Immune Health®

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Immune Health® - Mission and Vision

- ## Mission
  - Central hub for performing, curating, and analyzing patient immune assays, and driving new discoveries
    - Apply cutting-edge, multiplexed, real-time profiling and integrated data analysis of patient samples
    - Translate these data into quantitative, actionable immune health information
    - Deliver these results to discovery and clinical care teams
    - Help develop diagnostic and predictive readouts and understand how to use therapies that modulate immune response

- ## Vision
  - Deploy routine human immune profiling for real-time clinical decision making – impact across medical disciplines
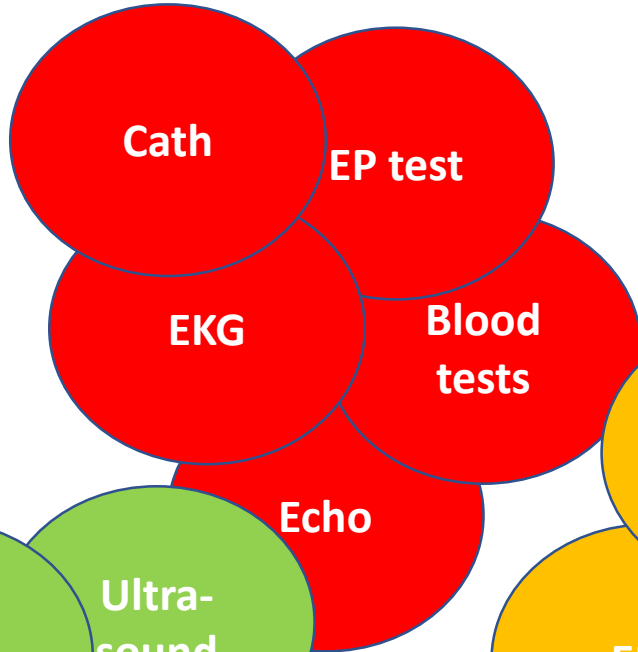
(Remember how 20 years ago we started sequencing patient tumors and reported back mutational data to clinicians and researchers for them to figure it out....?)
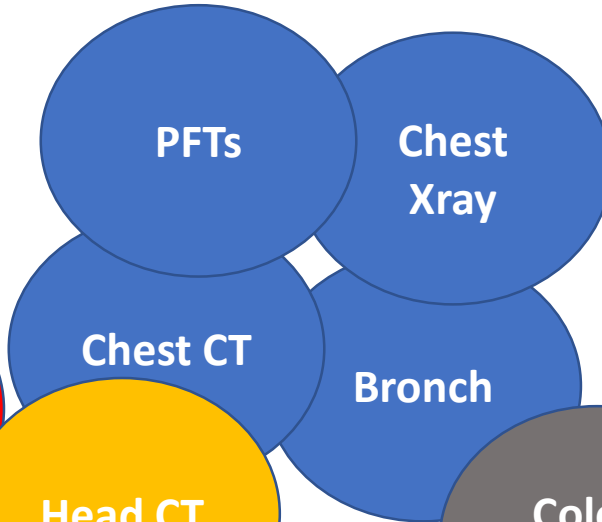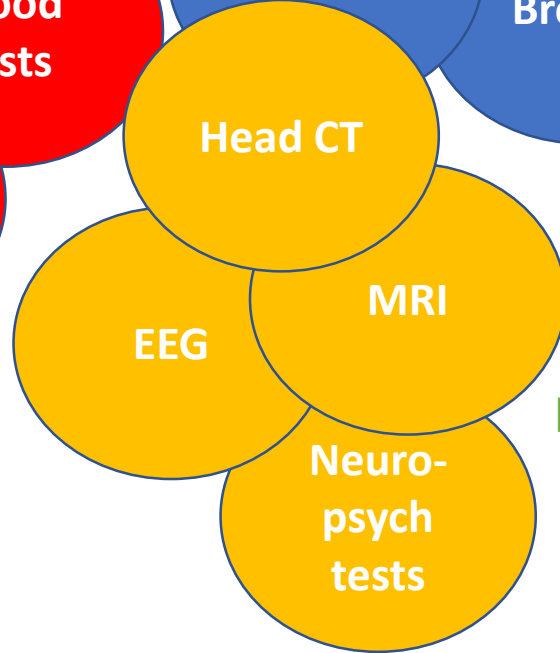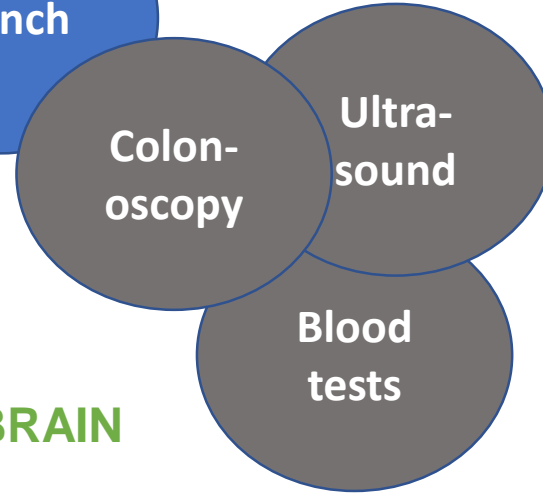
(It's like that except immunology)

IMMUNE HEALTH®
Penn Medicine

Current approach in the clinic

Immune Health® - work flow

Hypotheses → Cohorts — Clinical teams

Processing Banking

Samples → Hospital Labs and Tumor Mutational Profiling (already CLIA)

Assay Development

Assays

Other research 'Omics (if CLIA)

Cellular
RNA
DNA
Protein → if/when CLIA → EMR (Immune Health Report)
Metabolites   *Clinical immune boards*
Tissue
Functional

Curated clinical metadata → Database

→ Analytics

De-identified or Identified (if consent)

Patient Care

Research/Discovery → **Pilot** → **Validate** → **Implement CLIA test**
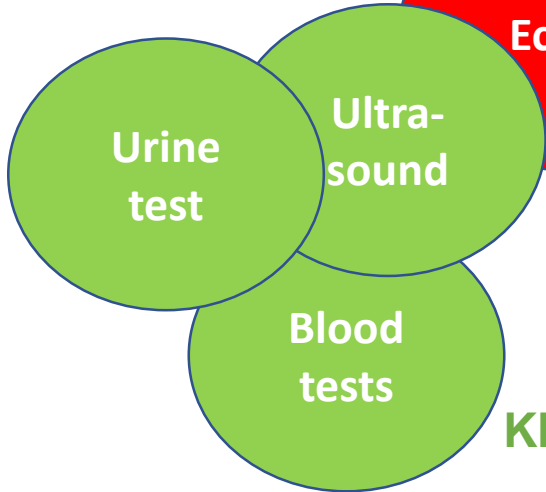
Immune Health® - three dimensions of data

Immune Health Report

2020 Digital Innovation
Enterprise Award

Philadelphia Alliance
for Capital and Technologies (PACT)

Immune Health – Projects and Clinical Cohorts

Projects	Cancer	Infection	Neuro	Autoimmunity	Cardiovascular
Cohorts	Checkpoint CART BMT	COVID Sepsis	MS	IBD	CHF Acute Coronary Syndromes

Options

Every patient	**Precision defined cohorts**	**Pre/post SOC interventions**	**Clinical trial subjects**
Clinically defined	Responders Exceptional responders Adverse events Poor outcome Molecularly defined Otherwise defined (e.g. diet)	Cohort plus: • Matched disease controls • Matched healthy	'Base module' for every trial

Dashboard of Projects and Prospective Cohorts

Project	Cohort	Status						Clinical Impact
		Dev.	Accrue.	Data Col.	Analysis	Pub.		
COVID-19	• Acute COVID-19							
	• Long term COVID-19							
	• COVID-19 vaccination in healthy subjects							
	• I-SPY							
Checkpoint blockade	• Melanoma, neoadjuvant anti-PD-1							
	• Melanoma, anti-PD-1, COVID-19 vaccine							
Lymphoma	• Lymphoma patients receiving the COVID-19 vaccine							
Multiple Sclerosis	• Anti-CD20 + COVID vaccine pilot							
	• Anti-CD20, fingolimod, IFNb							
Influenza	• Pediatric, childhood vaccines							
	• IBD, flu vaccine							
	• Melanoma, flu vaccine							

Sample traffic at Penn's Immune Health Processing Unit
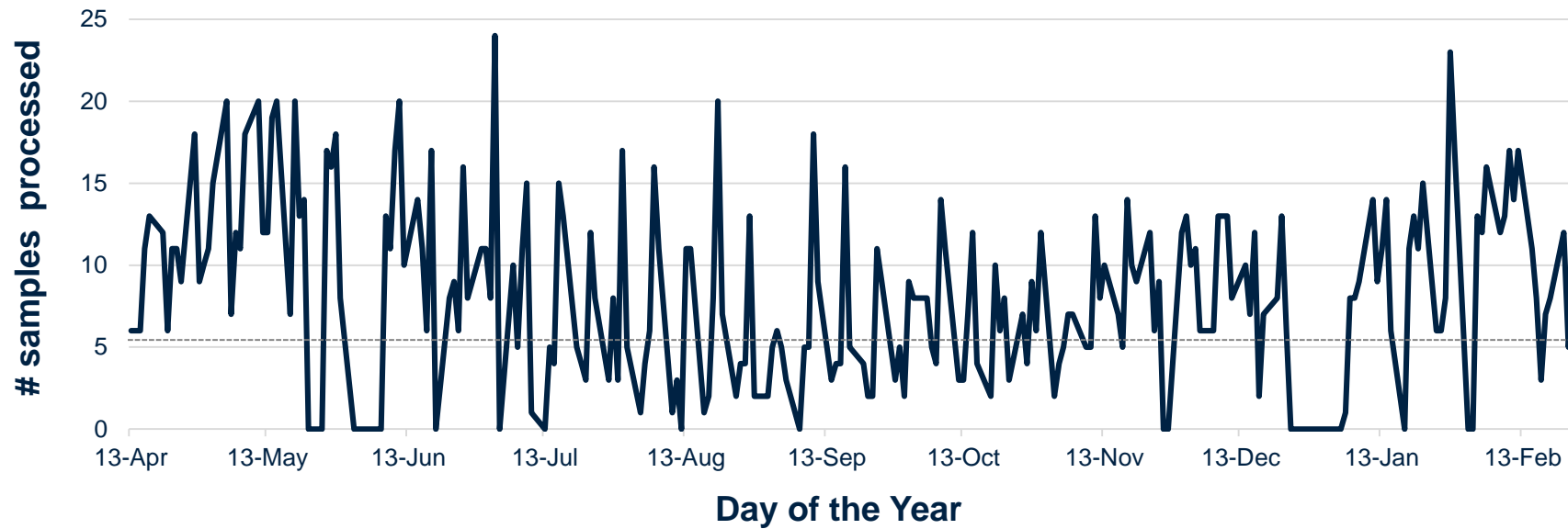
Processed to Date:
1,356 unique subjects
2,270 total samples
~16,000 tubes of blood

Immune Health Processing Unit

▸ **Allie Greenplate, IH Asso Dir**

▸ Sharon Adamski

▸ Kurt D'Andrea

▸ Ajinkya Pattekar

▸ Scott Korte

▸ Mandy Hicks

▸ Jake Hamilton

Philadelphia Inquirer

COVID-19 IMMUNE PROFILING

160 acute/recovered COVID-19 Patients
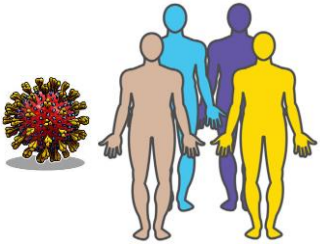
DEEP IMMUNE PROFILING
"PIPELINE"

→ **165,000** individual immune data points
  +1000s of clinical data points
→ **8M** immune-clinical pairwise comparisons
→ **27B** immune–immune pairwise comparisons

Dimensionality Reduction
(extensive computational analysis)
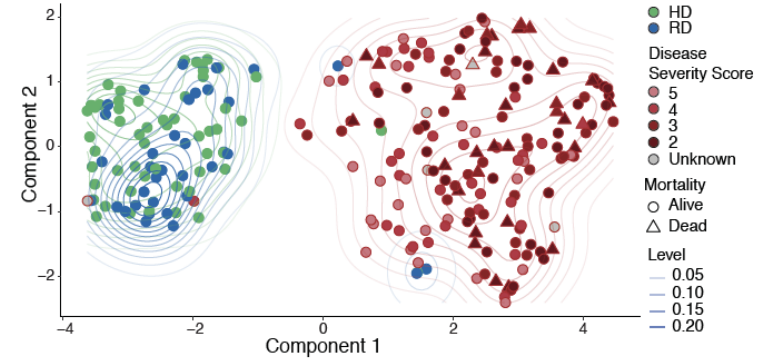
Mapping Immune Features
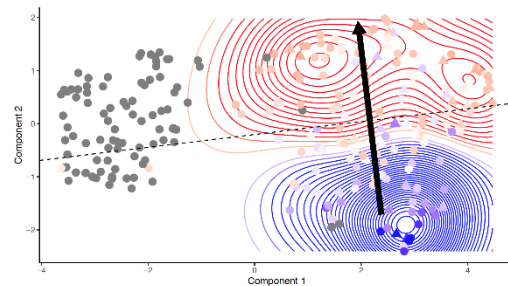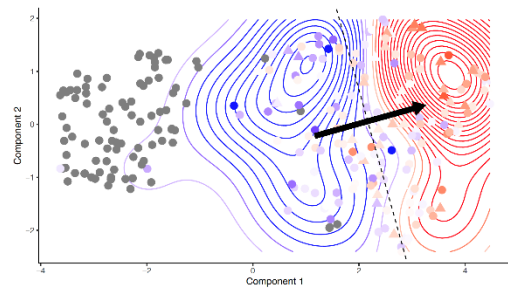
Temporal Changes
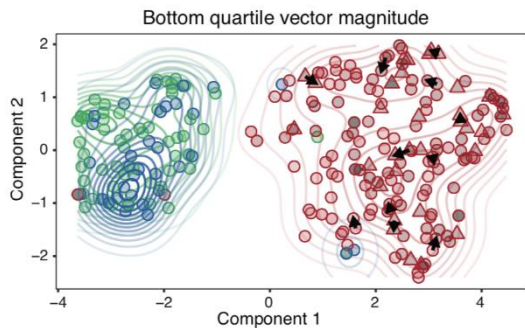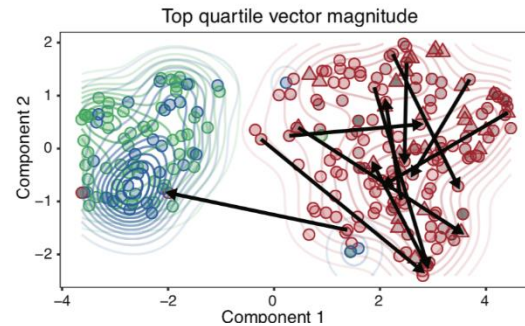
Applying an Immune Health strategy to COVID-19:

○ HETEROGENEITY IN IMMUNE RESPONSES

○ IMMUNE PROFILE LINKED TO CLINICAL DISEASE SUBTYPES

○ IDENTIFIES *IMMUNOLOGICAL* SUBGROUPS OF PATIENTS WHO MAY BENEFIT FROM DIFFERENT TREATMENTS

○ A ROADMAP FOR ANALYSIS OF VACCINE RESPONSES

Mathew et al, *Science*, 2020

SARS-CoV2 VACCINATION IN COVID-19 NAÏVE VS COVID-19 RECOVERED SUBJECTS

SARS-CoV2 mRNA vaccine

Long term immunity

d0
1⁰ Vac.

d15

d21
2⁰ Vac.

d28
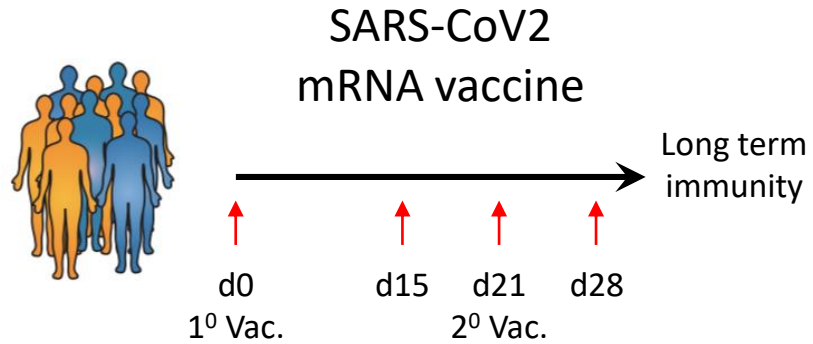
Two groups *prospectively* collected
- COVID Naive
- Previous COVID

IMMUNE HEALTH PROJECT

High Dimensional Cytometry
Serology
Ag-spec. Memory B cell analysis
Ag-spec. CD4/CD8 T cells
scRNA-seq
Serum cytokines

Integrated Analysis
UMAP etc
Long-term immunity
Side effects
Demographics
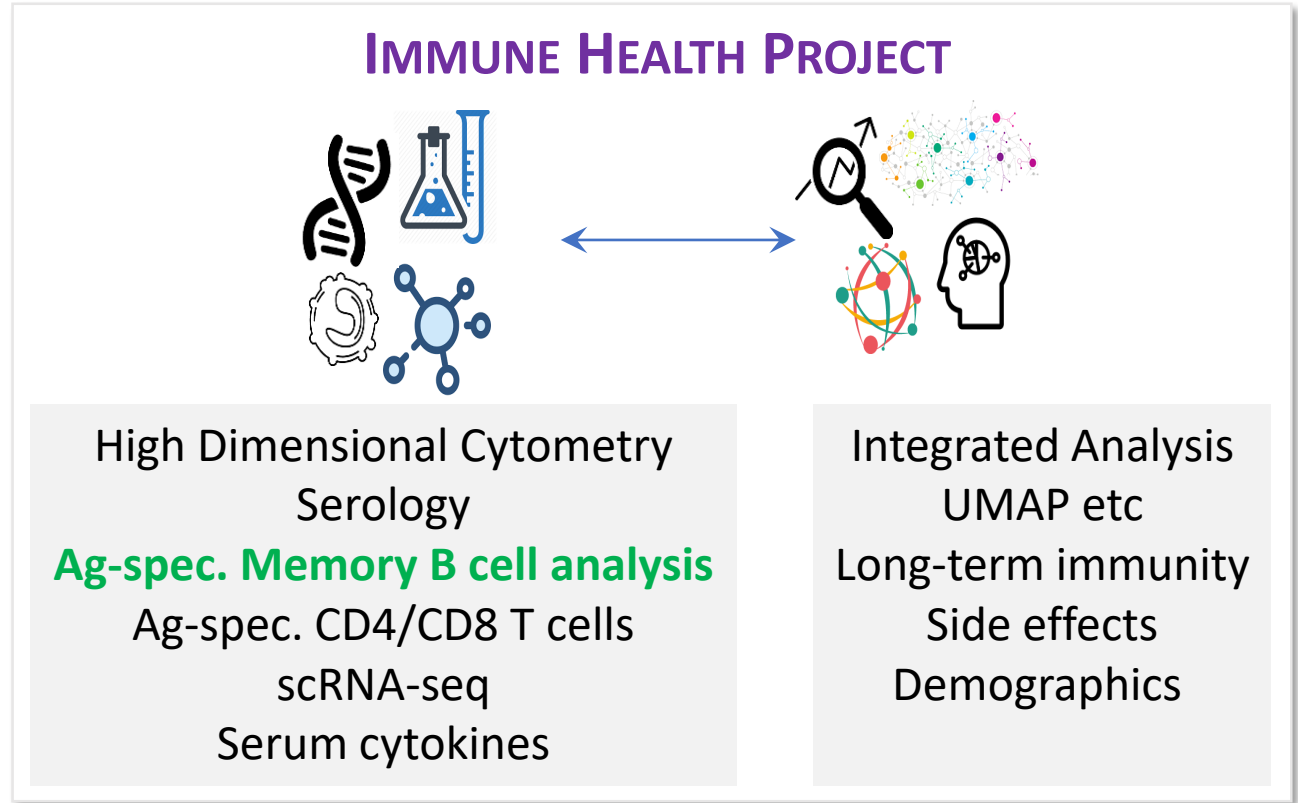
Allie Greenplate Rishi Goel

Divij Mathew

Mark Painter

Sokratis Apostilidis

Oliva Kuthuru

Goel et al, *Science Immunol*, 2021

Time from idea to publication:
3.5 months

SARS-CoV2 VACCINATION
IN COVID-19 NAÏVE VS COVID-19 RECOVERED SUBJECTS
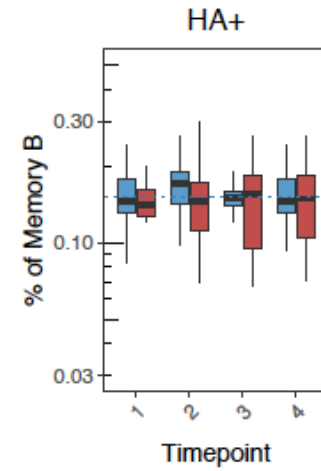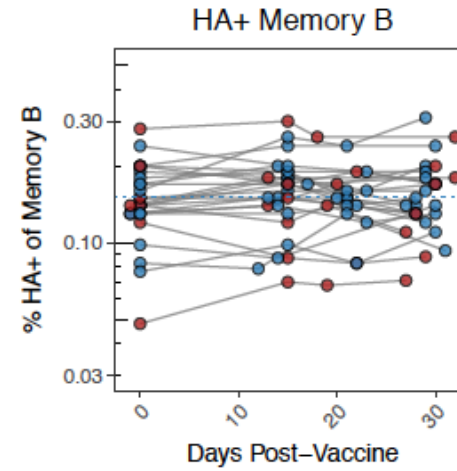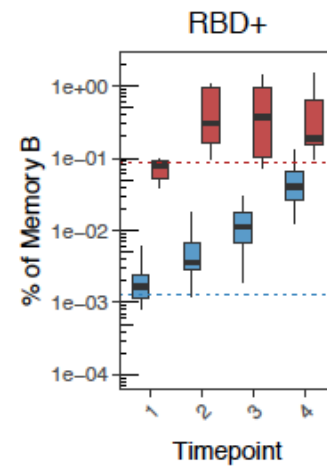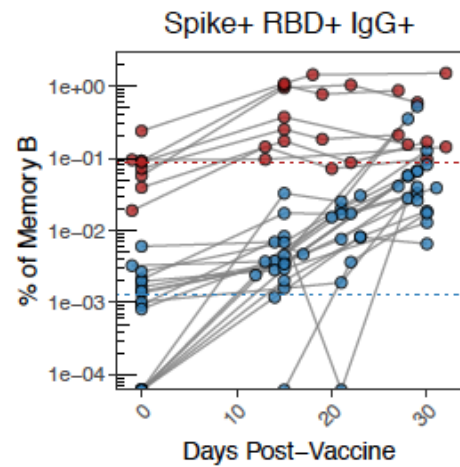
SARS-CoV2 Naive + mRNA Vaccine (n=17)
SARS-CoV2 Recovered (n=13)
SARS-CoV2 Recovered + mRNA Vaccine (n=8)

Goel et al, *Science Immunol*, 2021

METASTATIC MELANOMA PATIENTS RECEIVING PEMBROLIZUMAB

Huang AC et al, Nature 2017

Huang AC et al,
Nature Medicine 2019

Immune Health Institute !!
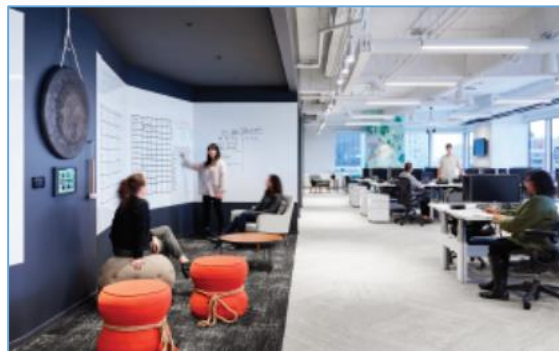
Artist rendering

SUMMARY: THE IMMUNE SYSTEM AS A "SENSORY" ORGAN
IMMUNE HEALTH® GAINS INSIGHTS INTO HEALTH/DISEASE FROM IMMUNE PROFILING

Nervous system

**Immune System:
Senses all tissues**
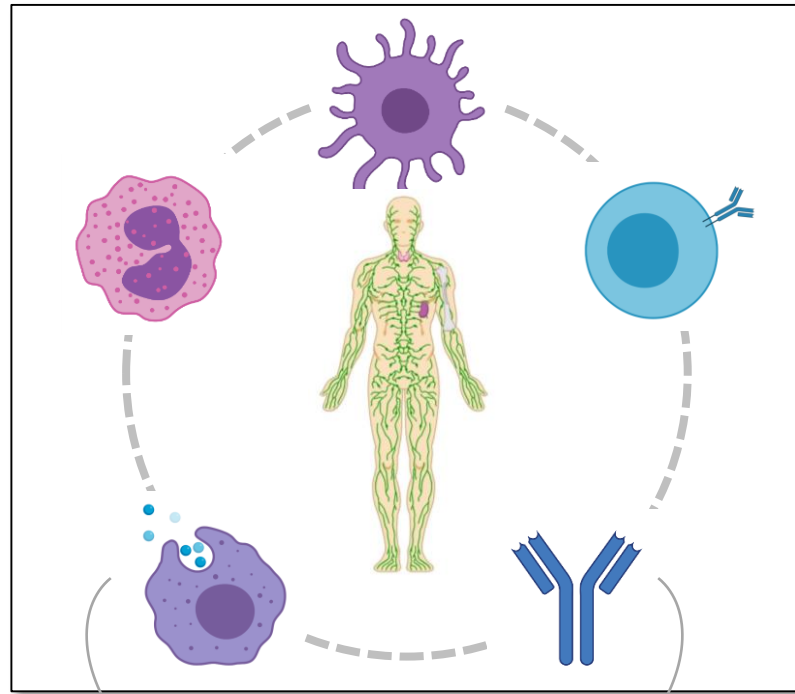
"Listening" to the Immune System

IMMUNE SIGNATURES IN:
- INFECTION, CANCER, AUTOIMMUNITY
- RECOVERY FROM SURGERY
- NEUROLOGY/PSYCHIATRY
- SLEEP DEPRIVATION
- PRE-ECLAMPSIA - OBGYN
- WESTERN DIET/OBESITY
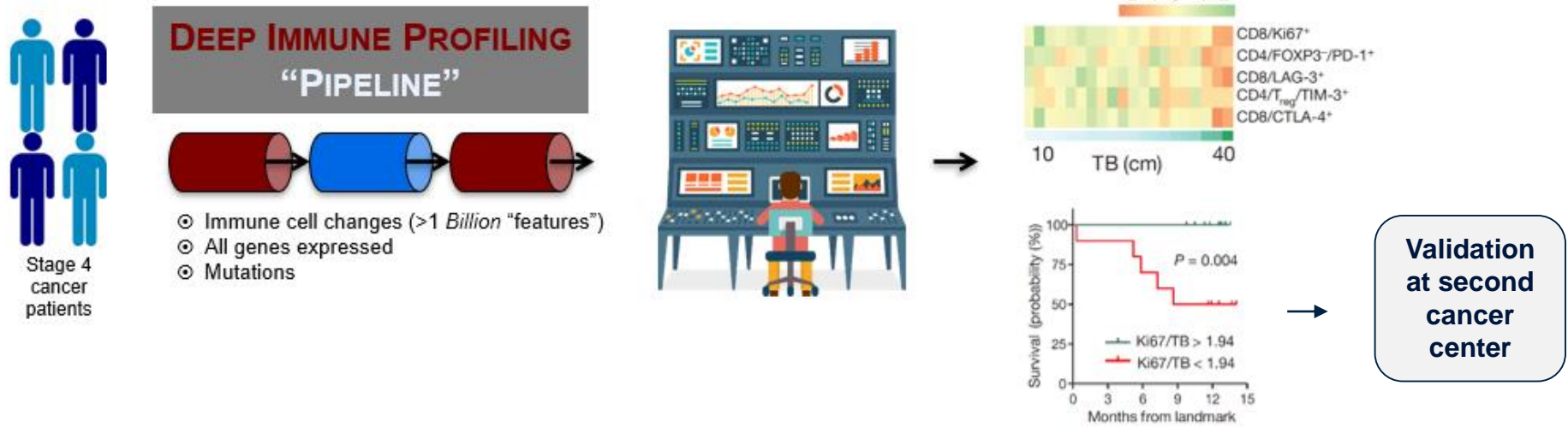- CARDIOVASCULAR DISEASE
- AGING

- EVERY HUMAN PERTURBATION CAN LEAD TO AN IMMUNE SIGNATURE

Immune Health® - Acknowledgements

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- **Pat Morin** – Admin IH Director
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- Ajinkya Pattekar
- Scott Korte
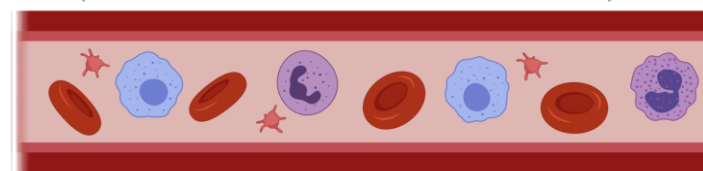- Mandy Hicks
- Jake Hamilton

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