PARKER INSTITUTE
for CANCER IMMUNOTHERAPY

Advanced correlative assays: Challenges and Opportunities

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OUR MISSION

To accelerate the ***development of breakthrough immune therapies*** to turn cancer into a ***curable disease***.

The PICI Model is centered around collaboration

7 Research Institutions

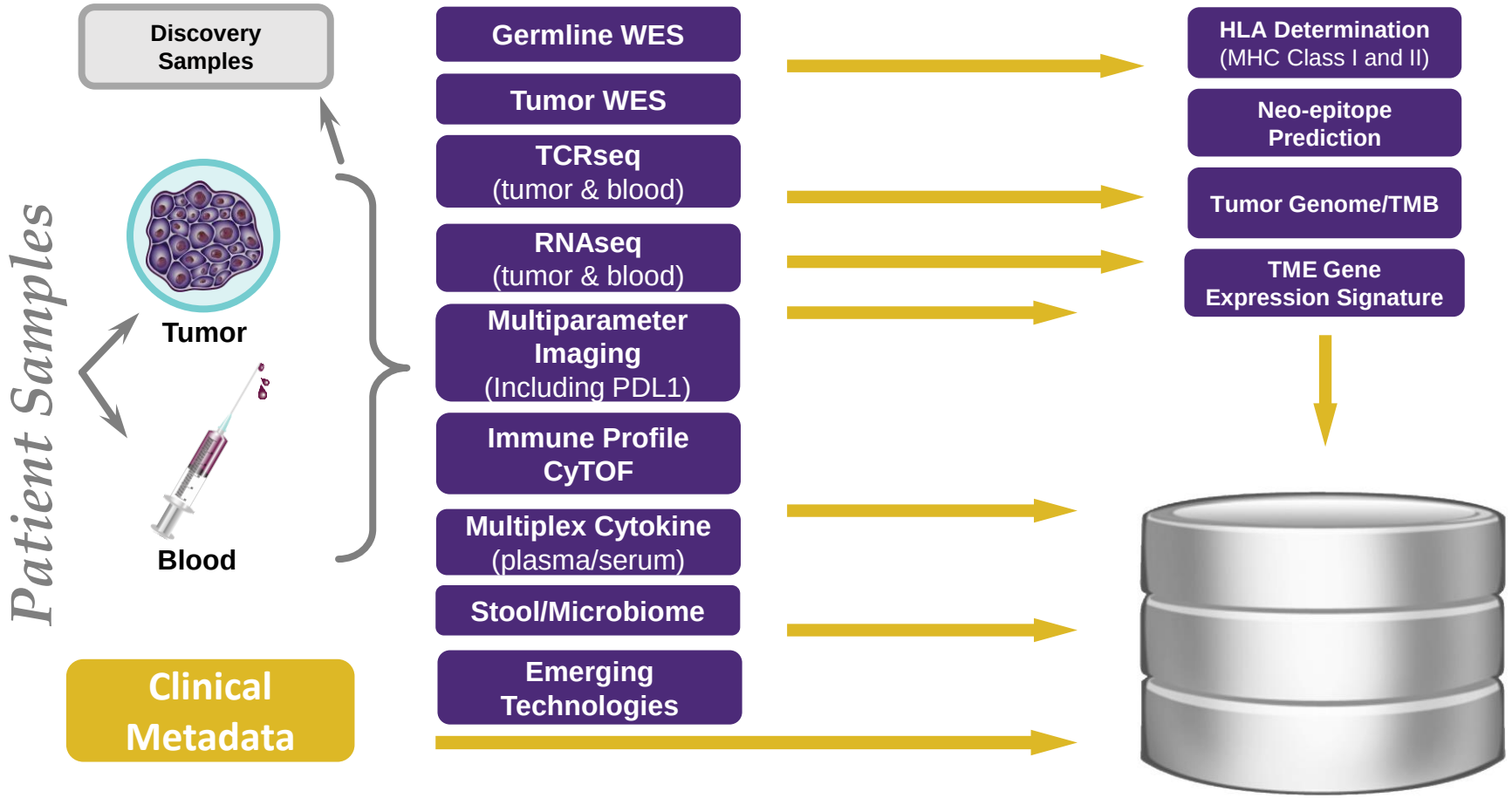
300+ Nation's Top Researchers

60+ Laboratories

40+ Industry & Nonprofit Collaborations

- Founded by Sean Parker with $250 million donation
- Launched in April 2016
- Currently ~50 employees in San Francisco, CA
- Activities span clinical development, translational research, bioinformatics, public outreach, and enabling collaborations

More measurements mean more opportunities for understanding

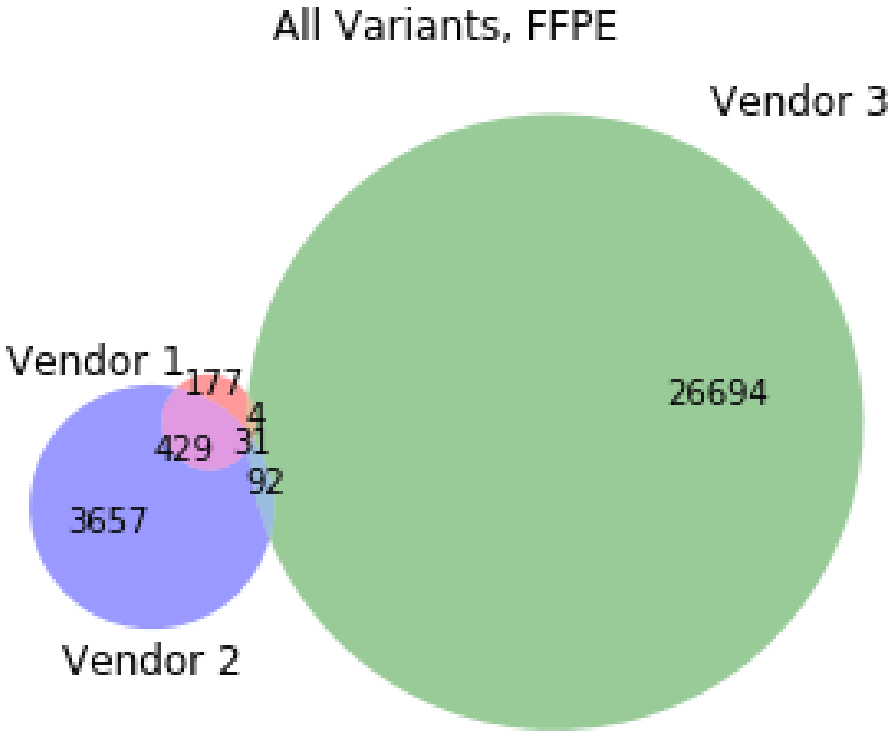


What are the challenges in implementing this idea?

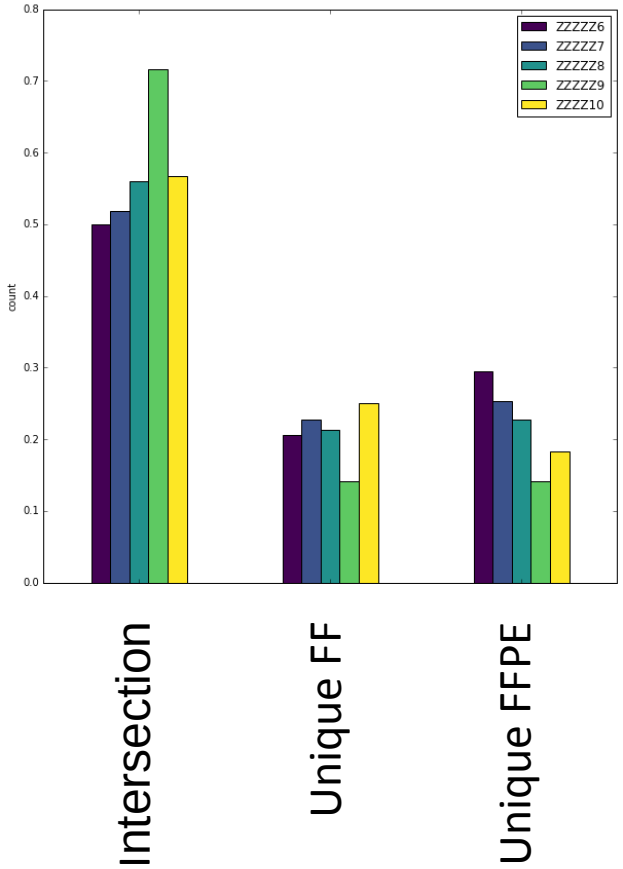
- Technology
- Logistics
- Analysis


Technology

Variant calling is far from being a “done deal”



Concordance between Fresh-frozen and FFPE varies by vendor



We are constantly working to be at the forefront of assay technology

- Flow cytometry
  - 31-marker CyTOF panel with space for drop-ins
  - Packaged by Fluidigm and available to investigators
  - Developing population specific panels for BD's FACS Symphony
  - Computational infrastructure to analyze datasets with thousands of flow files
- Making significant efforts to implement advanced imaging technologies
  - Vectra, MIBI, CODEX
- Single-cell sequencing
  - Working to harmonize dissociation protocols

Logistics

“Amateurs talk strategy. Professionals talk logistics.”

Logistics are where aspirations meet reality

- Are these samples available in the clinic?
  - Fresh dissociation is the main bottleneck for scRNAseq
  - Obtaining fresh frozen samples is still a challenge

- Is assay X worth doing?
  - High bar to clear due to sample availability

- Can anybody run my samples?
  - The fact that it can technically be done, does not mean you will find a way to do it in the real world

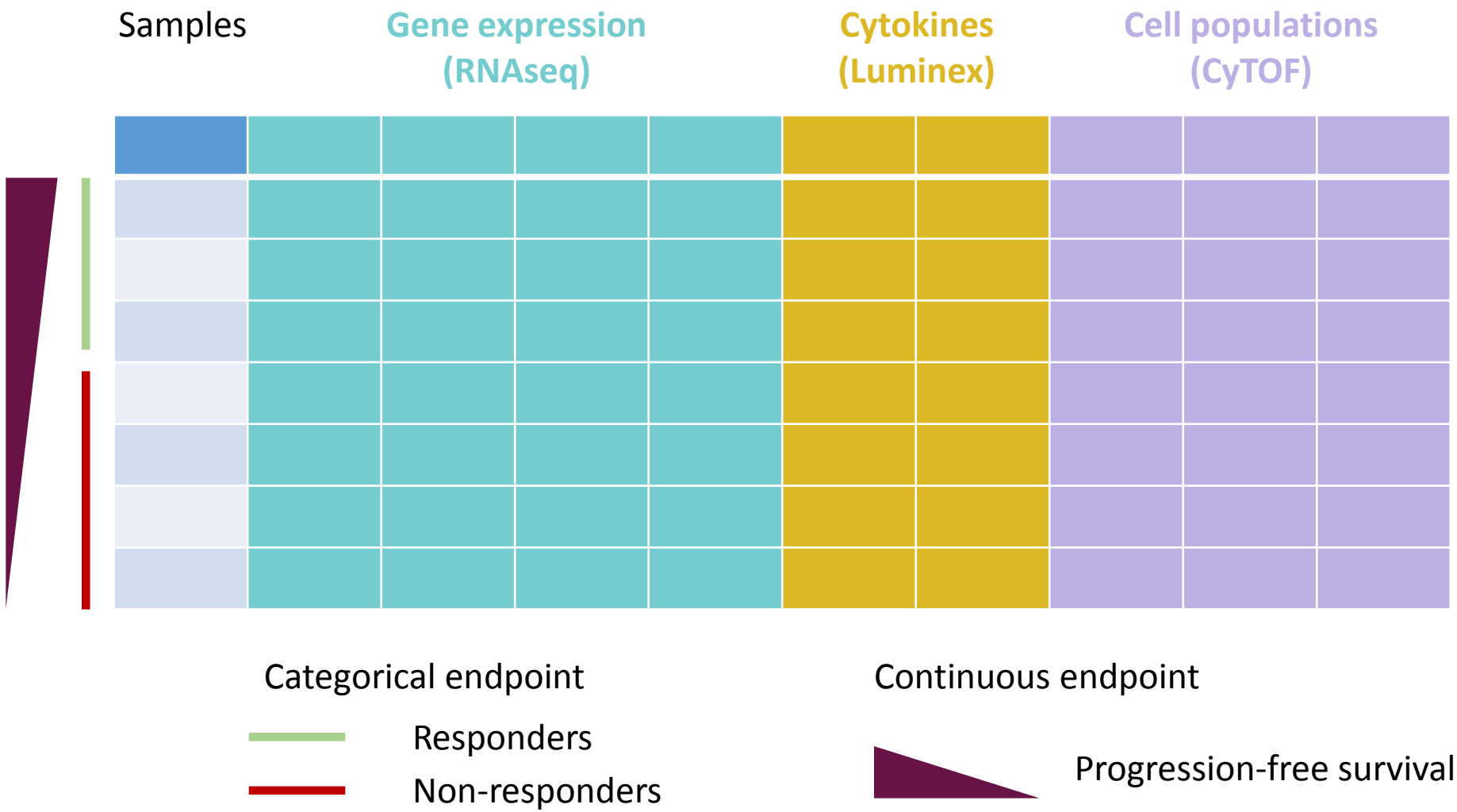
Being smart about aliquots is essential to run multiple assays

Sample	Viability (%)	Total PBMC (M/ml)	# 5M aliquots	# dry pellet (2M)	# 2M aliquots	Viability Post-thaw (%)
1	98.1	0.94	2	3	15	95.8
2	95.8	1.19	2	3	15	93.4
3	98.8	1.12	2	3	14	94.5
4	97.4	1.36	2	3	15	97.9
5	98.6	1.87	2	3	10	97.6

- Centralized biobanking with a commercial partner
- Broad consent protocol

Analysis

Each sample is annotated with multiple molecular measurements (features)



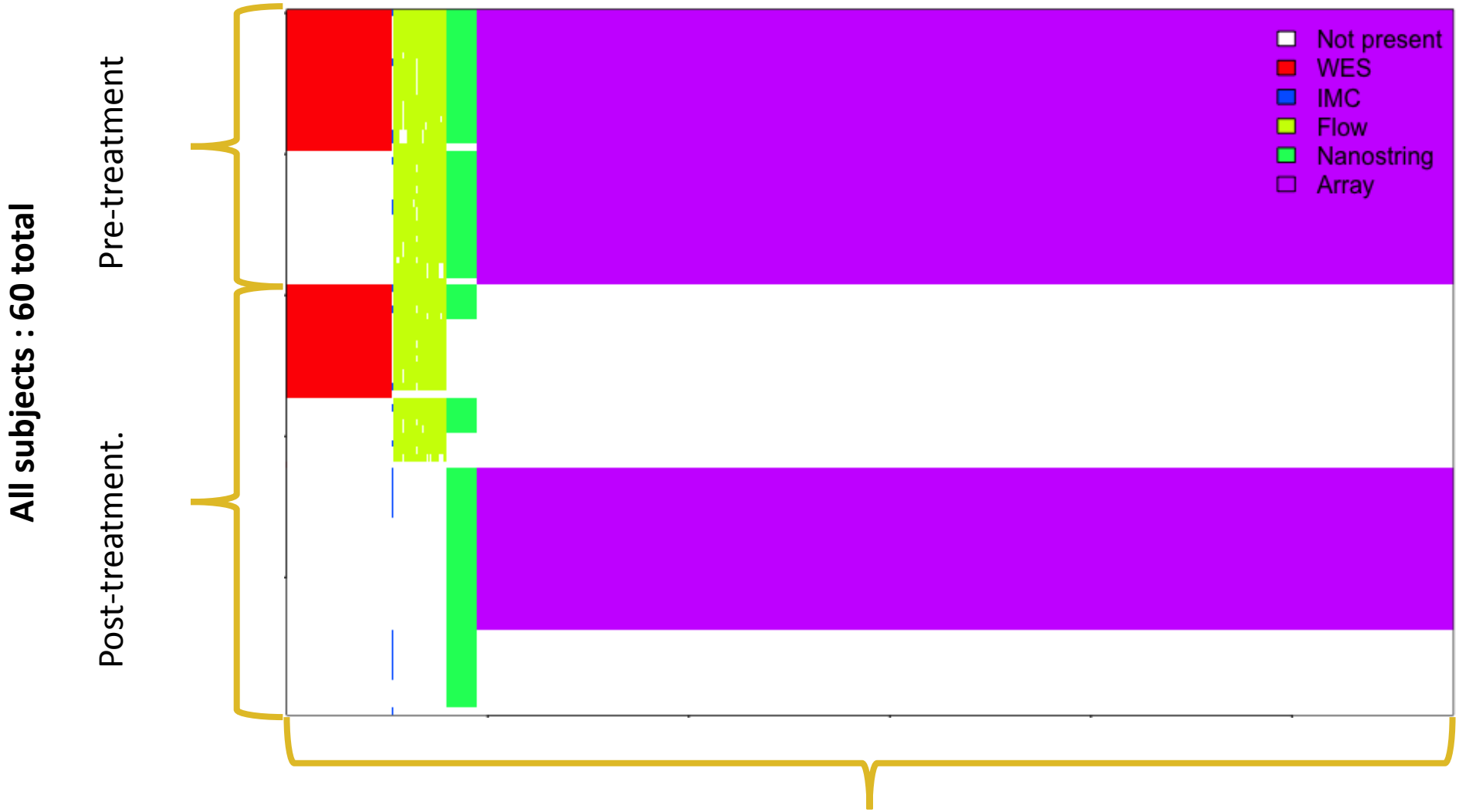
In order to get to that matrix you need broad computational expertise

- Central computational biology team with expertise across multiple datatypes

Fluorescence flow cytometry	Whole Exome Sequencing	Luminex
CyTOF	TCRseq	
RNAseq (bulk and single-cell)	VECTRA	
ATACseq (bulk and single-cell)	Imaging Mass Cytometry	

- Take best approaches when they exist
- Develop them when they are needed
  - https://github.com/ParkerICI

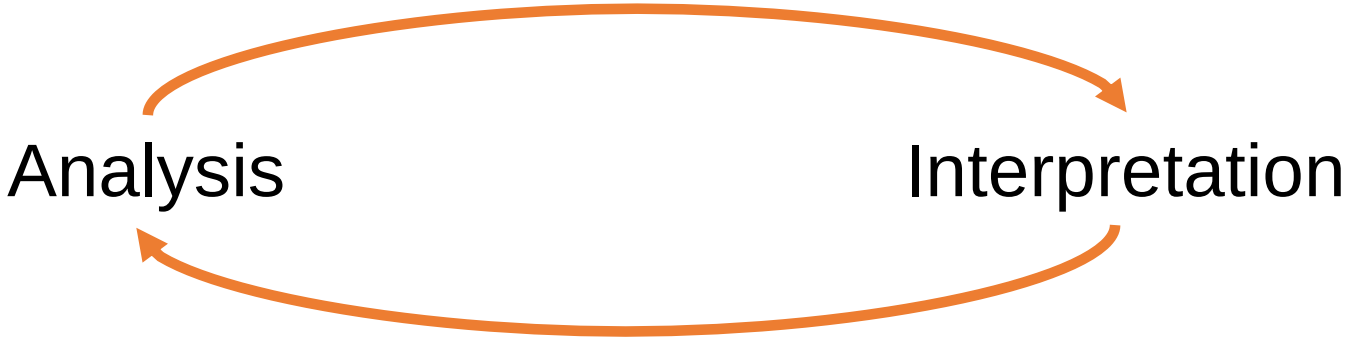
No matter what, real-world data is incomplete



This is not a Deep learning problem

- The output is not clearly defined
  - What is *response*?
  - Collecting good molecular data is harder than collecting good clinical data
- Datasets are small (n << p) and incomplete
- The encoding is ambiguous
  - What is the best way to translate assay data into numeric features?
- Deep Learning can help solve specific technical problems
  - Examples include variant calling, image segmentation, tissue annotation

The role of computational methods is to help human reasoning



- Have people that understand biology
- Close collaboration with investigators

- Visualization methods
- Queryable databases

What can we do with “more data”

- Increase the amount of “reference knowledge”
  - Look at how individuals differ from the reference
  - Increase statistical power

- Contextualize
  - Have we observed this signal before in other contexts?

- Ask questions we can’t anticipate today

Acknolwedgments

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