



Penn Medicine

Immune Health®

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May 6, 2021



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



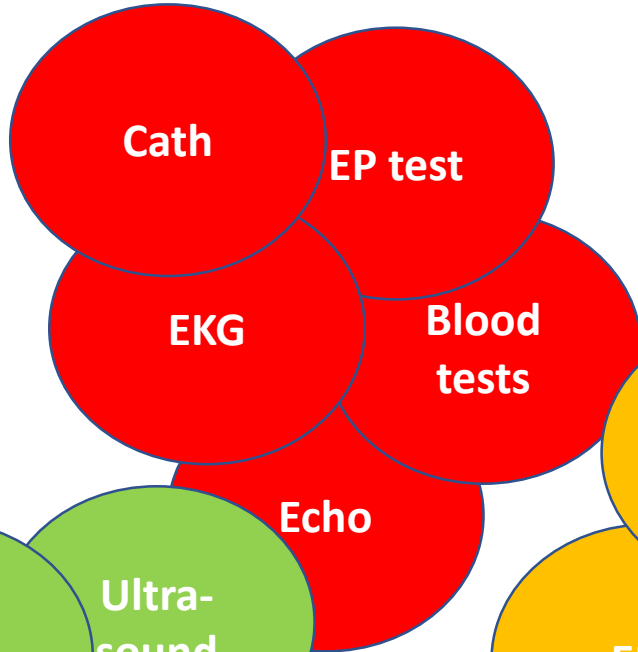
(Remember how 20 years ago we started sequencing patient tumors and reported back mutational data to clinicians and researchers for them to figure it out....?)

(It's like that except immunology)

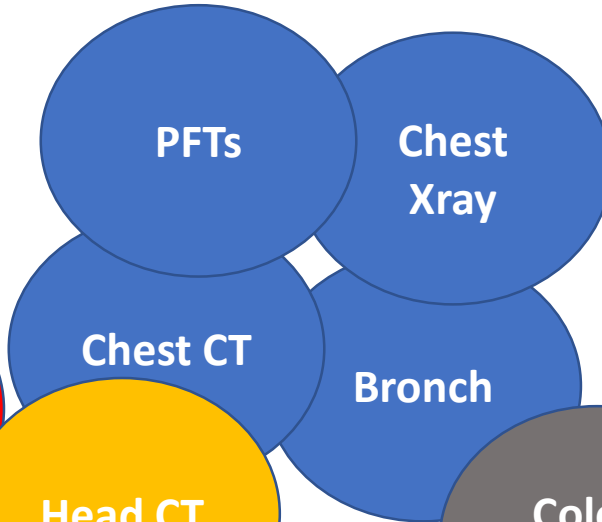


Current approach in the clinic

HEART



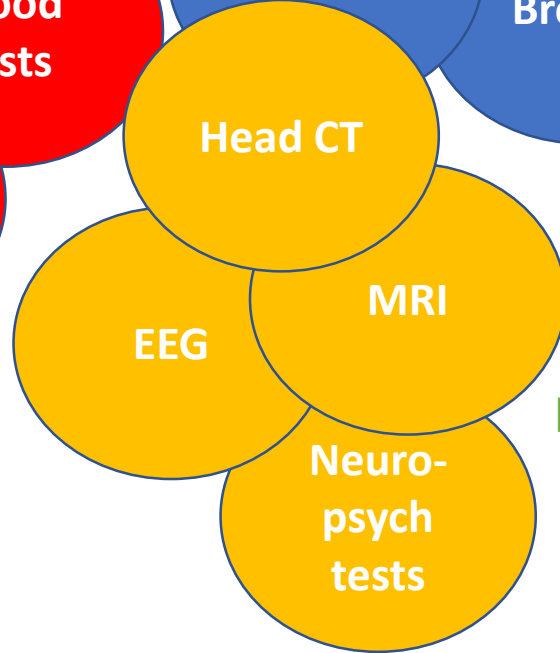
LUNG



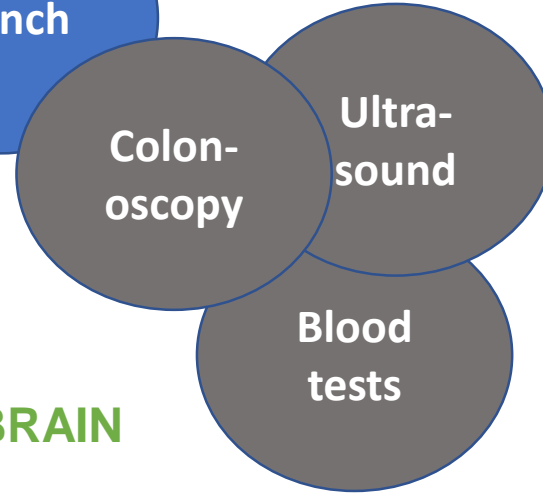
IMMUNE



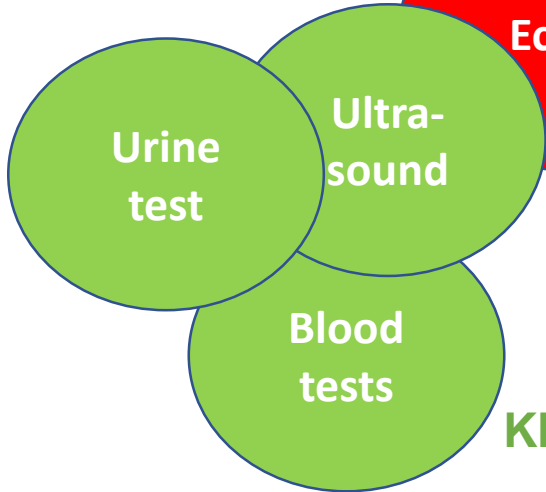
BRAIN



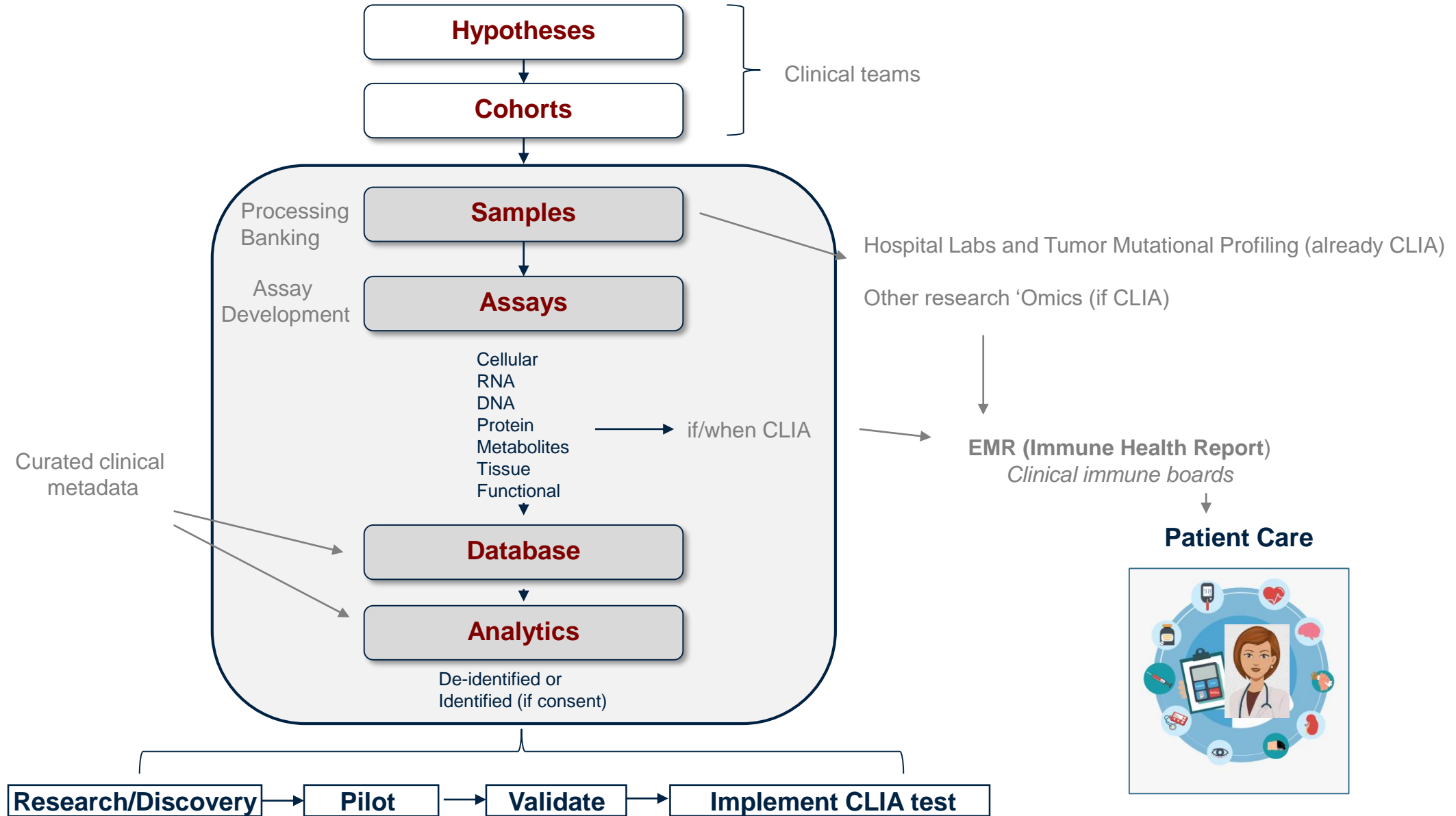
GI TRACT



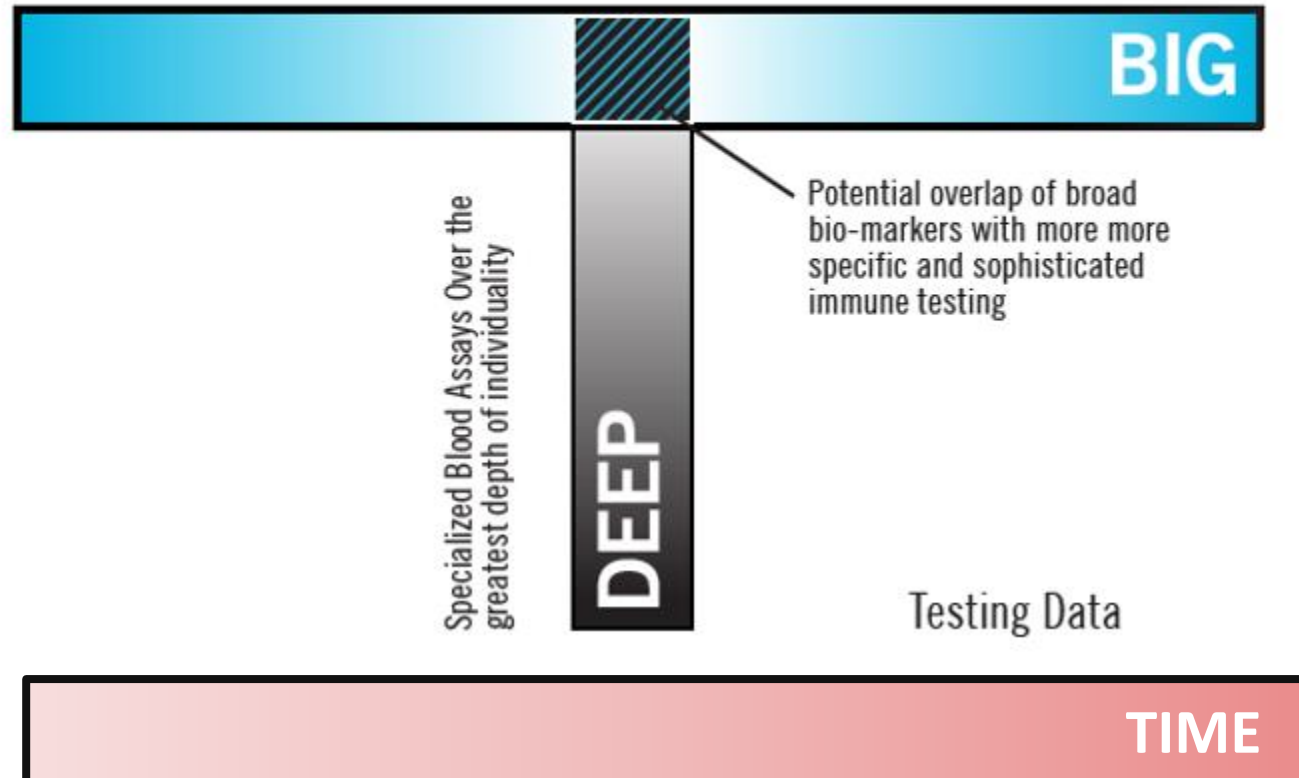
KIDNEY



Immune Health® - work flow



Immune Health® - three dimensions of data



Immune Health Report

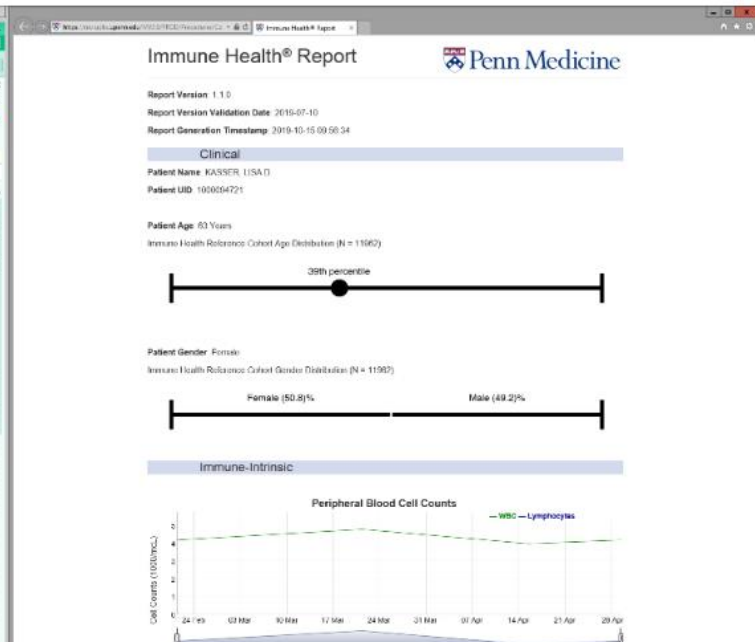
Production Application Server 39 - apicgw@PDA0017 - AFHERES - ANDREW RECH

Chart Review | Care Everywhere | Config | Document List | Search Results | Search Results | Medication | Care Everywhere | Individuals | Open Orders | Immune Health Report

Encounters | Lab | Imaging | Procedures | Cardiology | Medications | Other Orders | Precision Medicine | Epitopes | Labs | Notes | Media | LMS | Referrals | Misc Reports

Medications and orders also used in active treatment plans: ONCOLOGY SUPPORTIVE CARE PLAN

Date/Time	Test	Status	Scan Desc/Description	Encounter Type	Auth Provider
8/27/2020 08:12	HEMOGLOBIN BLOOD DRAW	Active - Future		Telephone	Thompson, JA
8/27/2020 07:34	AUTOMATED DIFF	Completed - Final result		Lab	Agarwal, Chk
8/27/2020 07:34	HEMATOCRIT - ELECT DIFF	Completed - Final result		Lab	Agarwal, Chk
8/27/2020 07:34	COMPLETE BUNEL METABOLIC PANEL	Completed - Final result		Lab	Agarwal, Chk
8/23/2020 11:15	CHLORINEL (HEMORR)	Active - Future		Telephone	Agarwal, Chk
8/27/2020 09:22	AUTOMATED DIFF	Completed - Final result		Lab	Wade, J EB
8/27/2020 09:22	HEMATOCRIT - ELECT DIFF	Completed - Final result		Lab	Wade, J EB
8/27/2020 09:22	COMPLETE BUNEL METABOLIC PANEL	Completed - Final result		Lab	Wade, J EB



2020 Digital Innovation Enterprise Award

Philadelphia Alliance for Capital and Technologies (PACT)

UPHS Links

ANDREW RECH Search

Open Orders Immune Health Report

Media LDAs Referrals Misc Reports

Position Add to Bookmarks

PD-L1 IHC

Show report for PS-19-0002907

Accession PS-19-0002907

Result

70116864 IHC

CPD Solid Tumor Panel Report

Show report for PD-19-0002171

Accession PS-19-0002907

COLLECTION DATE/TIME: 3/27/2019 13:43 EDT RECEIVED DATE/TIME: 3/28/2019 09:07 EDT PATHOLOGIST: Post, Frank MD Dr. med

CPD Solid Tumor Panel TMB R

Panel Type Case Number SOLID_V2_0 PD-19-0002171

CPD Solid Tumor Panel Mutat

Show 10 entries

Panel Type	Case Number
SOLID_V2_0	PD-19-0002171
SOLID_V2_0	PD-19-0002171
SOLID_V2_0	PD-19-0002171

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

Clinically defined

Precision defined cohorts

Responders
 Exceptional responders
 Adverse events
 Poor outcome
 Molecularly defined
 Otherwise defined (e.g. diet)

Pre/post SOC interventions

Cohort plus:

- Matched disease controls
- Matched healthy

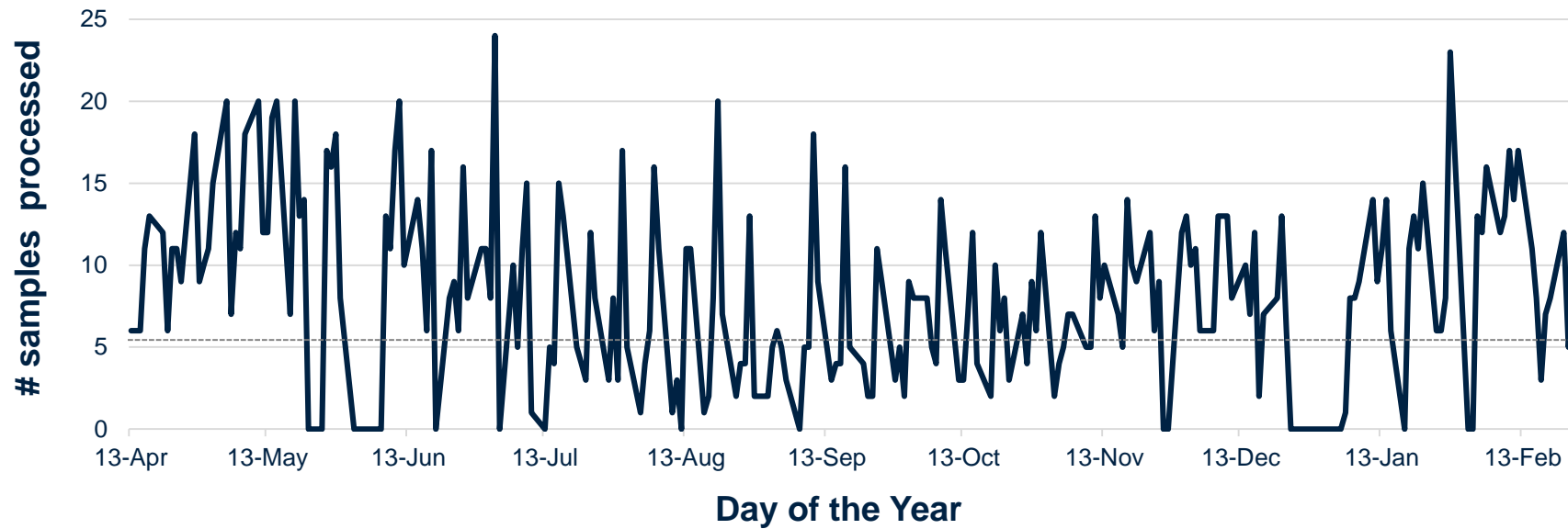
Clinical trial subjects

‘Base module’ for every trial

Dashboard of Projects and Prospective Cohorts

Project	Cohort	Status					Clinical Impact
		Dev.	Accrue.	Data Col.	Analysis	Pub.	
COVID-19	<ul style="list-style-type: none"> Acute COVID-19 Long term COVID-19 COVID-19 vaccination in healthy subjects I-SPY 	[Red bar spanning from Dev. to Pub.]					
		[Red bar spanning from Dev. to Accrue.]					
		[Red bar spanning from Dev. to Data Col.]					
		[Red bar spanning from Dev. to Analysis]					
Checkpoint blockade	<ul style="list-style-type: none"> Melanoma, neoadjuvant anti-PD-1 Melanoma, anti-PD-1, COVID-19 vaccine 	[Dark blue bar spanning from Dev. to Pub.]					
		[Dark blue bar spanning from Dev. to Data Col.]					
Lymphoma	<ul style="list-style-type: none"> Lymphoma patients receiving the COVID-19 vaccine 	[Grey bar spanning from Dev. to Data Col.]					
Multiple Sclerosis	<ul style="list-style-type: none"> Anti-CD20 + COVID vaccine pilot Anti-CD20, fingolimod, IFNβ 	[Black bar spanning from Dev. to Data Col.]					
		[Black bar spanning from Dev. to Accrue.]					
Influenza	<ul style="list-style-type: none"> Pediatric, childhood vaccines IBD, flu vaccine Melanoma, flu vaccine 	[Blue bar spanning from Dev. to Data Col.]					
		[Blue bar spanning from Dev. to Data Col.]					
		[Blue bar spanning from Dev. to Analysis]					

Sample traffic at Penn's Immune Health Processing Unit

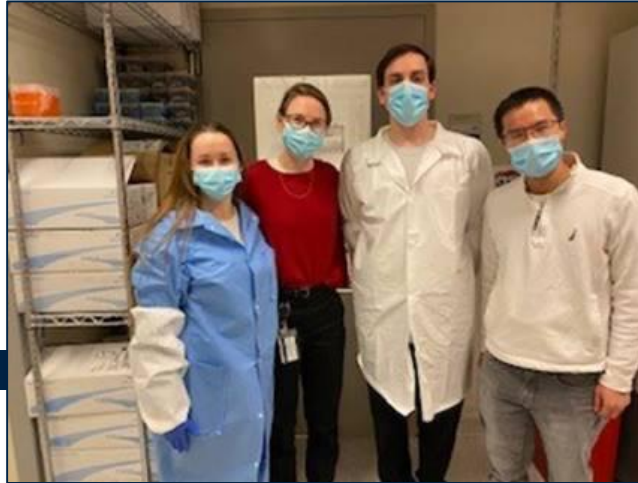
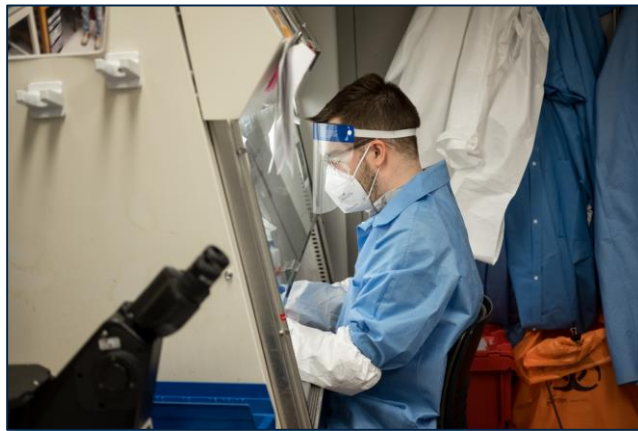


Processed to Date:
1,356 unique subjects
2,270 total samples
~16,000 tubes of blood



Immune Health Processing Unit

- ▶ Allie Greenplate, IH Asso Dir
- ▶ Sharon Adamski
- ▶ Kurt D'Andrea
- ▶ Ajinkya Pattekar
- ▶ Scott Korte
- ▶ Mandy Hicks
- ▶ Jake Hamilton



Spread

Continued from A1

work in the real world. The answer to this complex question has been on the minds of scientists ever since November, when the first large-scale studies suggested the vaccines could prevent up to 95% of illness.

But those promising results came from rigorous clinical trials, in which participants who met specific criteria were assigned at random to receive either the vaccine or a placebo, allowing their outcomes to be compared. All sorts of people were excluded: pregnant women, people who had previously been infected with COVID-19, and patients with certain cancers, HIV, or severe allergies.

The Penn study, led by E. John Wherry, is among many new underway to answer a variety of open questions. Can some vaccinated people become infected but have no symptoms, thereby potentially transmitting the virus without realizing it? How well do the vaccines work in people with various medical conditions? Is previous COVID-19 infection equal in protection to a first dose of vaccine? And for all vaccine recipients, how long does the protection last?

None of the uncertainties is reason to hesitate in getting the vaccines, which are safe and remain our best hope of curbing the pandemic. But the answers will be complicated by the emergence of new coronavirus variants, which could reduce the vaccine's effectiveness, and by the fact that the real world is inevitably messier than a clinical trial.

Said Wherry, an immunologist at Penn's Perelman School of Medicine: "These are all things keeping all of us up at night."

Tracking prevention

When they say a vaccine prevents 95% of illness, that's an estimate. What it really means is the number of illnesses among vaccinated people is 95% lower than the number among unvaccinated people.

That certainly suggests the vaccine is preventing most cases of disease. But we can never pin down the exact number of avoided illnesses without knowing how many people in each group were exposed to the virus — that is, on how many occasions was the vaccine actually put to the test.

Large, randomized clinical trials nevertheless provide a solid estimate of disease prevention, counting on the likelihood that similar numbers of vaccinated and unvaccinated people will be exposed. But measuring a vaccine's punch in the real world, when everyone can (eventually) get it, is trickier.

And for a variety of reasons, no vaccine quite lives up to its track record in a clinical trial, said Gregory Poland, a Mayo Clinic vaccine researcher and fellow at the Infectious Diseases Society of America.

People might delay or skip the second dose. Or they may engage in more risky behavior than the health-conscious types who enrolled in a clinical trial. Or, with vaccines that require special handling, something can go amiss. The two COVID-19 vaccines to receive U.S. authorization so far, for example, consist of genetic instructions in the form of RNA, which starts to degrade after vials are removed from cold storage.

Still, an Israeli health system reported this week that the RNA vaccine made by Pfizer and BioNTech may indeed come close to the level of success demonstrated in the clinical trials. The Israeli study was not randomized, and the details have not yet been published, but it's a good sign.

Other studies, meanwhile, suggest that new variants of the coronavirus can partly "escape" the immunity that is provided by the vaccines. Yet even partial protection is much better than none. And so far, the drugs still seem to prevent severe cases of disease.

Can vaccinated people spread disease?

A key reason the coronavirus has posed such a challenge is that some people become infected with mild or no symptoms, but meaning they can spread the virus unknowingly.

It is possible that is happening to some degree with vaccinated people, too, said Briane Barker, a Drew University biologist who studies the immune system's response to viruses. In other words, for some people, the vaccines may prevent disease but not prevent the virus from invading and making copies of itself — the definition of infection.

But if measuring a vaccine's ability to prevent disease is a challenge, measuring its ability to prevent transmission is far harder.

"You both have to show that someone is infected, then you have to be able to document the transmission opportunity and

the level of success demonstrated in the clinical trials. The Israeli study was not randomized, and the details have not yet been published, but it's a good sign.

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Does infection equal a dose of vaccine?

Recipients of the RNA vaccines have been reporting that any side effects, such as fever and headache for a day or two, tend to occur after the second shot.

But for those previously infected with COVID-19, side effects may be more likely after the first shot. Does that suggest that a prior infection is just like getting a first dose?

That's among the questions that Wherry hopes to answer in his lab at Penn. The short answer is no, as shown by the antibodies that are present only in those who've been infected.

Yet the immune system has many agents besides antibodies. Wherry's team also is measuring various kinds of white blood cells, including "helper" T cells that can act as sentinels, marshaling support to fight an infection, and "killer" T cells that, as the name suggests, fight infection by killing cells that the virus has penetrated.

These cells are extracted from blood samples and chemically tagged with various fluorescent markers — allowing each type of cell to be counted with a laser inside a boxy device called a flow cytometer.

So far Wherry's team has enrolled 35 vaccinated people to participate, a third of whom were previously infected. Others, including cancer patients who take immune-suppressing drugs, will be added later.

"There's this idea that previous infection may leave an imprint on your immune response," he said. "Then when you get the vaccine, how your vaccine-induced response evolves could be different than if you've never seen the virus before."

And like many others, he plans to measure how the immune response changes over time.

Plenty of unanswered questions. But on one front, the scientists who study the vaccines are united: Vaccination is the best weapon we have. Make an appointment as soon as you're eligible, and get it done.

University of Pennsylvania immunologist E. John Wherry is studying various aspects of how well the COVID-19 vaccines work, such as what happens when a recipient has previously been infected. Penn Medicine

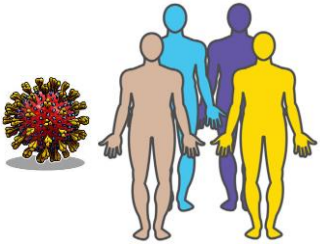
At a Penn lab, Sharon Adamski extracts plasma from blood collection tubes to study how well the vaccines work against COVID-19. At right, Scott Korte prepares a centrifuge to separate white blood cells from the blood of people vaccinated against COVID-19.

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Philadelphia Inquirer

COVID-19 IMMUNE PROFILING

160 acute/recovered COVID-19 Patients

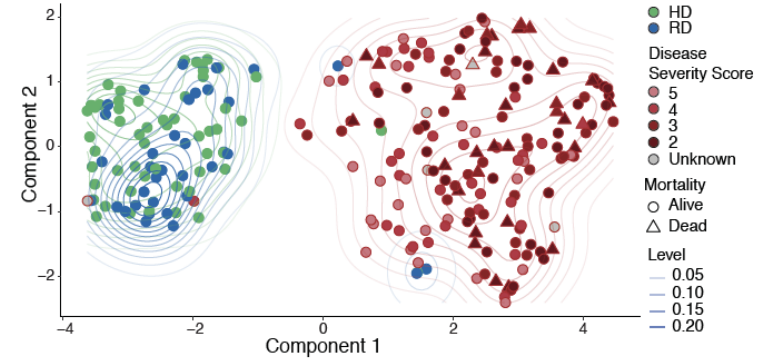


DEEP IMMUNE PROFILING
"PIPELINE"

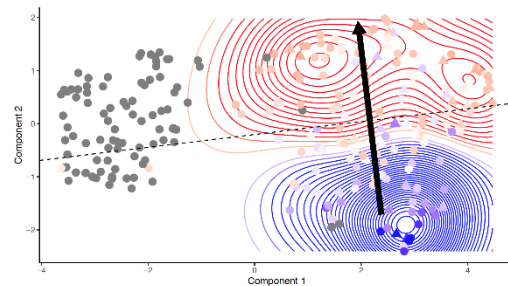
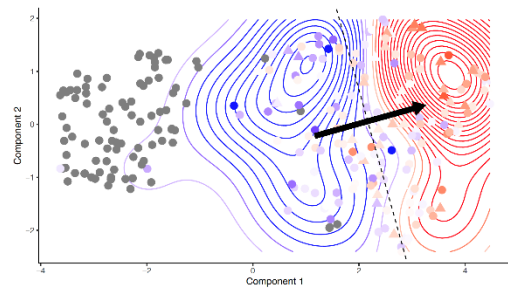


- 165,000 individual immune data points
- +1000s of clinical data points
- 8M immune-clinical pairwise comparisons
- 27B immune-immune pairwise comparisons

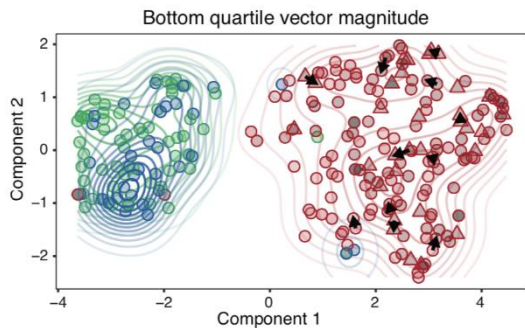
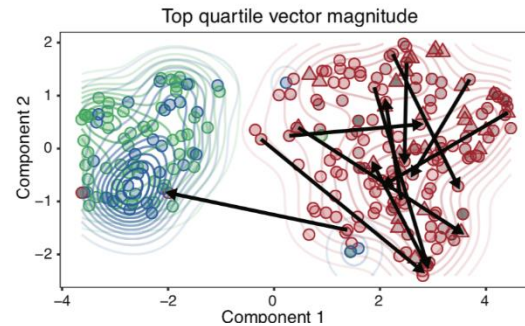
Dimensionality Reduction
(extensive computational analysis)



Mapping Immune Features



Temporal Changes

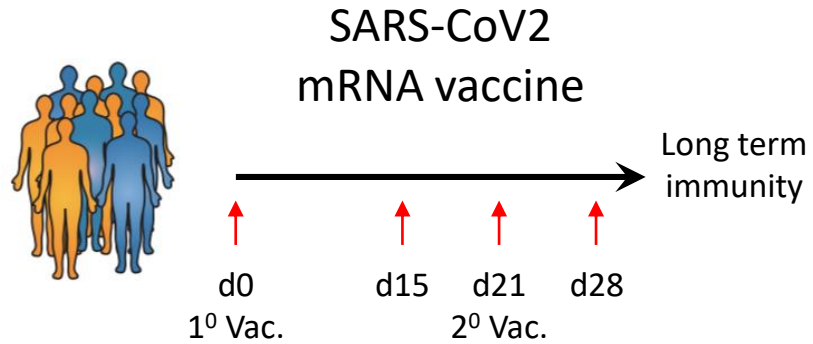


Applying an Immune Health strategy to COVID-19:

- 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

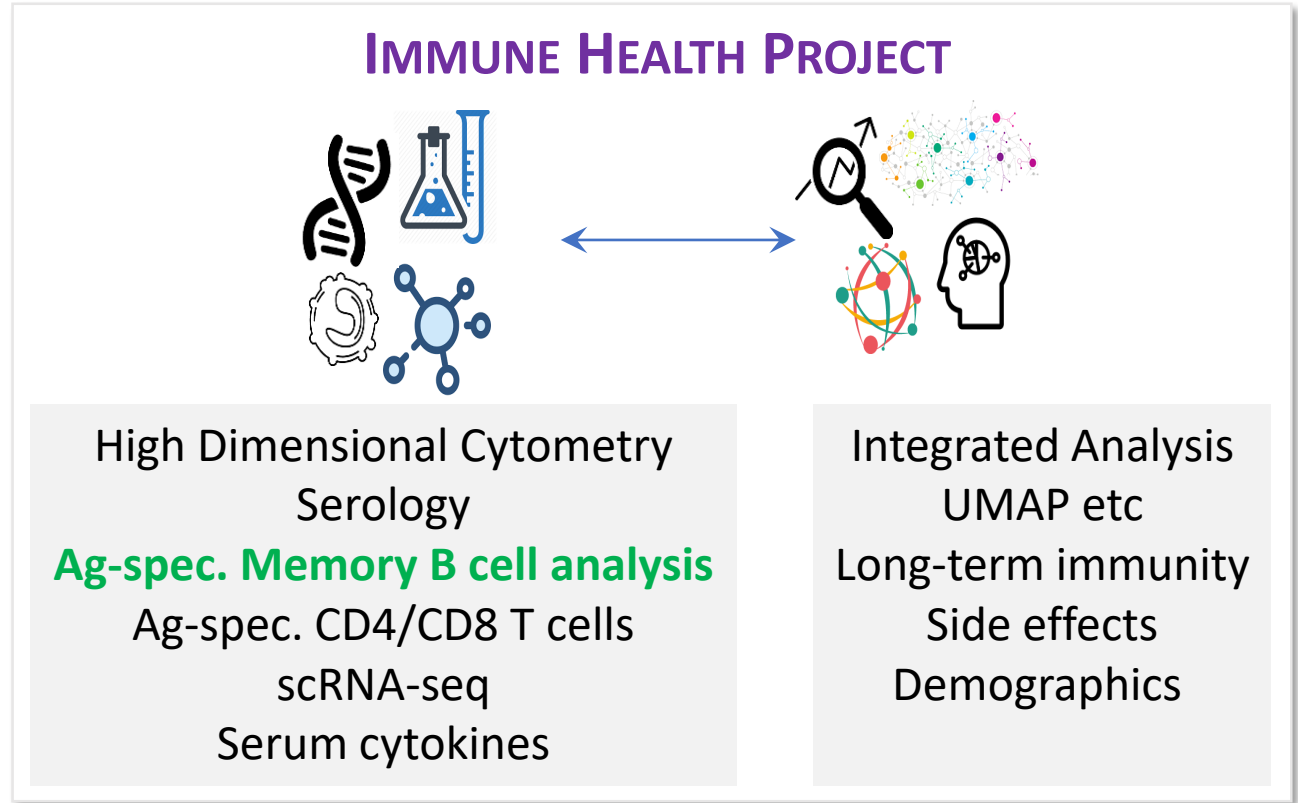
Mathew et al, *Science*, 2020

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



Two groups *prospectively* collected

- COVID Naive
- Previous COVID



Allie Greenplate



Rishi Goel



Divij Mathew



Mark Painter



Sokratis
Apostilidis

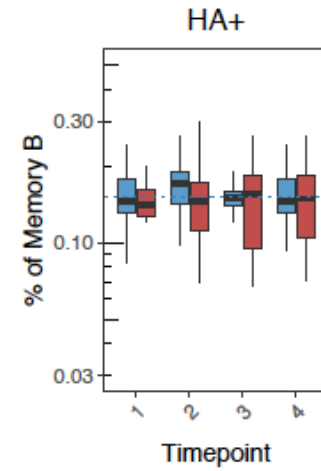
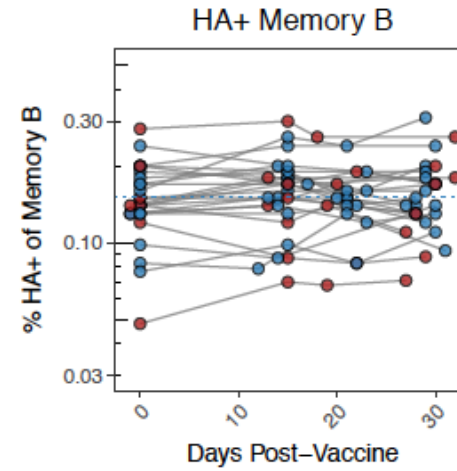
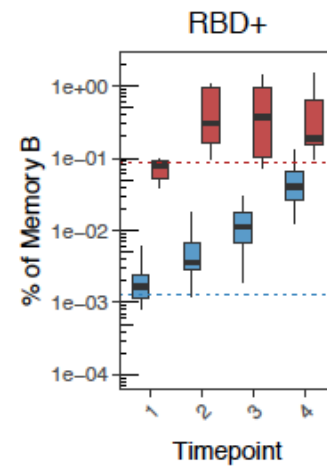
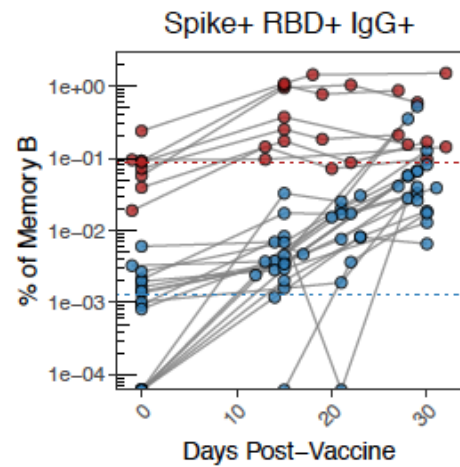


Oliva Kuthuru

Goel et al, *Science Immunol*, 2021

Time from idea to publication:
3.5 months

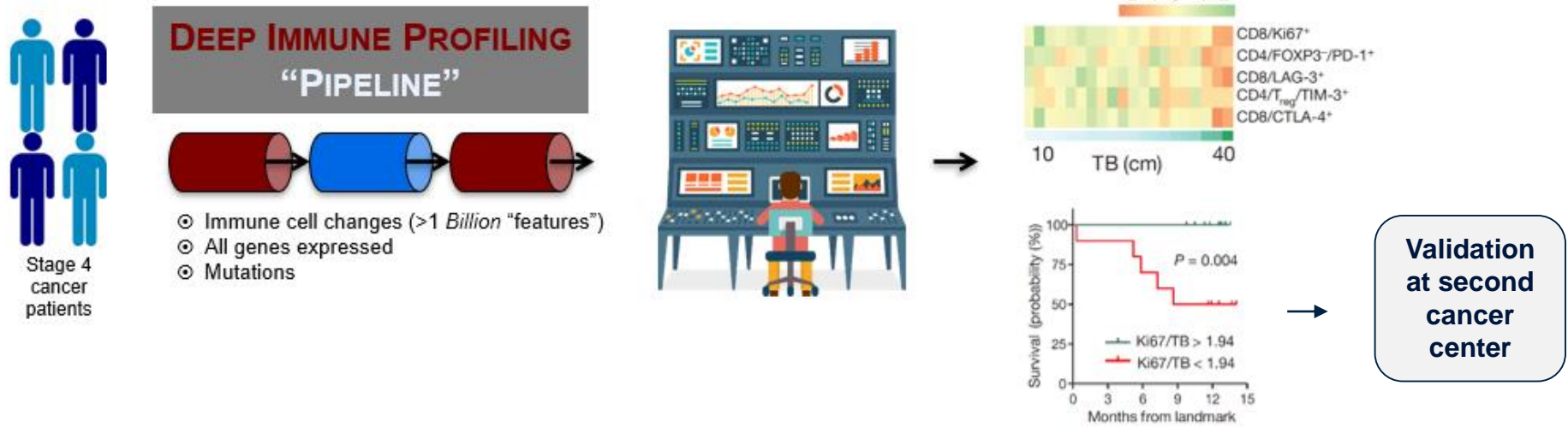
SARS-CoV2 VACCINATION IN COVID-19 NAÏVE VS COVID-19 RECOVERED SUBJECTS



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

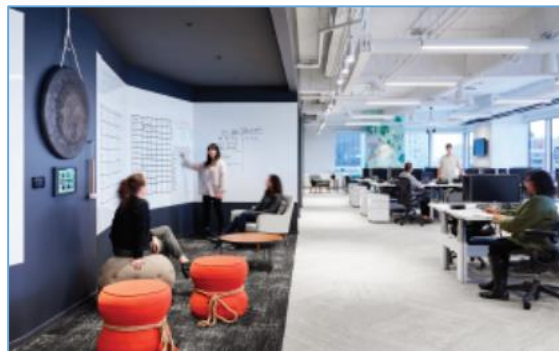
METASTATIC MELANOMA PATIENTS RECEIVING PEMBROLIZUMAB



Huang AC et al, Nature 2017

Huang AC et al, Nature Medicine 2019

Immune Health Institute !!



Artist rendering

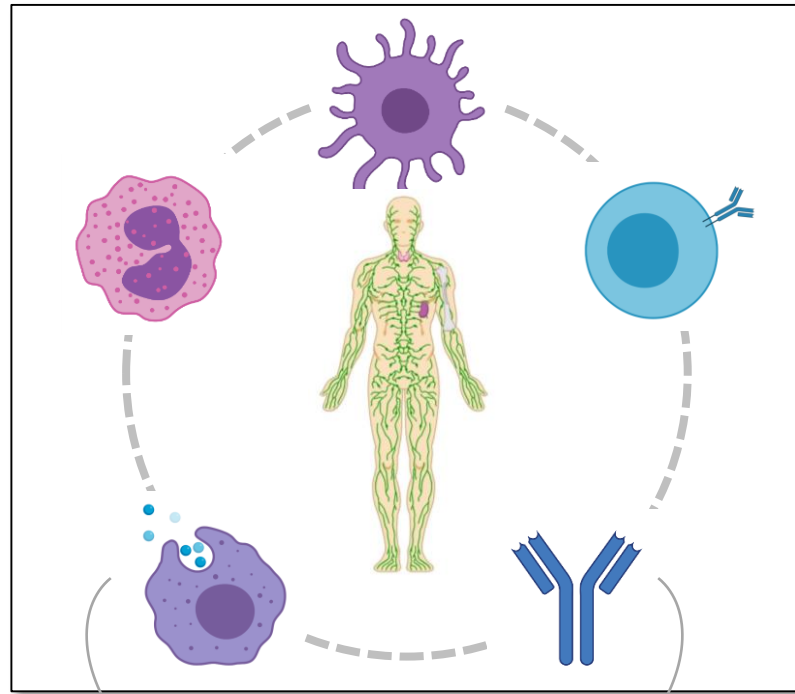
SUMMARY: THE IMMUNE SYSTEM AS A “SENSORY” ORGAN

IMMUNE HEALTH® GAINS INSIGHTS INTO HEALTH/DISEASE FROM IMMUNE
PROFILING

Nervous system



Immune System:
Senses all tissues

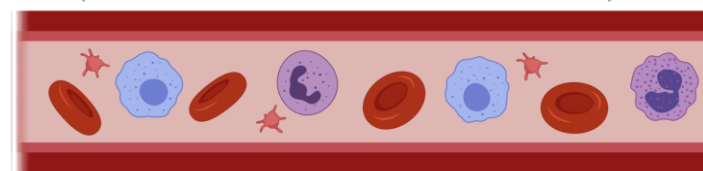


“Listening” to the
Immune System

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

- **E. John Wherry** – IH Director
 - **Pat Morin** – Admin IH Director
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 - Ajinkya Pattekar
 - Scott Korte
 - Mandy Hicks
 - Jake Hamilton
- Immune Health Council
 - Robert Vonderheide (Chair)
 - David Roth (Co-Chair)
 - Michael Feldman
 - Katherine Nathanson
 - E. John Wherry
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 - Allie Greenplate
 - Derek Oldridge
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