimus, everolimus
			Sensitive
PIK3CA	H1047R	SNV	sirolimus, temsirolimus, everolimus
			Sensitive
PIK3CA	E545K	SNV	Erlotinib/Gefitinib
			Resistant
PIK3CA	H1047R	SNV	Erlotinib/Gefitinib
			Resistant
PIK3CA	E545K	SNV	Imatinib
			Resistant
PIK3CA	H1047R	SNV	Imatinib
			Resistant

Variant Type: Variants of Unknown Significance

Gene	AA Change	Genomic Event	Drug
			Indication
RARG	D95G	SNV	Retinoic Acid
			Sensitive



NMTRC 009 Treatment Memo

Molecular Tumor Board held on : 11 / 16 / 2015 Subject Study ID: MGT9-209-08

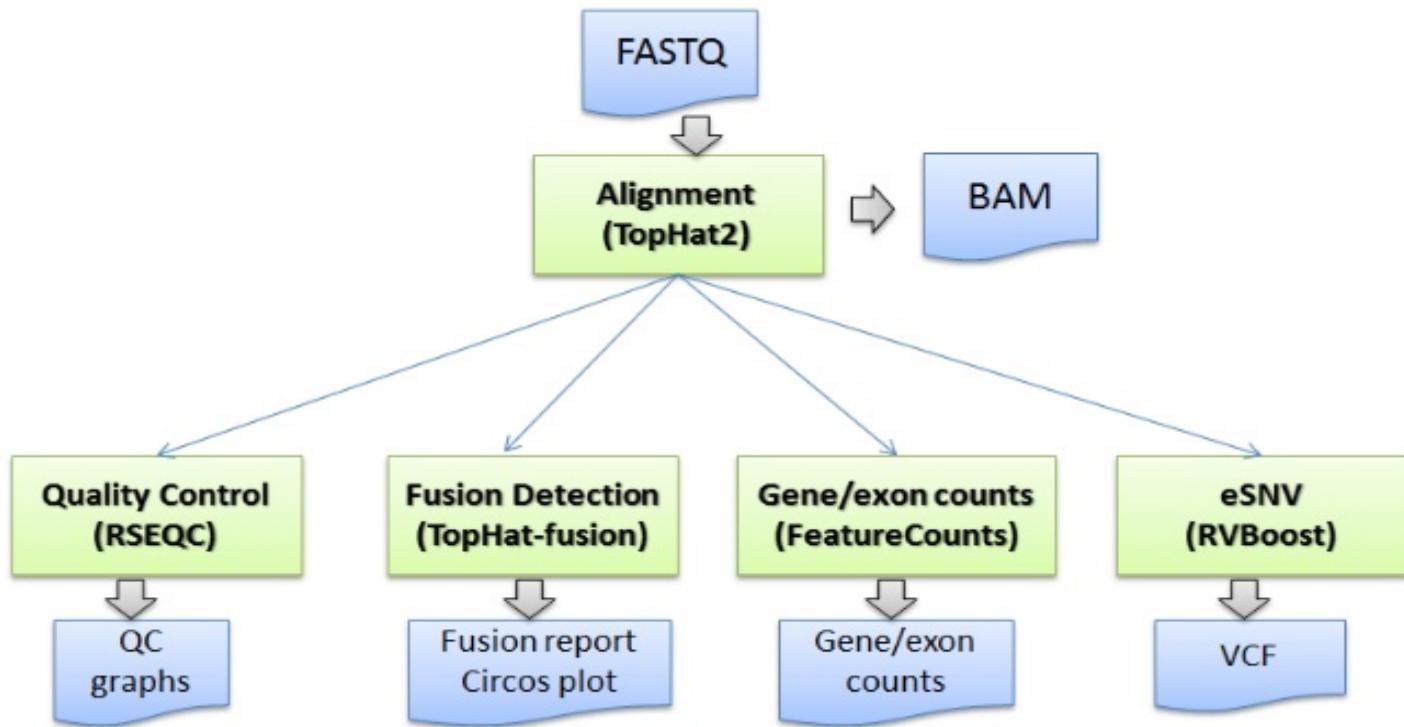
Chemotherapy Administration:

Cycles will be 21 day cycles of:

	Drug Name	Dose	Route	Schedule
1	Etoposide	125 mg/m ² /dose	IV	Give on Days 1-3 of each 21 day cycle.
2	Dasatinib	65 mg/m ² /dose	PO	Take 50mg orally twice daily on every day of a 21 day cycle.
3	Tensirolimus	35 mg/m ² /dose	IV	Give on Days 1, 8, and 15 of a 21 day cycle. Pre-medication with Benadryl 30 minutes prior to dose.
4	Vandetanib	65 mg/m ² /day	PO	Take 50mg (1/2 of 100mg tablet) once daily on every day of a 21 day cycle. *Please ask pharmacy to cut tablets in half prior to dispensing May replace with Thalidamide if not able to order Vandetanib due to limited access program.



Problem 5: Integrate RNA and other data to get improved accuracy.



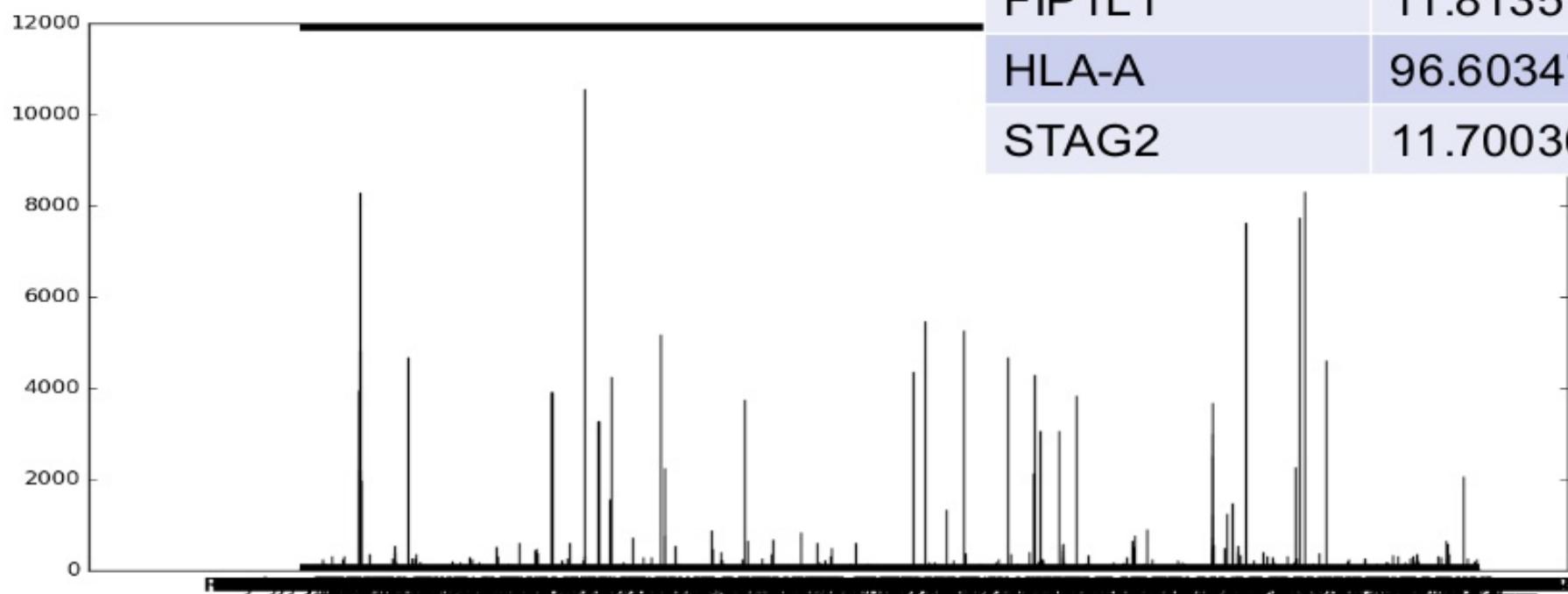
MAPRSeq

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RNAseq Stats:

	Number of Transcripts
RPKM > 1	17651
RPKM > 0	38320
ALL	57773

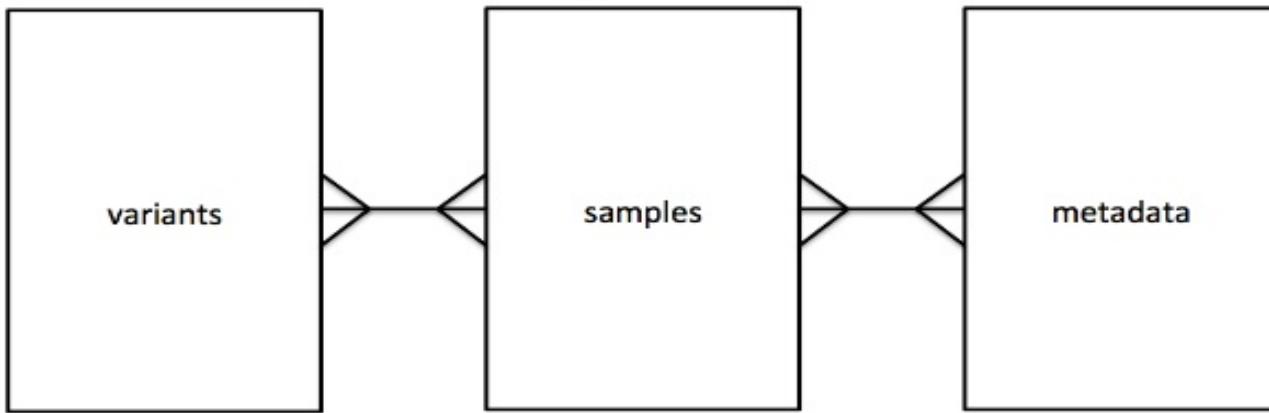


Gene	RPKM
Average RPKM >1	16.2921
H3F3A	23.844392374
ACVR1	7.87217392506
PIK3CA	3.67493145428
FGFR3	27.3744042904
FIP1L1	11.8135796235
HLA-A	96.6034792985
STAG2	11.7003663476



Problem 6: Metadata

Samples and the metadata about them link genotypes and phenotypes



- Studies on the research side mostly ‘managed’ in excel files – semi-structured/denormalized.
- Each investigator collects the information they need to answer a specific question.
- Can come from clinical notes in the EMR; free text – this requires NLP!**
- Limited information can come from the EDT for example ICD 10 codes, birthdate, ect.
- Information is decentralized and not easy to query

Diagnosis	UC vs. IC Vs. CD
Date of Current Diagnosis	date listed in Month/Year format
Initial Diagnosis	for example: if 1st dx as UC, then dx with CD
Date of Past Diagnosis	date listed in Month/Year format
Gender	Male / Female

Birth date	month/day/year
Race	
Ethnicity	

Pyoderma Gangrenosum	Yes or No
Erythema Nodosum	Yes or No
Metastatic Crohn's disease	Yes or No
Uveitis/iritis	Yes or No
Episcleritis/scleritis	Yes or No
Primary Sclerosing Cholangitis	Yes or No
Arthritis - small joints (hot swollen joints)	Yes or No
Arthritis - large joints (hot swollen joints)	Yes or No
Amyloidosis	Yes or No
Ankylosing Spondylitis	Yes or No
Sacrolilitis	Yes or No
IBD-related mouth ulcers	Yes or No
Veno us thrombosis	Yes or No
Arterial thrombosis	Yes or No
Kidney stones	Yes or No
Colon or rectal cancer	Yes or No
perianal procedure	Yes or No
abcess	Yes or No
fistula	Yes or No
stricture	Yes or No
seton placed	Yes or No

Crohn Phenotype	B1 or B2 or B3
Crohn's Location	Ileocolonic, Colonic, Ileum

UC Location	E1 or E2 or E3
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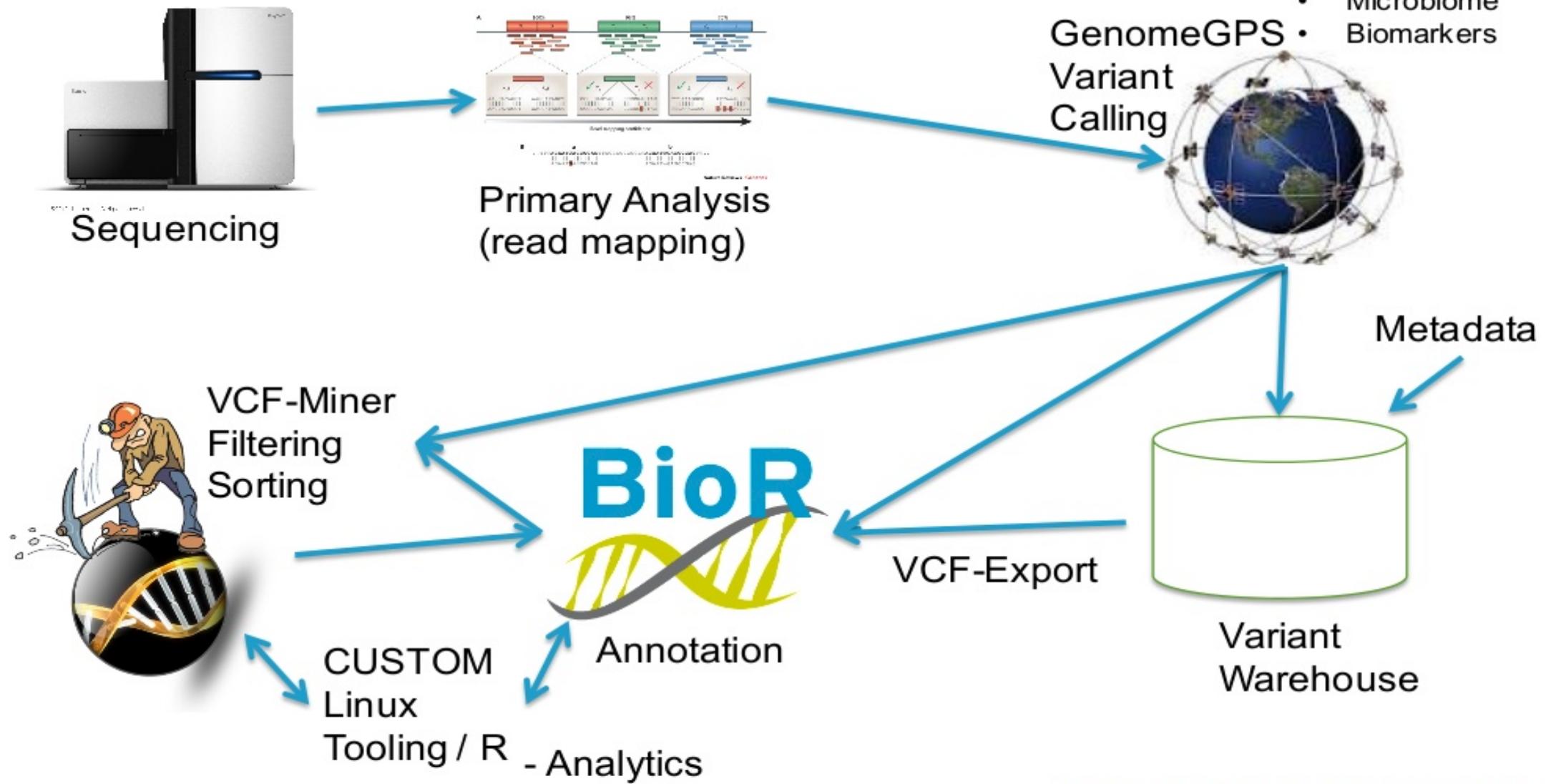
Number of IBD related surgeries	# value
Number of resections	# value
Number of strictureplasties	# value
Anti-TNF Ever	Yes or No
Any 1st degree family members with CD	Yes or No
Any 1st degree family members with UC	Yes or No
Ever Smoked	Yes or No
Smoke When Diagnosed	Yes or No
Currently Smoke	Yes or No
Current Smoke Amount	packs per day, can be decimal, or pack per week
Average Pack Per Day Over History	packs per day, can be decimal, or pack per week
Years Smoked	# value

Medication for IBD	See separate list
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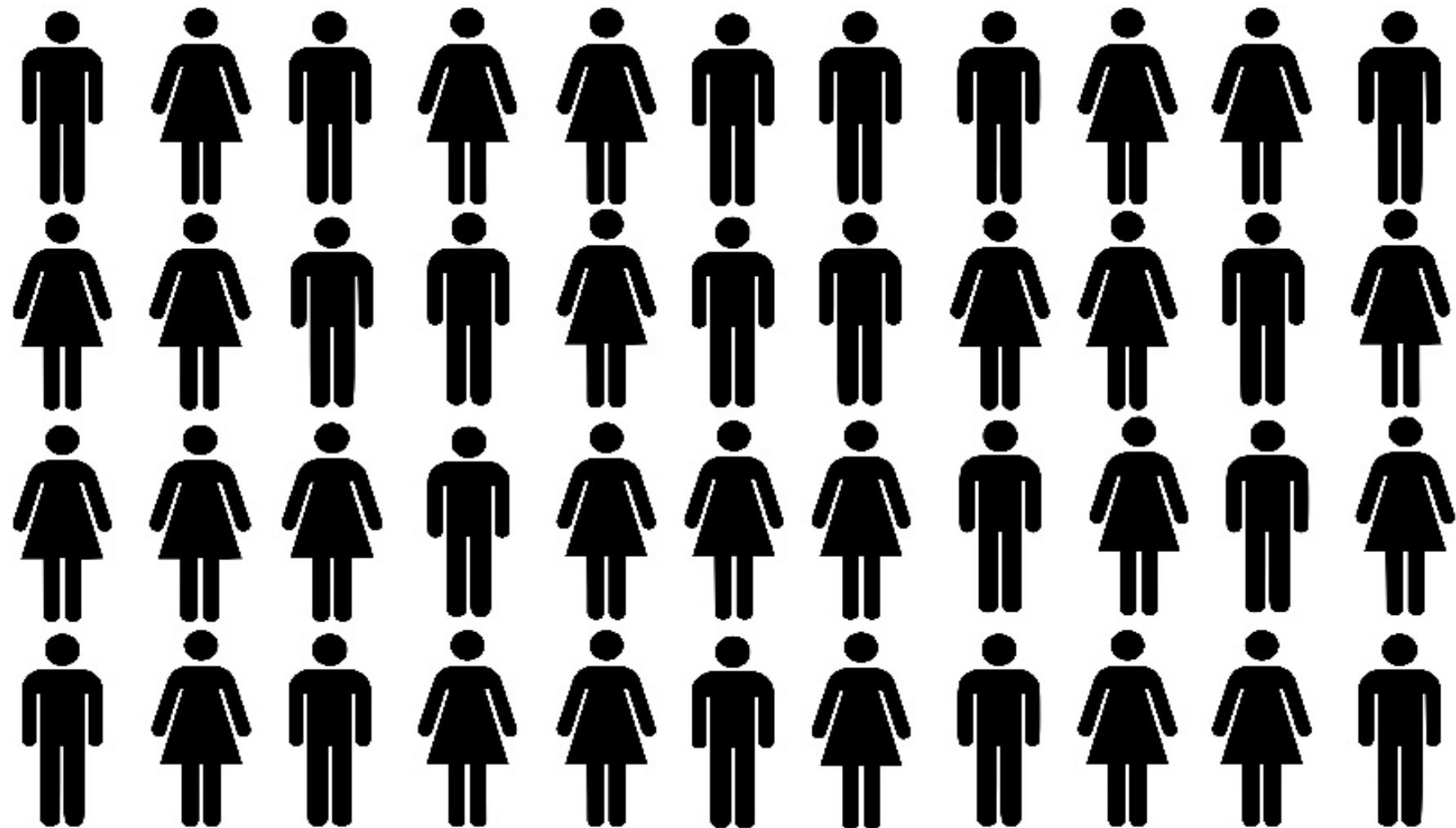
Example Study Collection Form
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Review: Components



Problem 7: Cohort Identification (N+1)



Metadata Query Builder

```
select id from patient where (
    gender = 'f',
    smoking = 'false',
    Contains(diagnosis, 'DIPG'),
    age < 10
...
)
```



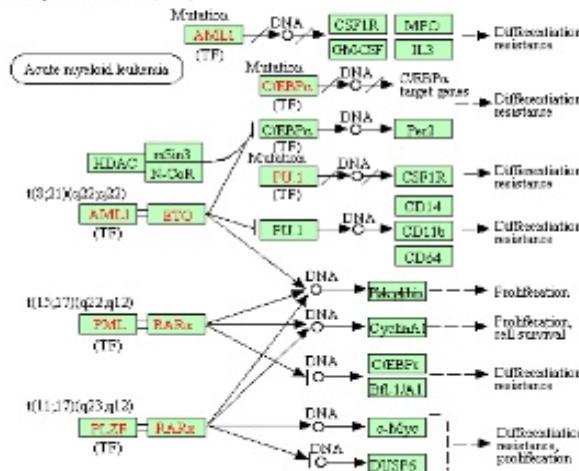
TRANSCRIPTIONAL MISREGULATION IN CANCER

TF: Transcription factor
Transcription factor fusion:

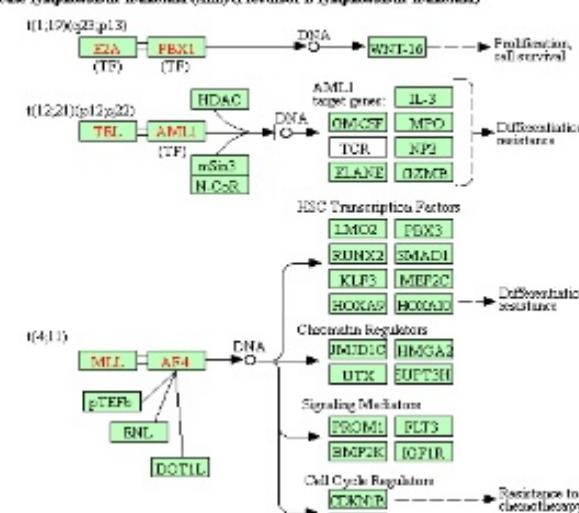
 2-Partner 3-Partner

Cancers of hematopoietic and lymphoid tissues

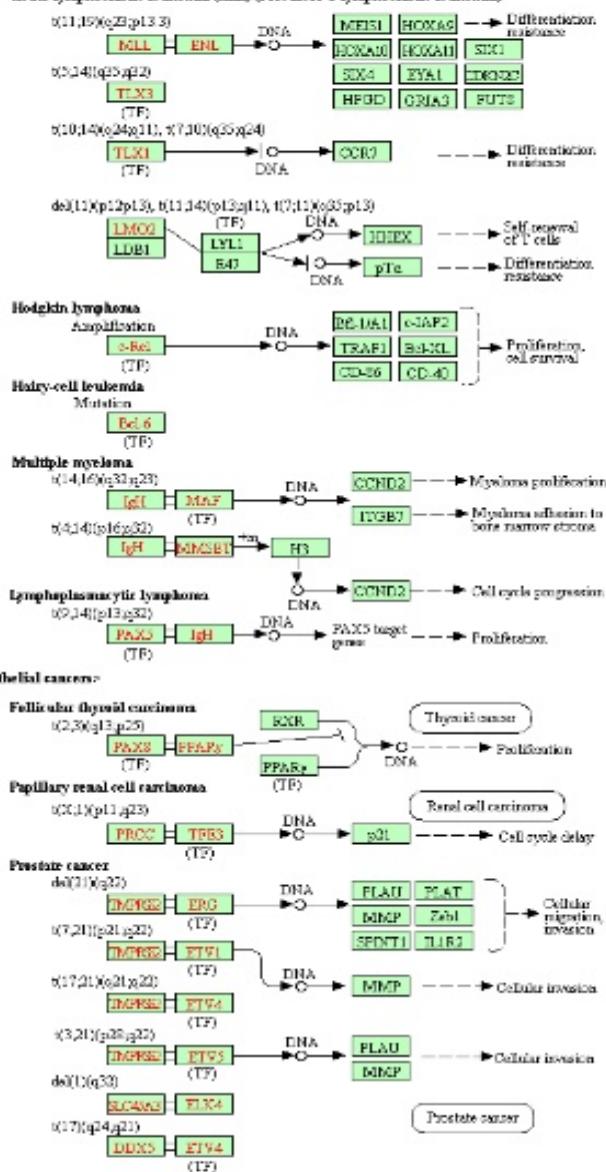
Acute myeloid leukemia (AML)



Acute lymphoblastic leukemia (ALL) (Precursor B lymphoblastic leukemia)

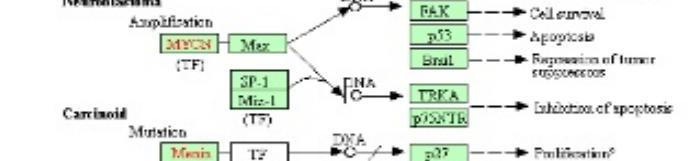


Acute lymphoblastic leukemia (ALL) (Precursor T lymphoblastic leukemia)



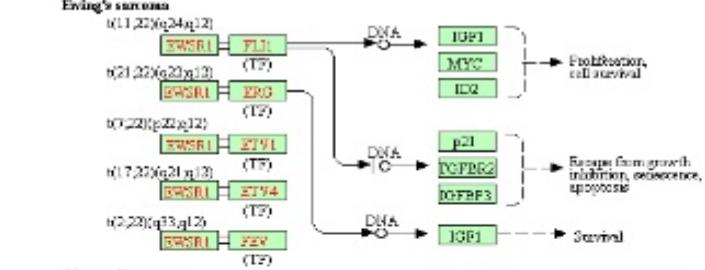
* Neurodegenerative diseases

Neuroblastoma

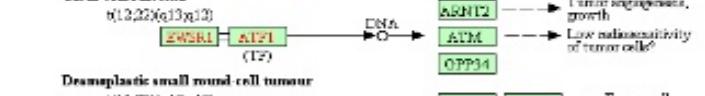


-8-

<500X600B>



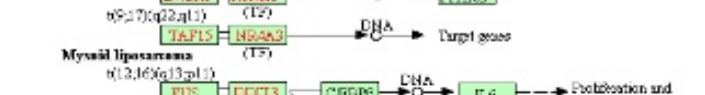
Cleavage



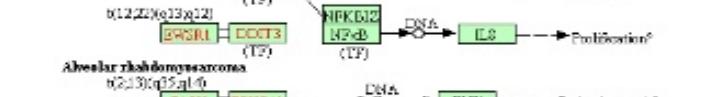
011220013d12



ANSWER = **NEEDS**



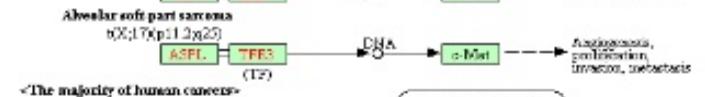
PLS ELLIS



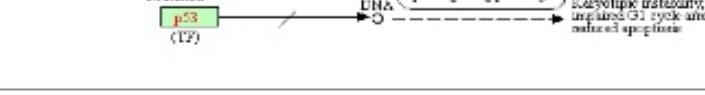
PAX3 = P08001A

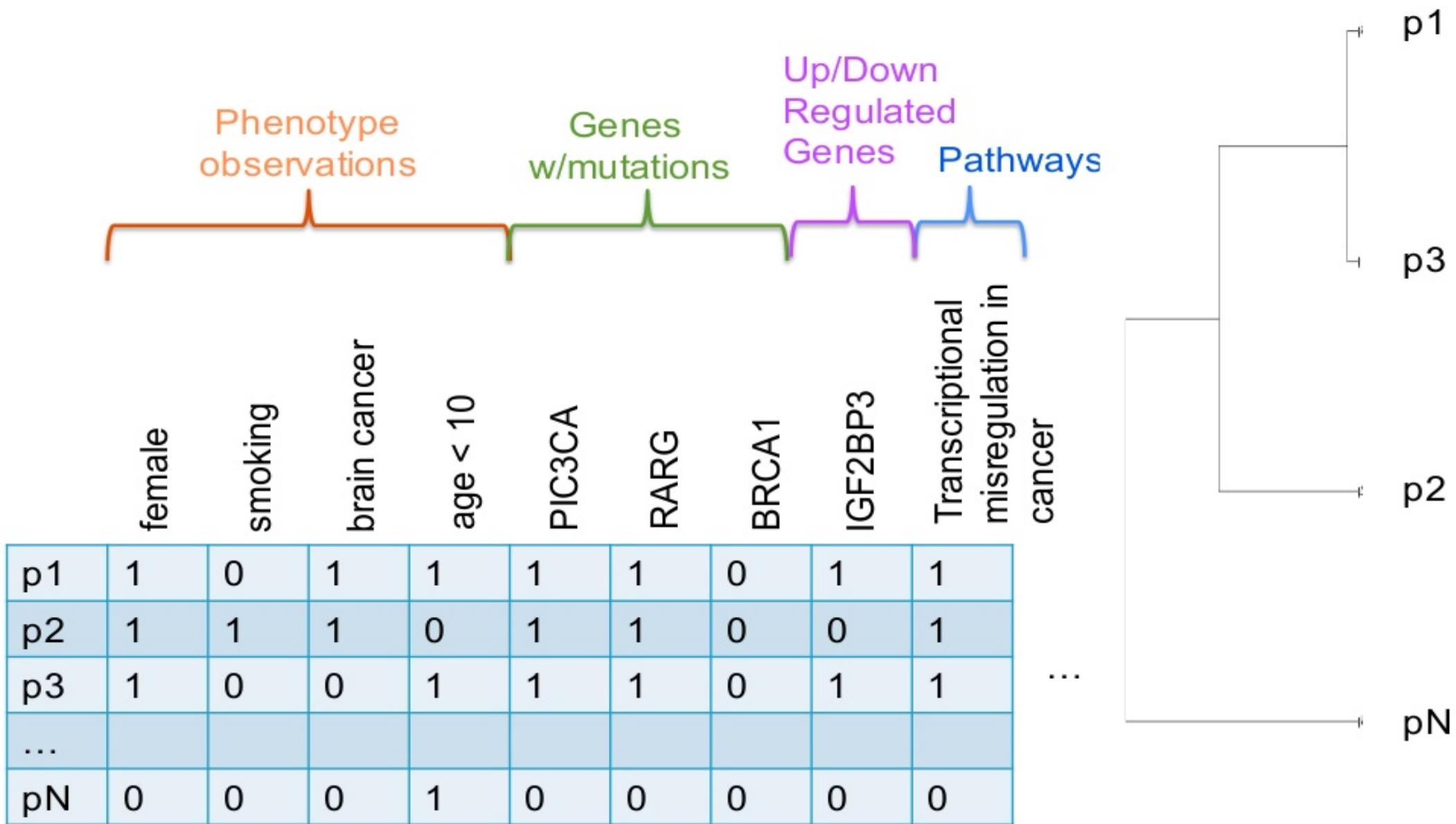


SYT = **SSX**



The majority of human cancers - mutation





Problem 8 Dynamic Recalculation and Analytics

A large set of records (~70 Million) records each needs be touched in recalculating statistics.

- Statistics need to be recalculated because we often are dealing with incomplete data or incompatible technologies (e.g. gene panels versus whole genome sequencing)

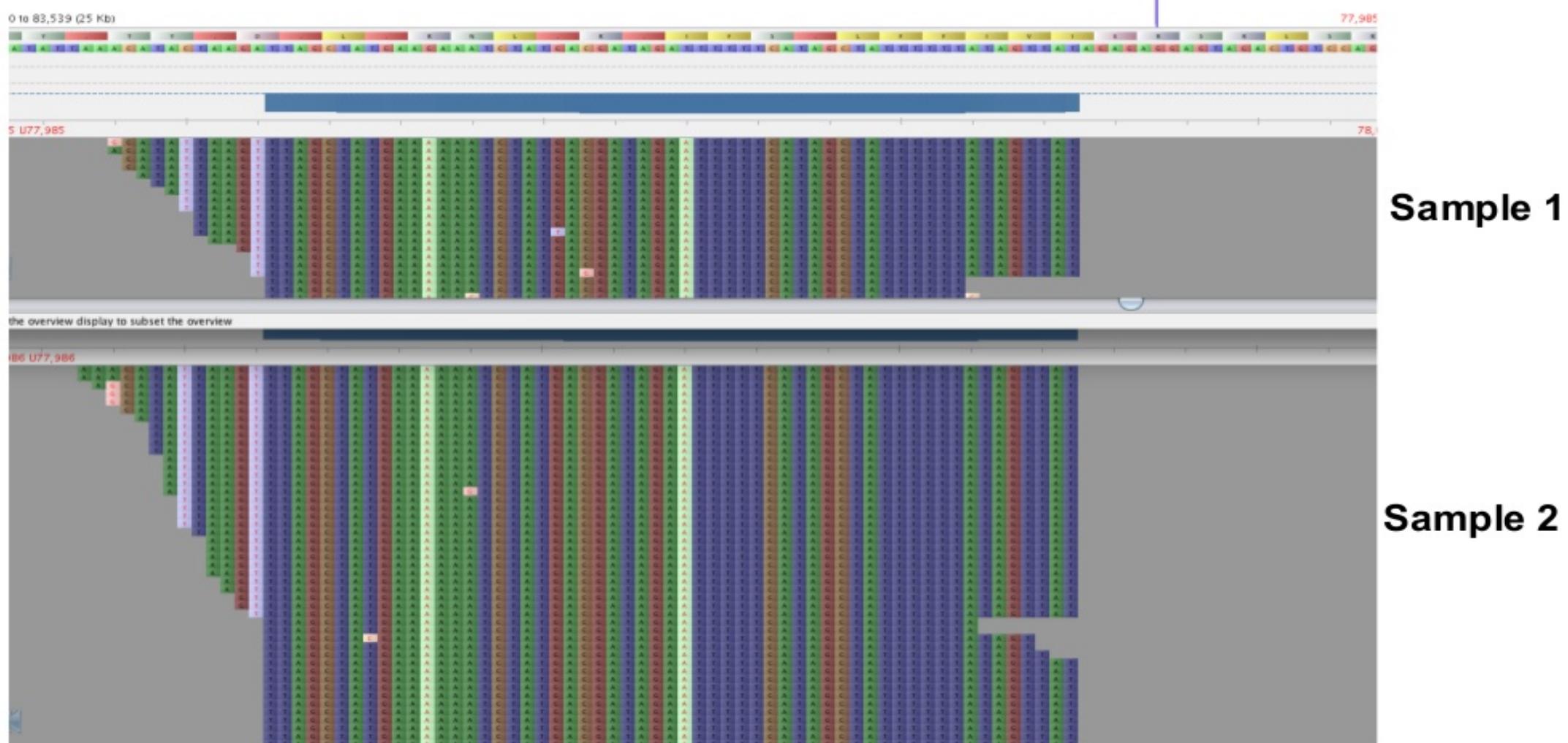
After a user selects the cohort set, important statistics need to be recalculated based on the cohort set.

$$V \begin{bmatrix} 0110 \\ 0001 \\ 1010 \\ 0101 \end{bmatrix} \wedge S \begin{bmatrix} 0101 \end{bmatrix} = R \begin{bmatrix} 0100 \\ 0001 \\ 0000 \\ 0101 \end{bmatrix} = AF \begin{bmatrix} \frac{1}{2} \\ \frac{1}{2} \\ 0 \\ 1 \end{bmatrix}$$

Variant Database Samples Selected Based on the Metadata Bitwise OR used for calculating frequencies Resulting Allele Frequencies (sortable and dynamic)



Different Coverage Results in Errors!



We have to normalize all of the data to make it comparable!



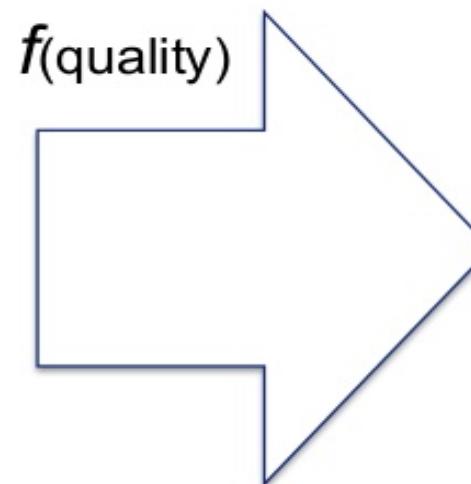
Each of these files come in one at a time, could be from different intuitions and could be years apart!

VCF1	VCF2	VCF3
S1	S2	S3
V1:0/1	2:1/1	V5:1/0
V2:1/1	3:0/1	
V4:1/0	4:0/1	

Variants

GVCF1	GVCF2	GVCF3
S1	S2	S3
V1	V2	V2
V2	V3	V3
V3	V4	V5
V4		

Coverage



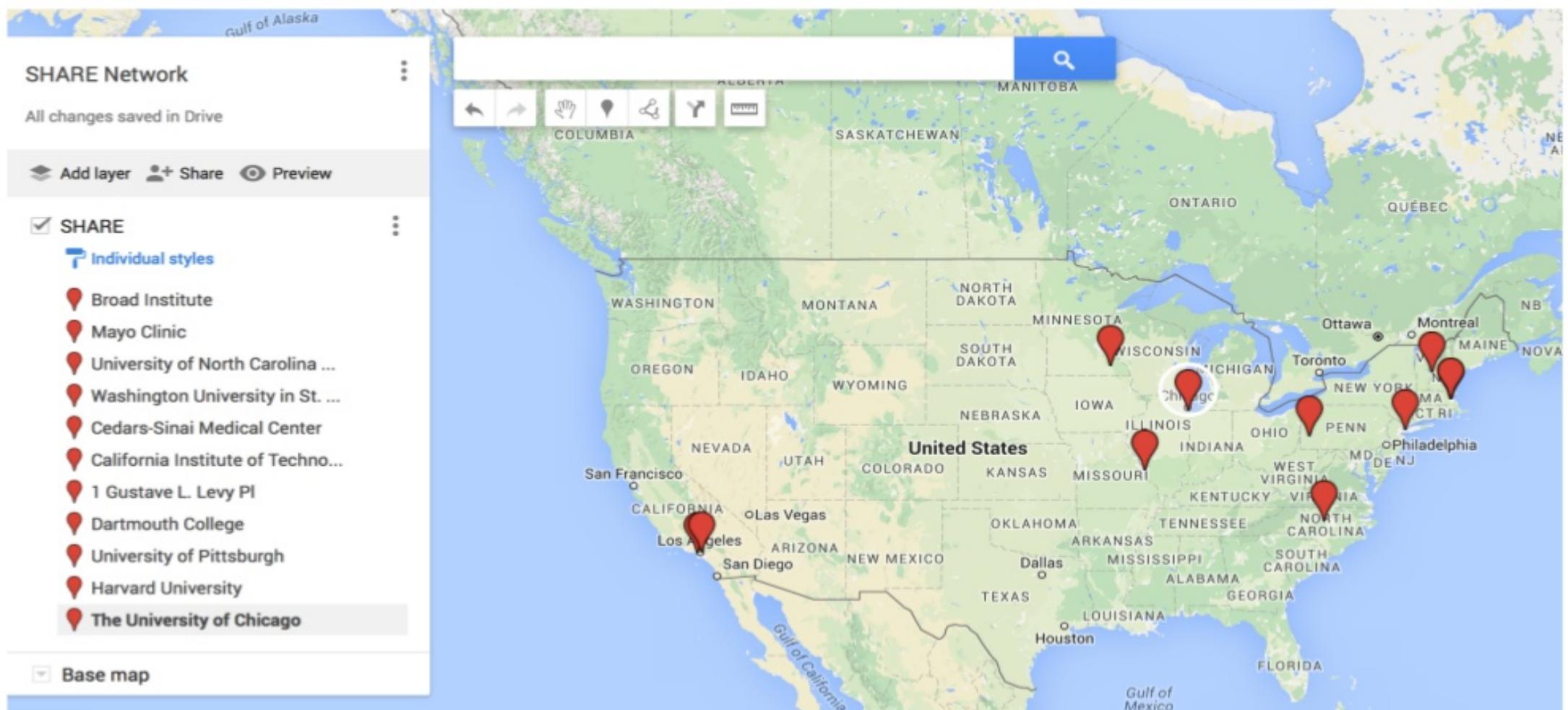
The Cohort Analysis requires a complete table of the following form:

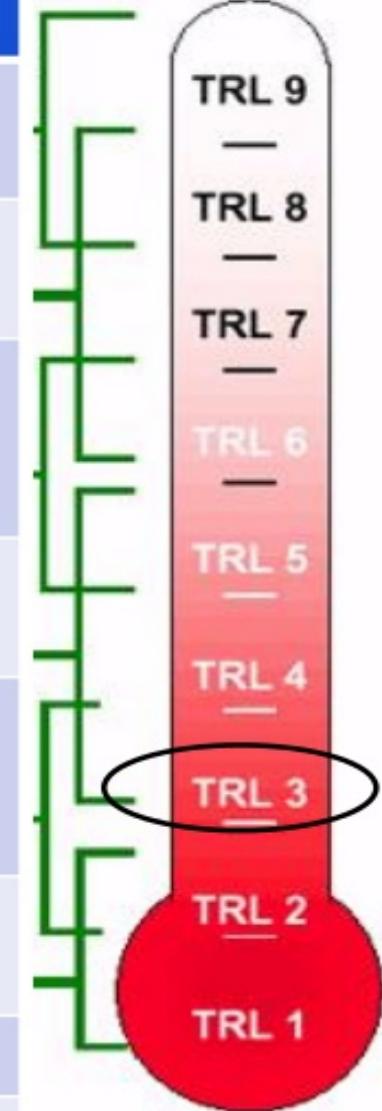
	S1	S2	S3
V1	0/1	.	.
V2	1/1	1/1	0/0
V3	0/0	0/1	0/0
V4	1/0	0/1	.
V5	.	.	1/0

Different technologies have different coverage!



Problem 9: Data Sharing – ConsortiaDB SHARE



Problem	Legacy	Future State / Being Evaluated	
1 – Variant Calling	GATK	GATK4 on Spark /Adam	 A vertical scale on the right side of the table, labeled TRL 1 at the bottom and TRL 9 at the top. It features a red gradient bar with a black circle highlighting TRL 3.
2 - Annotation	Linux Commands - SGE	Spark	
3 – Variant Filtering	MongoDB – can only filter 10,000 samples	Spark – being evaluated; could be a Spark SOLR hybrid.	
4 – Clinical Oncology	Oracle	Spark / Hortonworks Stack	
5 - Metadata	Elastic Search + STORM + MapReduce	Spark/SOLR Hybrid?	
6 – RNA and Other Data	Linux Commands - SGE	Spark/Hadoop?	
7 – Cohort Identification	DB2	Spark/Hbase Hybrid	
8 – Dynamic Recalculation	Custom Distributed Java	Spark	
9 – Consortium and Data Sharing	None	Spark / Hortonworks Stack	DUALIZED MEDICINE ARAGATAGATACTTCA GCGA

(2) Ride for DIPG

https://www.facebook.com/rideforDIPG/

Ride for DIPG

Daniel Home Find Friends 1 1 Create Page



 THE CURE STARTS NOW FOUNDATION
www.thecurestartsn.org
Nebraska

RideForDIPG.org

Ride for DIPG · Medical Research · Pediatrics

Donate Now Liked Message ...

Timeline About Photos Reviews More

Medical Research · Omaha, Nebraska
5.0 ★★★★★

Status Photo / Video

HUMANS OF NEW YORK

Pediatric Cancer Series

in association with



Memorial Sloan Kettering
Cancer Center

Thanks

Advanced Analytics

- ▶ Dan Blezek
- ▶ Yaxiong Lin
- ▶ Paul Bleimeyer

Natural Language Processing

Vinod Kaggal, Josh Pankratz,
Sean Murphy, Pradip Kanjamala.

UDP

Mat Raveling, Brian Brownlow, Bob Domnick

Bioinformatics Systems

- ▶ Iain Horton
- ▶ Patrick Duffy
- ▶ Mike Meiners
- ▶ David Rider
- ▶ Matt Bockol
- ▶ Mike Kalembach
- ▶ Greg Dougherty
- ▶ David Mead

Adam Team!

Michael Heuer

Bioinformatics Core

- ▶ JP Koche
- ▶ Steve Hart
- ▶ Raymond Moore
- ▶ Mike Zimmerman
- ▶ Dan O'Brien
- ▶ Saurabh Baheti

Advanced Analytics and Infrastructure Support

- ▶ Jason Ross

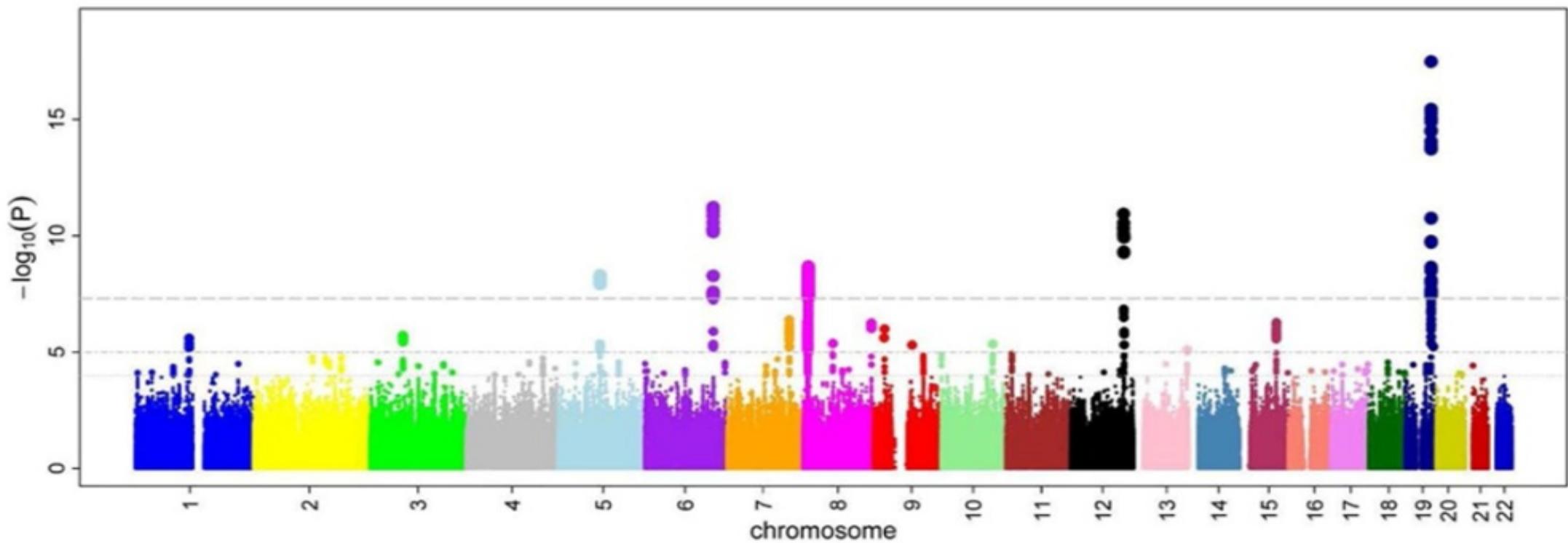
Example Personalized Medicine Case

- ▶ Jesse Shumaker
- ▶ Giselle Sholler
- ▶ Jeffry Bond



Data (!Hypothesis) Driven Discovery

What we do today – collect data to answer a question (GWAS):

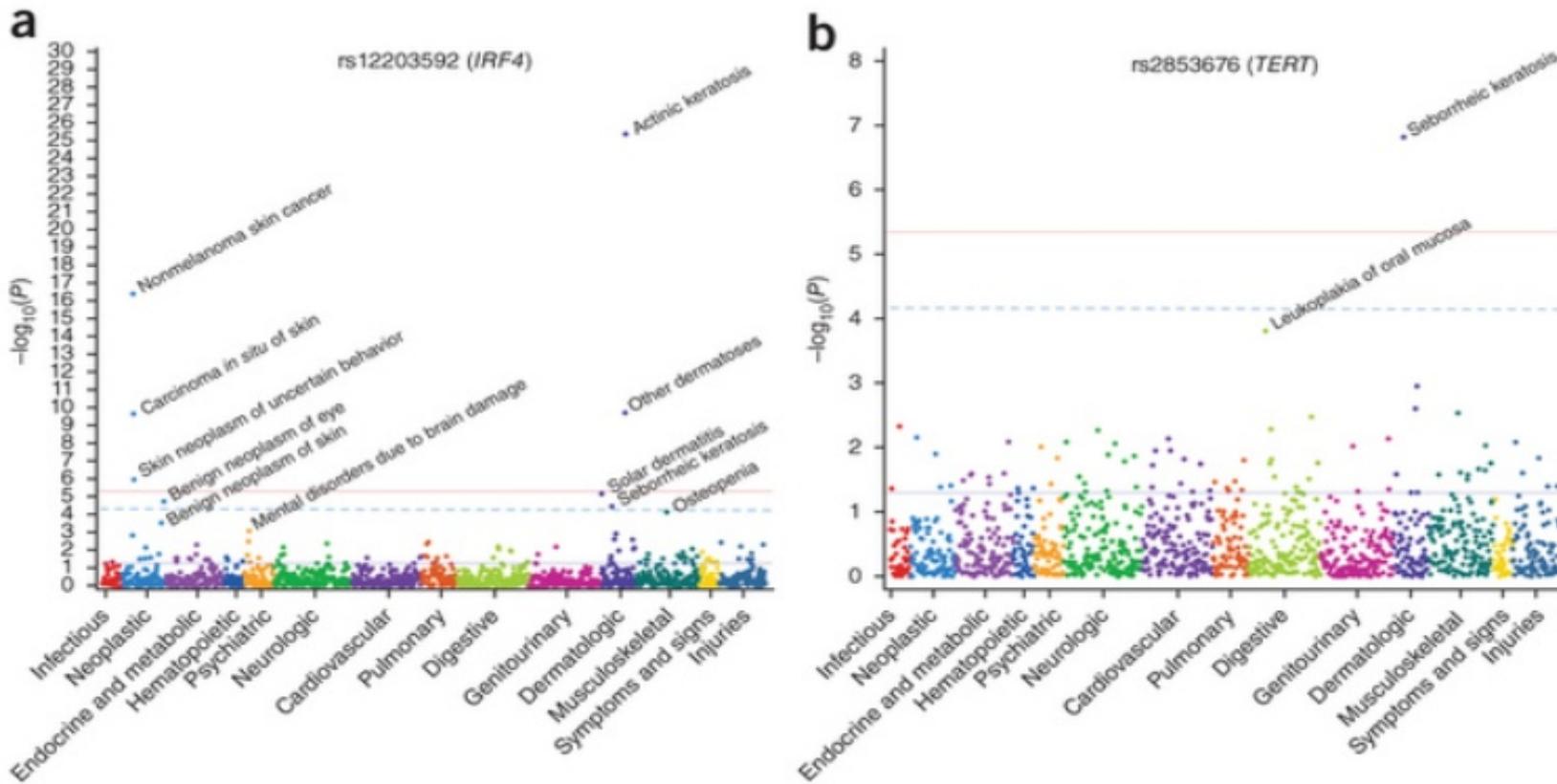


An illustration of a [Manhattan plot](#) depicting several strongly associated risk loci. Each dot represents a [SNP](#), with the X-axis showing genomic location and Y-axis showing [association level](#). This example is taken from a GWA study investigating [microcirculation](#), so the tops indicate genetic variants that more often are found in individuals with constrictions in small blood vessels.¹¹



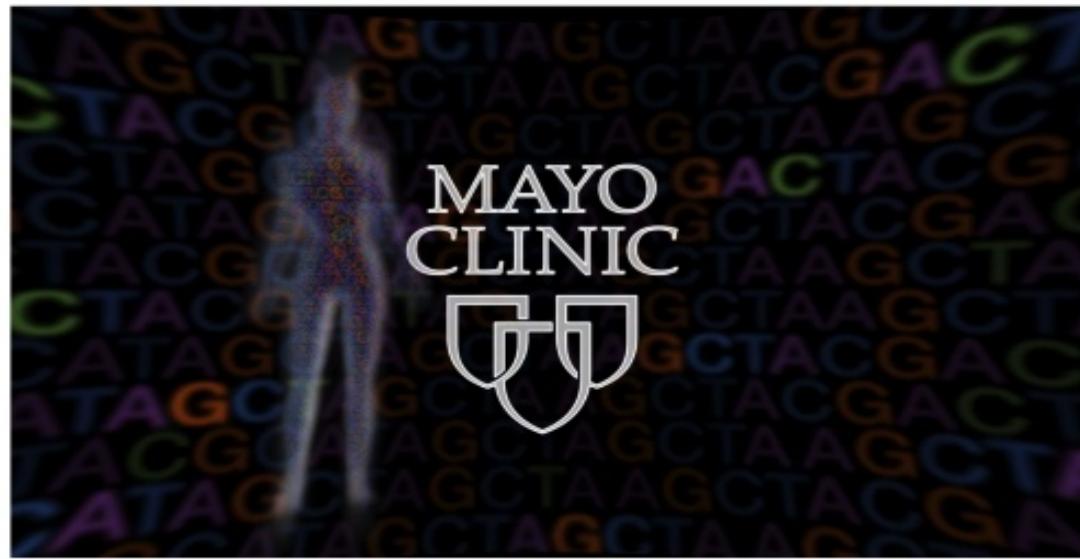
Data (!Hypothesis) Driven Discovery

What we want to do – have the data to answer a multitude of questions (PheWAS):



An illustration of a [Manhattan plot](#) depicting several strongly associated risk variants for a variety of diseases. Each dot represents a [SNP](#), with the X-axis showing conditions and Y-axis showing [association level](#).





Center for INDIVIDUALIZED MEDICINE





■ **Figure 2.** Example of a Clinical Note

Patient Information		Date: 10/06/2004		Time: 10:00 AM		Room: 101	
File #		Name:		Phone:		Fax:	
100-123456		Hurt, John S.		(404) 555-1234		(404) 555-1234	
Address:		City:		State:		Zip:	
123 Main Street		Atlanta, GA		GA		30303	
City:		State:		Zip:			
Phone:		Fax:		Email:			
(404) 555-1234		(404) 555-1234		jshurt@pacifier.com			
Social Security:		SSN:		DOB:		Gender:	
123-45-6789		123-45-6789		01/01/1950		Male	
Employer:		Occupation:		Employment Status:		Employer Address:	
None		None		None		None	
Primary Doctor:		Referring Doctor:		Other Doctor:		Other Doctor:	
None		None		None		None	
Medical Record #:		Patient Name:		Provider Name:		Last Visit:	
100-123456		Hurt, John S.		Dr. Mark E. Smith		10/06/2004	
Visit Date:		First Name:		Last Name:		Visit Type:	
10/06/2004		John S.		Hurt		New Patient	
Visit Reason:		Problem:		Diagnosis:		Treatment:	
None		None		None		None	
Initial Complaints:		History of Present Illness:		Physical Exam:		Diagnostic Test:	
None		None		None		None	
Chief Complaint and Purpose of Visit:		History & Test Note:		Treatment:		Plan:	
None		None		None		None	
History of Present Illness:		Physical Exam:		Diagnostic Test:		Plan:	
1. Elevated PSA:		None		None		None	
He has had PSA values greater than 7.0 ng/ml for a couple of years and prostate values somewhat proportionately emerged. Last check he had PSA over 7.0 with a prostate value of 34 cc which is significantly larger than his previous prostate size and was about twice as large than the reference suggested range. No test can be thought, nothing has been changed or done on an ultrasound and therefore would not feel that there were certain reasons for this. The patient stated that he physician's office concerned with that and just had to keep track of things closely at this time given by. He has no more testing done.		None		None		None	
2. Urinary difficulties:		None		None		None	
He has had difficulty with urination. It was recognized that he did have an ultrasound done. Because of that, we re-admitted him for a follow-up appointment in early October. He has had no subsequent complaints similar to what he had in the past year. Because of this additional studies had been done, which included another ultrasound, all of which were basically unchanged.		None		None		None	
3. Hearing Loss:		None		None		None	
Chronic problem, seems to be fairly stable.		None		None		None	
4. Abdominal pain:		None		None		None	
He has had fairly typical lower abdominal cramping. This seems to occur most often when he has eaten later than the recommended time for him. It does not really seem to make much difference on location. Some questions were raised whether this might be some form of food poisoning symptom but the pain is rather chronic for something. He gets a very little better with the provider of the oral anti-nauseants, which is a good water status. Sometimes he has to cough up "belches" but can have acid reflux.		None		None		None	
5. Headaches:		None		None		None	
He has had a few headaches who wakes a little or two a day at a very brief pace (approximately 5 miles per hour). When he is out along history would at this point such as pushing a mower, etc. No greater than half an hour he usually feels the leg fatigue. In a very best case he can get back to his activities. He has really no other complaints suggesting chronic problems in the lower extremities.		None		None		None	
6. Back pain:		None		None		None	
He has had a few episodes where he gets a sharp or a more or other rapidly to get fatigued and he actually gets some true vertigo-type conditions for an instant. He has been concerned by his local physician that this is related to aging of the ear and the start of Meniere's disease for benign paroxysmal vertigo.		None		None		None	
7. Heartburn:		None		None		None	
Last colonoscopy was in March of 1998. Last PSA checked during the past calendar year. His chest X-ray is clear.		None		None		None	
REVIEWED INFORMATION WITH PATIENT AS NOTED ON THE CURRENT VISIT INFORMATION FORM DATED 22 MAR 1998 AND ON THE PATIENT FAMILY HISTORY FORM DATED 01-MAR-1998.							
CURRENT MEDICATIONS:							
Loprin 10mg daily ASA 325mg daily Medrol 25mg/day daily on demand							
TOTAL SIGNS:							
Height: 176.0 cm, Weight: 76.0 kg, BSA: 1.95 m ² , DBM: 24.703 Hb/Hct							

This is an ambulatory care note for a nonexistent test patient. For this study, all available inpatient and outpatient notes were used.

