# Wearables for Managing Health


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Conflicts: Personalis, Genapsys, SensOmics, Qbio, January AI, Filtricine, Mirvie, Fodsel, Protos

# Medicine

## Presently

Focus on **Illness**
Reactive
Measure very few things
Infrequent
Population based

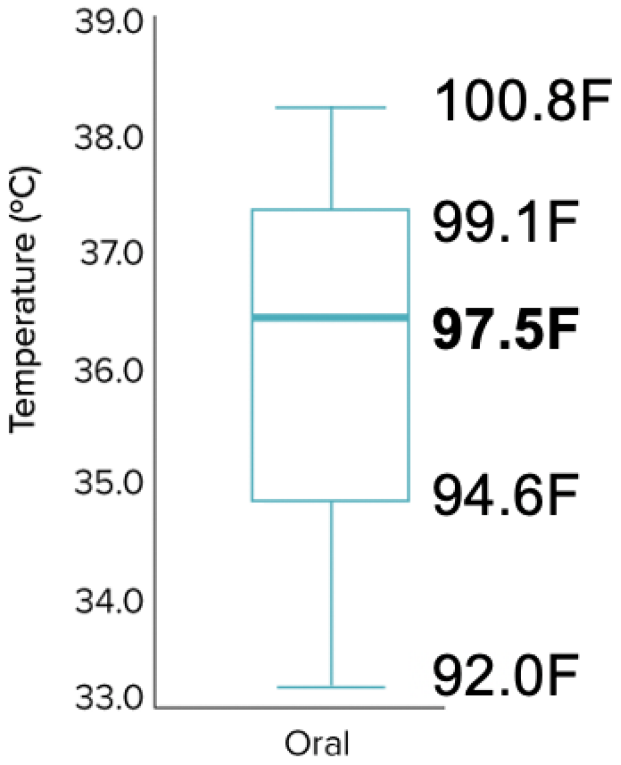
## Should be

**Precision Health**

Focused on **Health**
Proactive
Measure many things
Frequent
Individual based

# Importance in Individual Variation from “Normal”

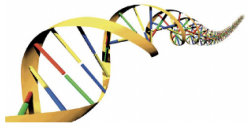
Oral temp in 2749 healthy individuals



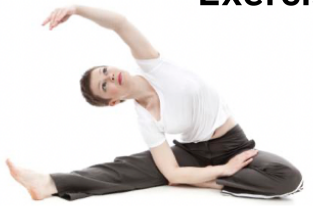

Sund-Levander M. Scand J Caring Sci 2002;122-8. & Souissi N. Chronobio Int 2007;24:739 -48

# Health is a product of Genome & Exposome

Genome



Exercise



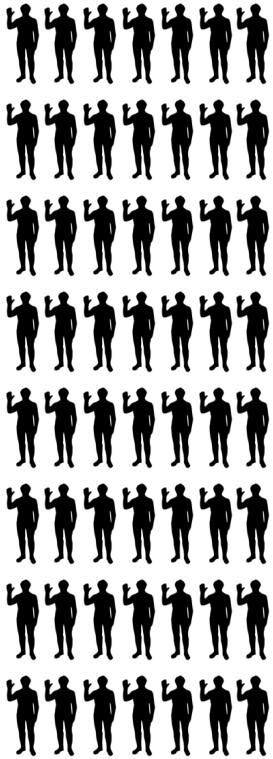
Pathogens

Food

Environmental Exposures

Stress

# Longitudinal Personal Omics Profiling



109 Individuals

**Omics Measurements**

**Biosensors**

Genome

Epigenome

Transcriptome

Proteome

Cytokines

Metabolome
Lipidomics

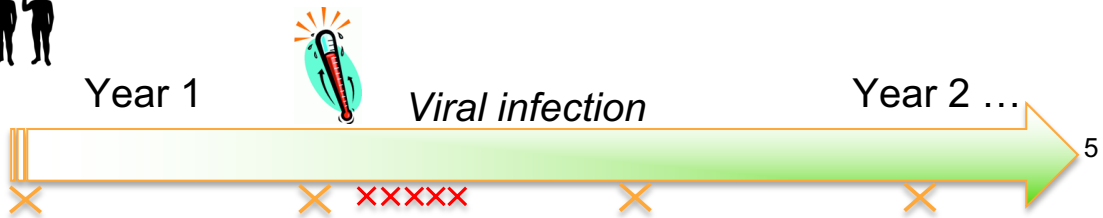
Autoantibody-ome

Microbiome (Gut, Urine, Nasal, Tongue, Skin)

**Billions of Measurements!**

**Clinical Tests**
**Questionaires**

**Stress Echos**
**Glucose Control**




9 yrs

# 49 Major Health Discoveries

## Metabolic

1 MODY mutation (gene)
1 ABCC8 Mutation (gene)
14 New Diabetes

## Cardiovascular

6 Carotid Plaques (imaging)
1 Atrial Fib. (wearable)
1 RMB20 mutation (gene)
1 Reduced LVEF/GLS (imaging)
3 Dilated L. Atrium (imaging)
1 Pharmagenomic (gene)

## Heme/Onc

7 Oncologic Risk Genes
(Thyroid Cancer in 1)
1 Lymphoma (Imaging)
1 MGUS (IgM)
1 Smoldering Myeloma (IgM)
1 α Thalassemia (Clinical)
1 β Thalassemia (Gene/Clinical)
1 Pros1 Mutation (gene)

## Other

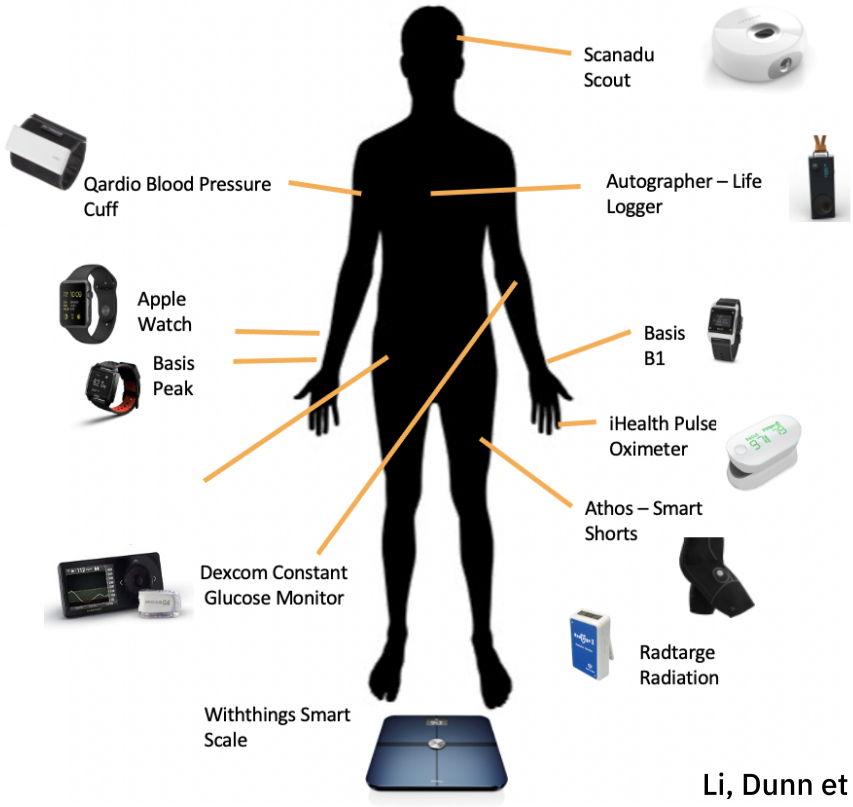
1 Sleep Apnea (wearable)
1 SLC7A9 mutation (cystinuria risk)
2 Macroalbuminuria

## Infectious

1 Lyme Disease (wearable)

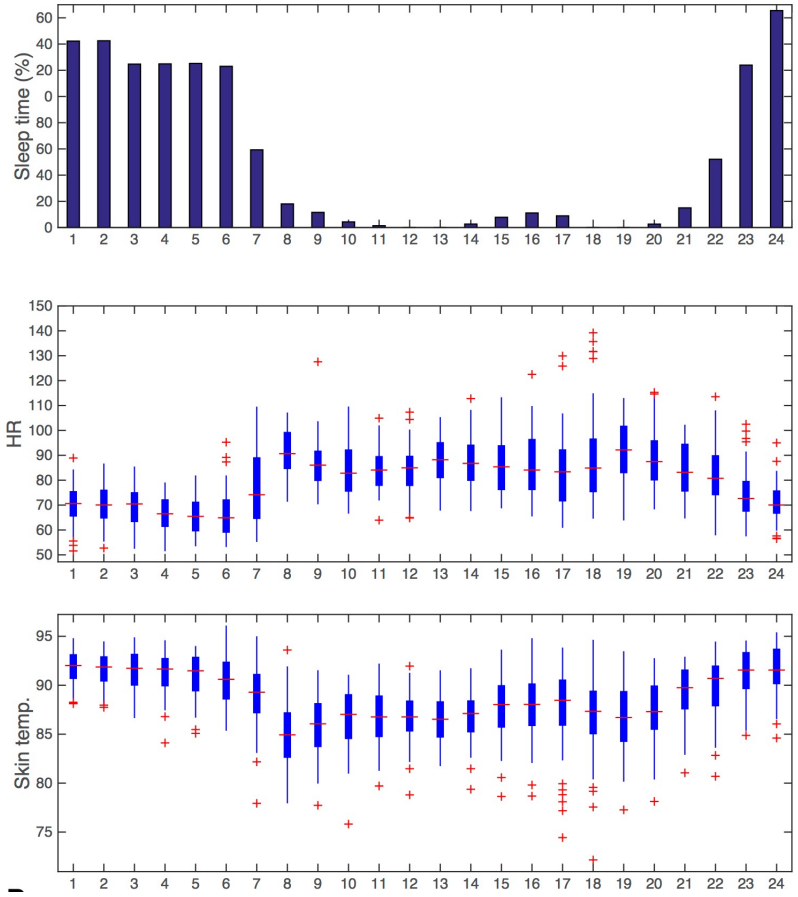
# Wearable Sensors: Over 900 Devices

- Worn by millions of people (20% of US)
- Make 100Ks of measurements each day
- Wearables can track many things: HR, HRV, Respiration Rate, SpO2, Skin Temp, Blood Pressure



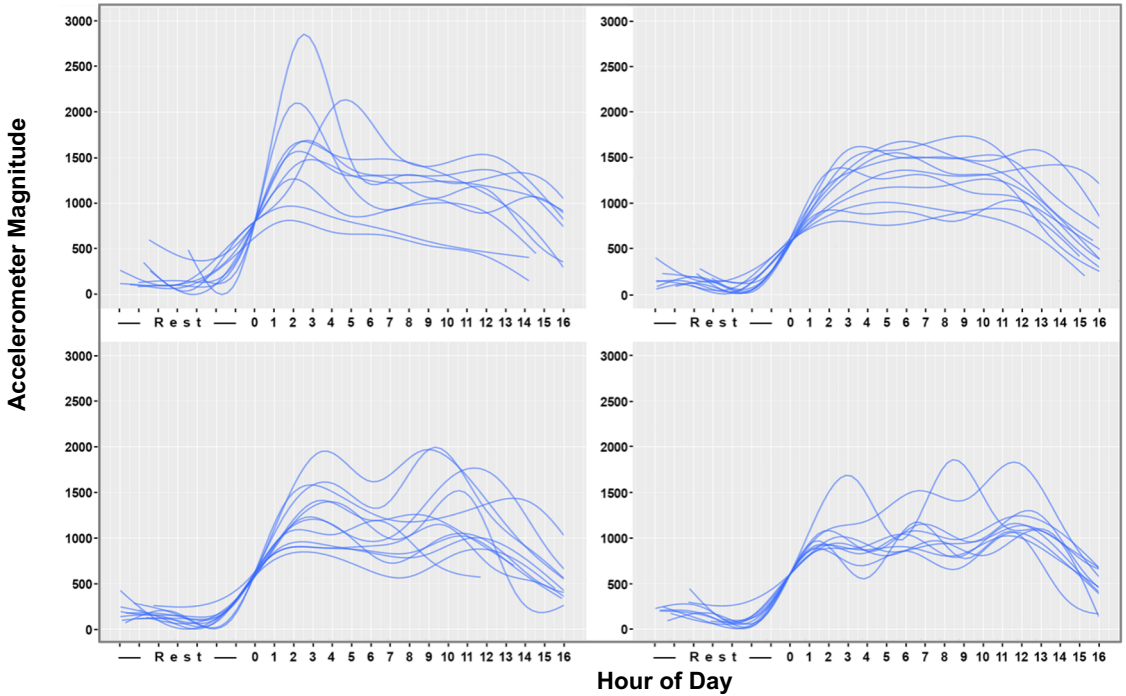

Li, Dunn et al.
PloS Biol 2017

# Circadian and Diurnal Patterns



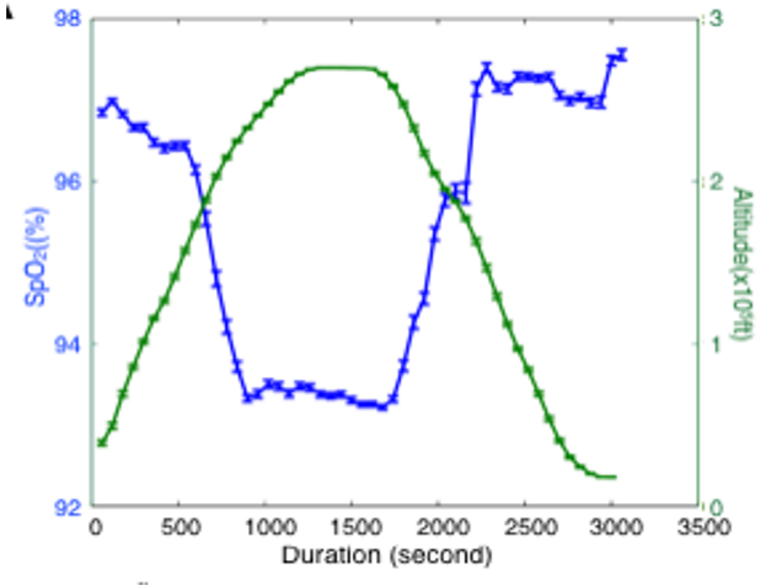

Li, Dunn et al. PloS Biol 2017

# Activity Phenotypes: 4 Patterns




Li, Dunn et al.
PloS Biol 2017

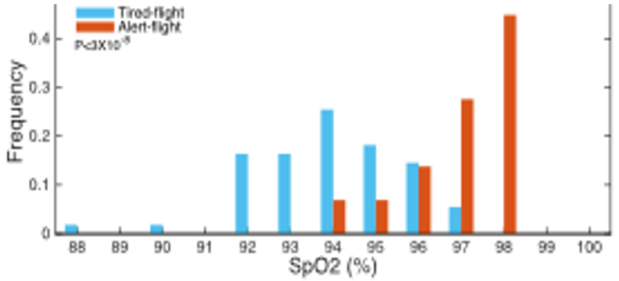
# SpO2 Levels Drop During Airline Flights

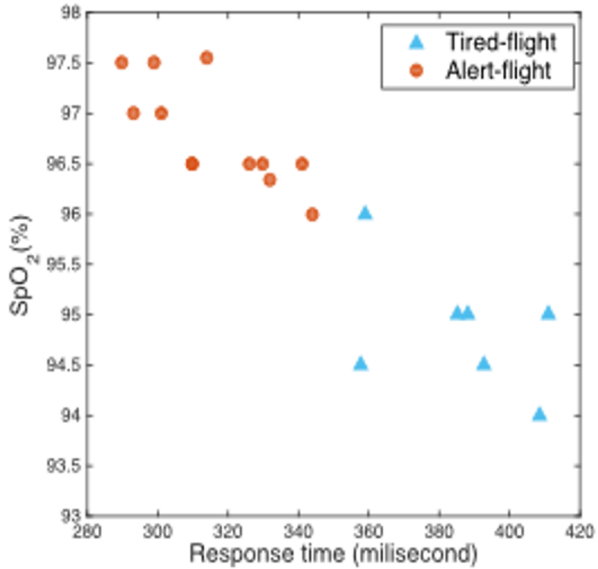



**SF to San Diego 2016**

# SpO2 Measurements

# Associated With Fatigue



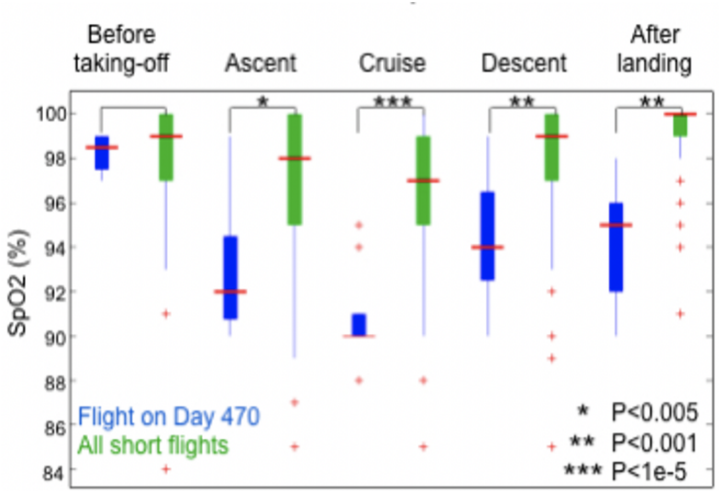

Li, Dunn et al. PloS Biol 2017

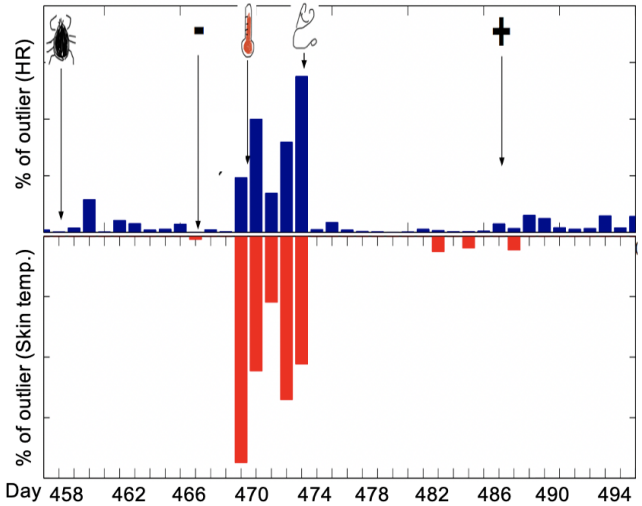
# Early detection of Lyme disease

## Digital Health: Tracking Physiomes and Activity Using Wearable Biosensors Reveals Useful Health-Related Information

Xiao Li, Jessilyn Dunn, Denis Salins, Gao Zhou, Wenyu Zhou, Sophia Miryam Schüssler-Fiorenza Rose, Dalia Perelman, Elizabeth Colbert, Ryan Runge, Shannon Rego, Ria Sonecha, Somalee Datta, Tracey McLaughlin, Michael P. Snyder

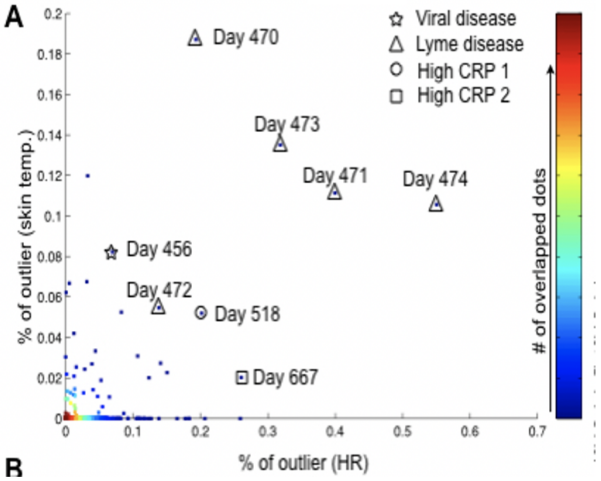
Published: January 12, 2017 • https://doi.org/10.1371/journal.pbio.2001402



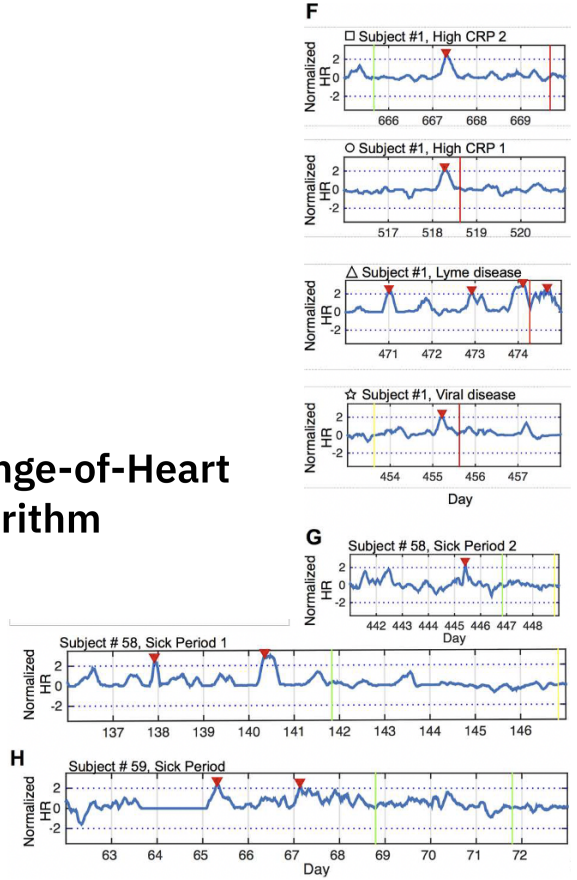



# Detects All Days of Illness

Li, Dunn et al.
PloS Biol 2017

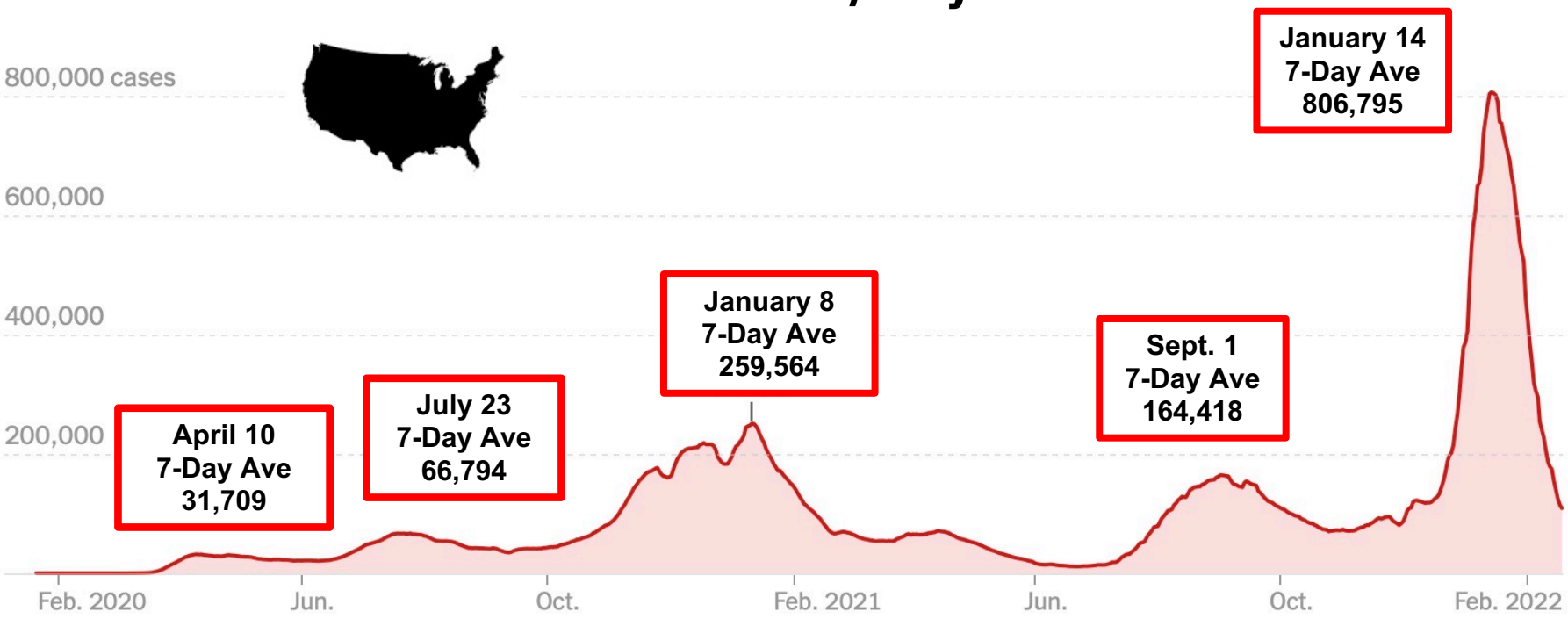



## Change-of-Heart Algorithm



# United States COVID-19 Cases/Day





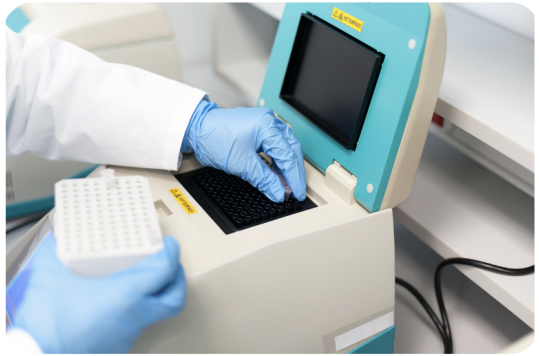

https://www.worldometers.info/coronavirus/country/us/

# Current Tests

## Thermometer

Does it work?

## PCR



Slow (1-2 days), Cost, Stochastic

# COVID-19 Infectious Disease Study

## Wearables Data Study

We are trying to find out if information from wearable devices, like Fitbit and Apple Watch, can be used to track infectious diseases like COVID-19. We hope to be able to predict the onset even before any symptoms start.

Healthcare workers and high-risk individuals are especially encouraged to enroll in the study.

Enroll >

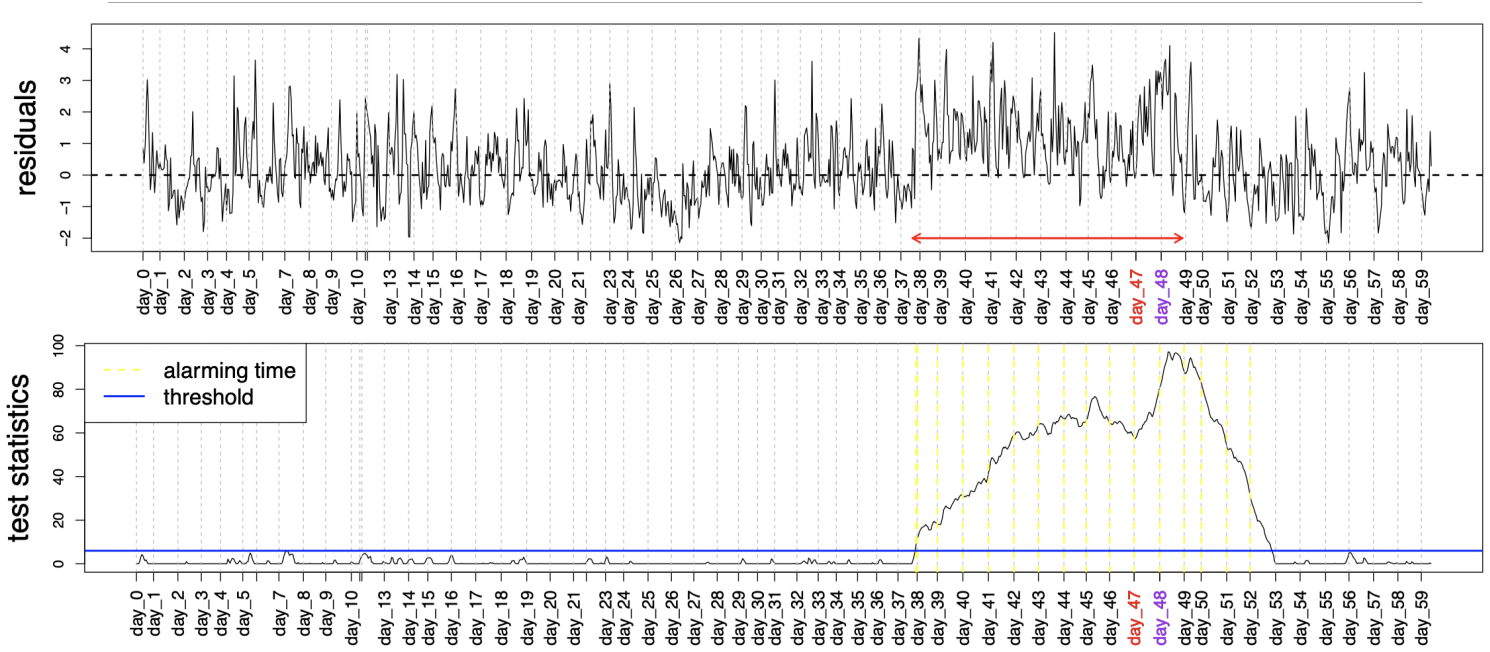
Study email: covid19_wearables@lists.stanford.edu
Participants' rights questions: 1-866-680-2906

**Launched IRB Approved Study**

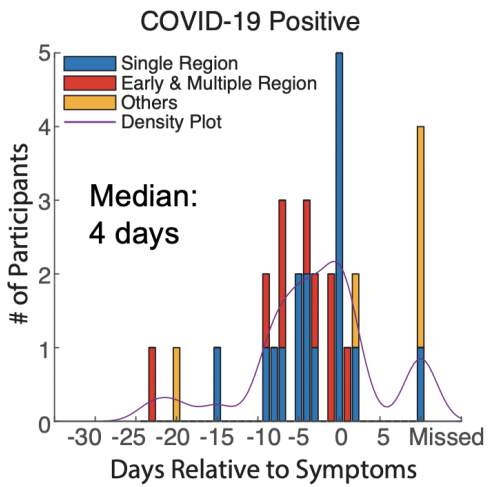
**Partnering with Leading Companies E.g. Fitbit, Garmin**

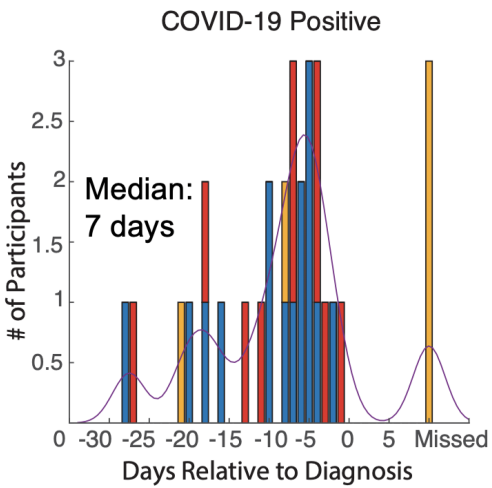
**>5000 Enrolled**
**>30 COVID-19 Positives (Golden dataset)**

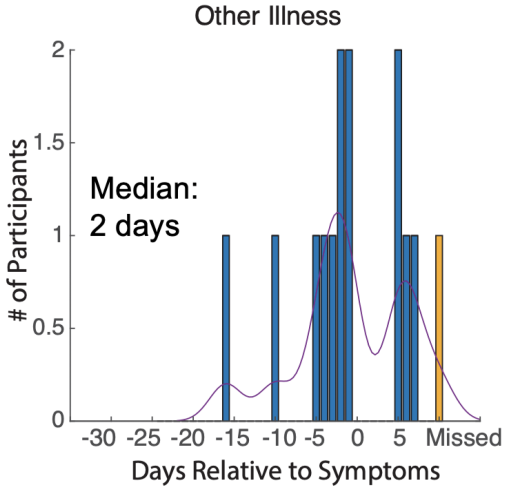
# Identifying COVID-19 at early stage



# Summary of Early Detection

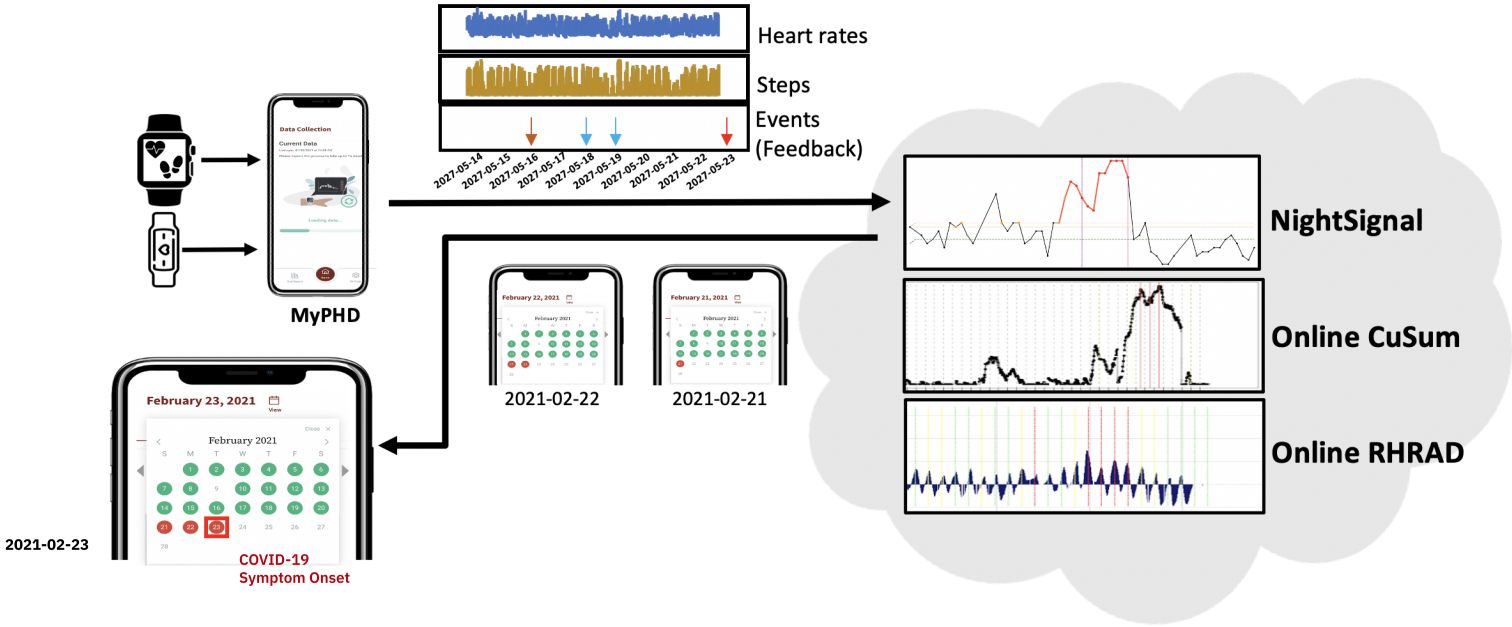



**Elevated Heart Rate: 7 Beats/Min**

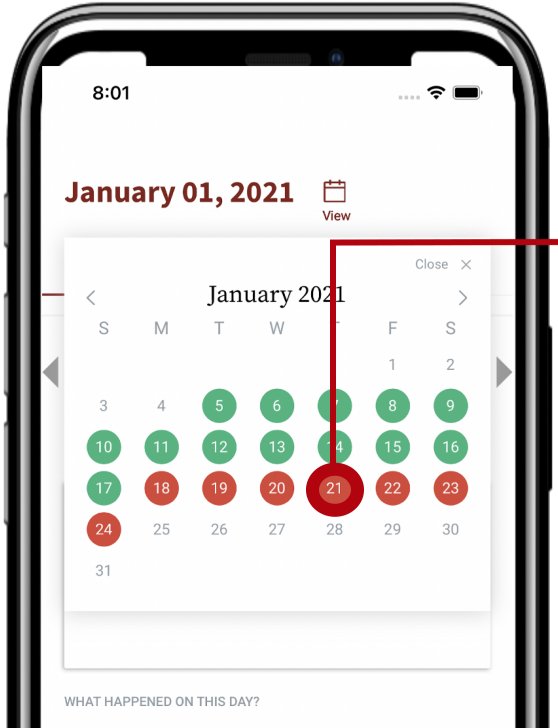
# Real-time Alerting Overview




**Real-time alerts**

innovations.stanford.edu

# Online Alerting System




## Real Covid positive case

**Symptom Onset ***

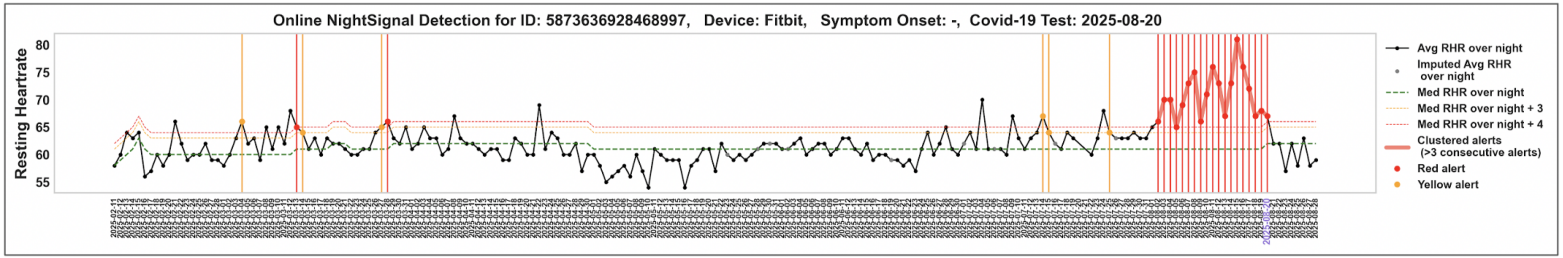
**Total = 80% (67/84) of cases**

*** For privacy reasons, actual dates have been slightly shifted**

# Asymptomatic Detection Examples

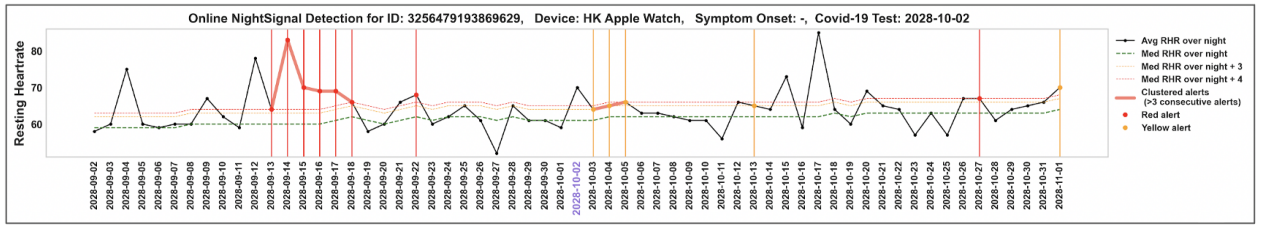
## Fitbit

NightSignal

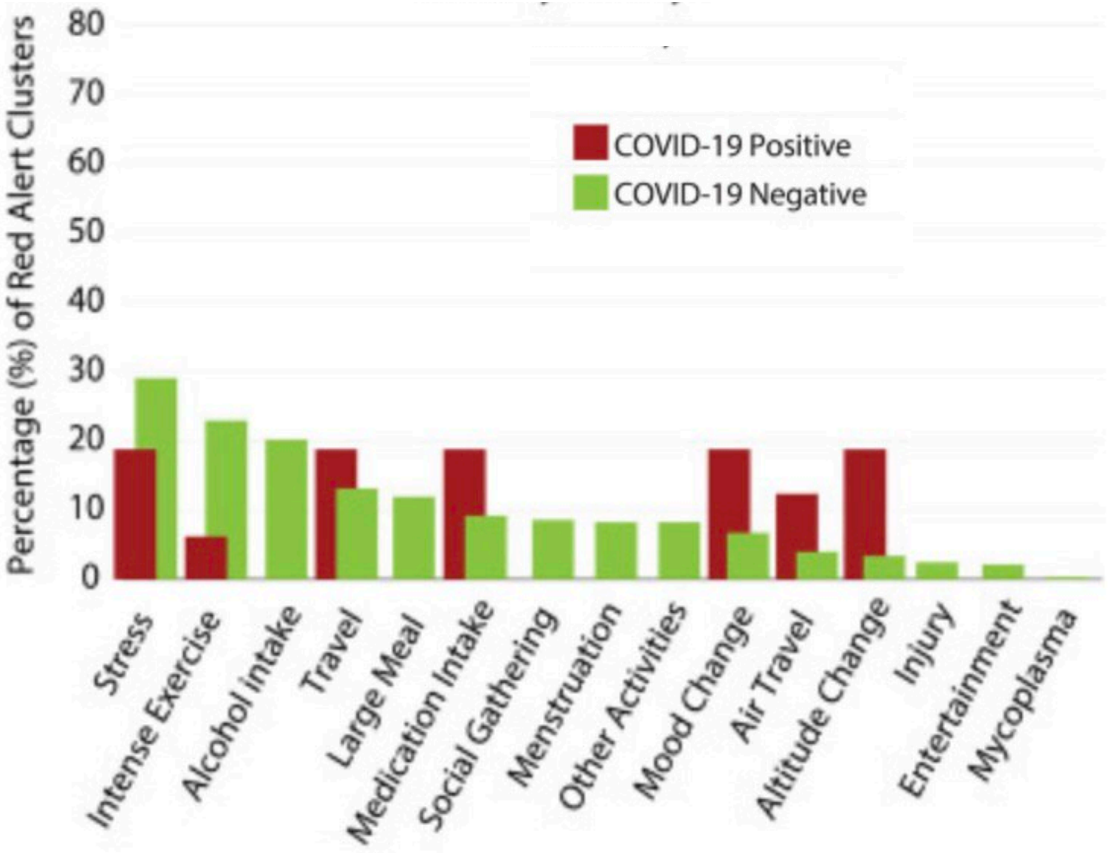



## Apple Watch

NightSignal

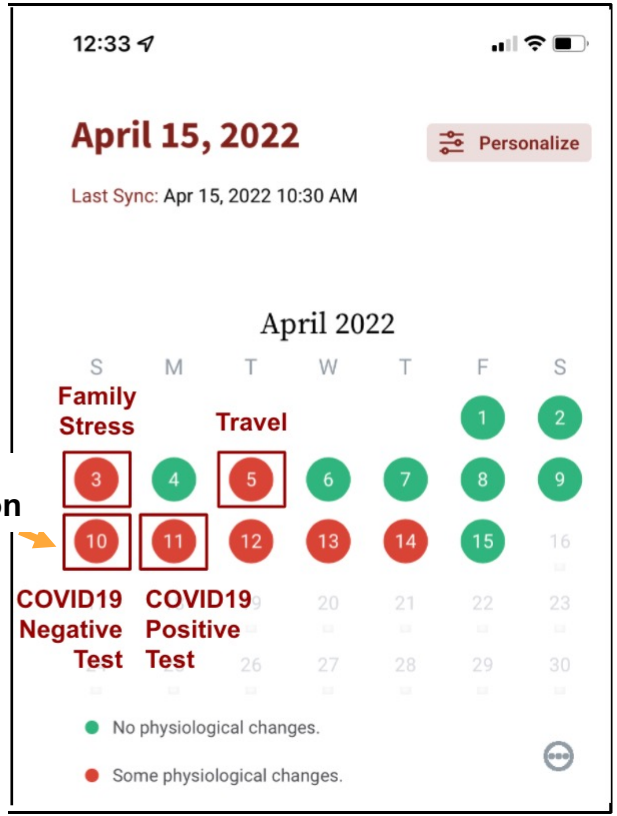


# Other Stress Triggers

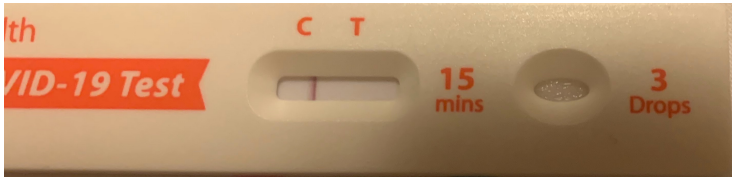


# COVID Detection Assays

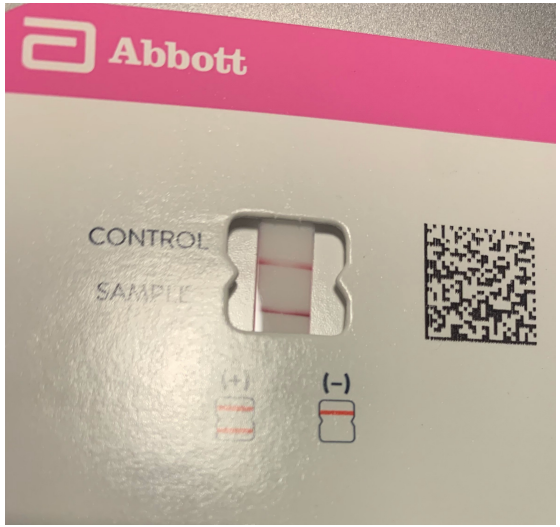
**FitBit Stress Signal Detection**




Congestion

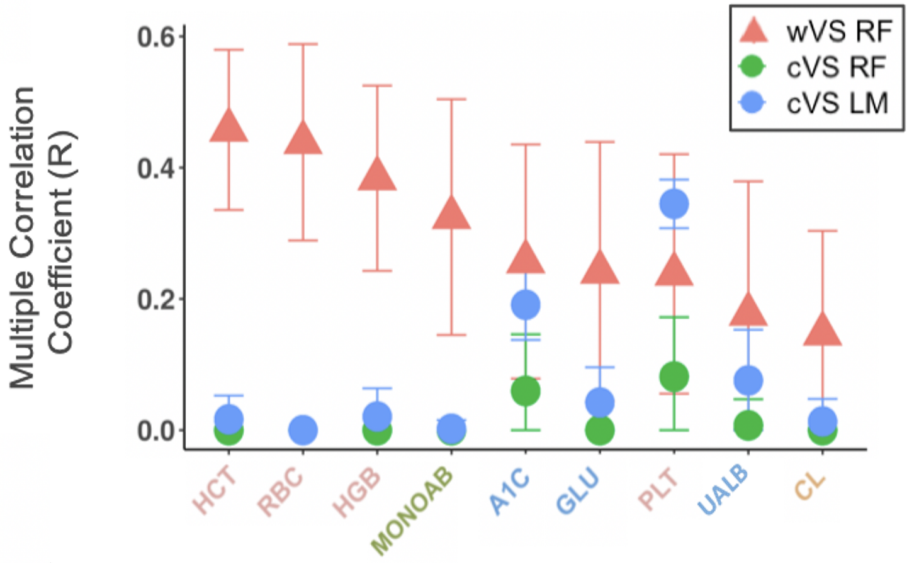



**CVS (-) Test 4/10**




**Abbott (+) Test 4/11**

# Prediction of Other Clinical Biomarkers From a SmartWatch



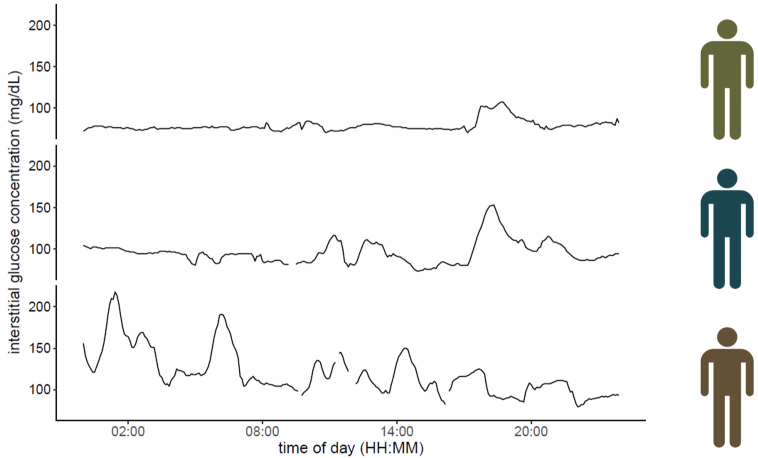

Dunn et al, 2021, Nature Medicine.

# Continuous Glucose Monitoring: Lots of Spikers

Hall et al. PloS Biol 2018

**2-4 Weeks**

**Dexcom G4**

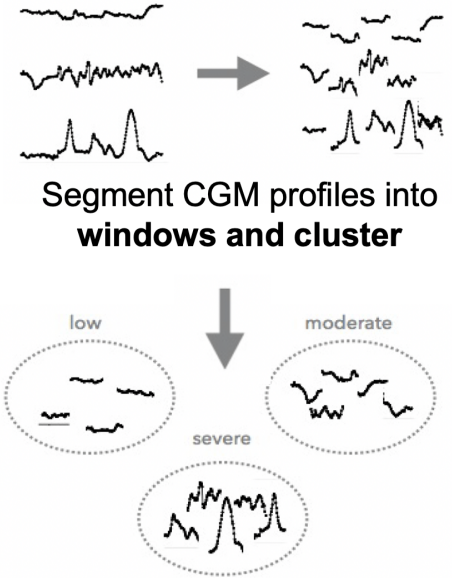


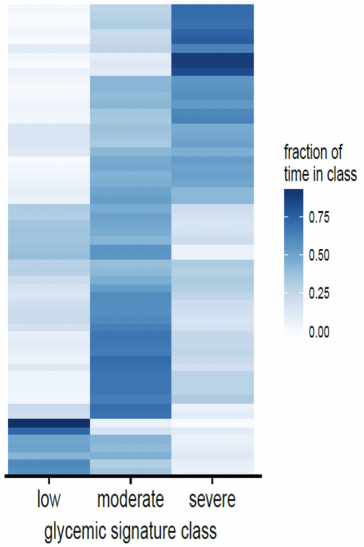

**24 hours**

# Classification of People into Glucotypes Based on CGM Profiles

## Glucotypes

Hall et al. PloS Biol 2018



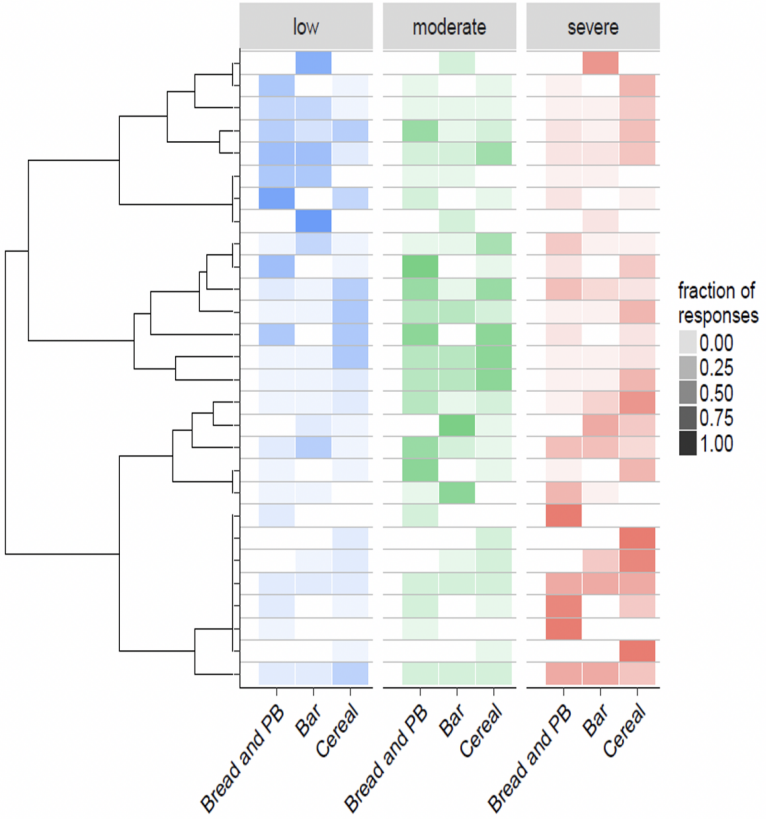
# The same meal triggers different glycemic responses in different people

Hall et al. PloS Biol 2018

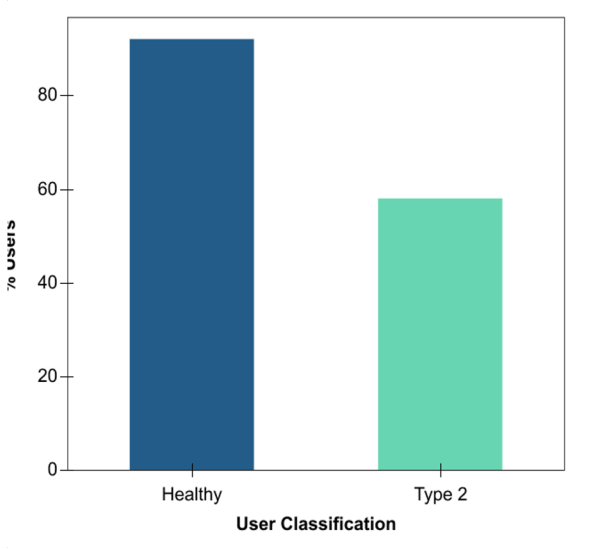
Bread + Peanut Butter

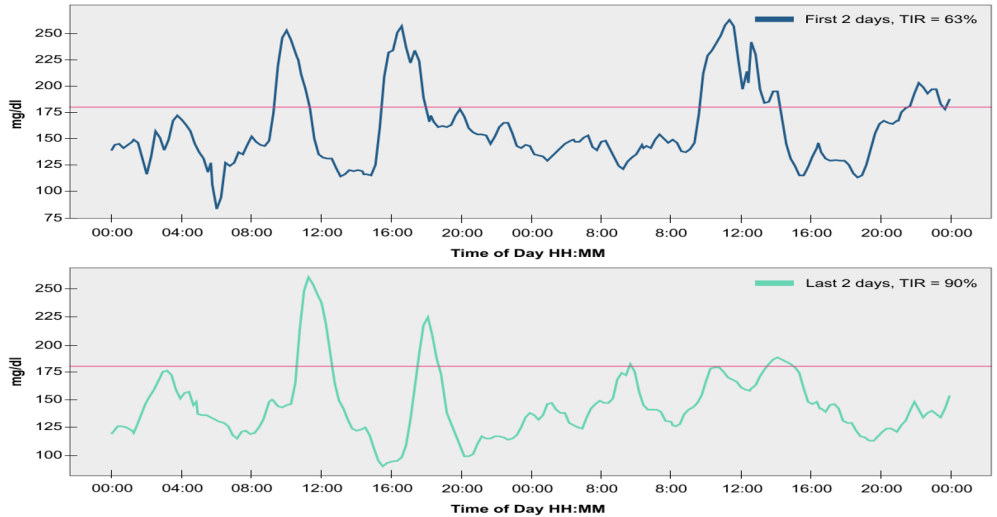
Protein Bar

Cornflakes + Milk



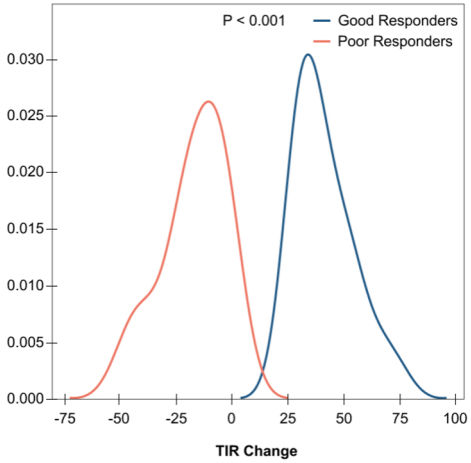
# Sugar Challenge (655 Participants with lots of data): CGM Plus Logging App Improves TIR in 10 days




January.ai

# Good Responders vs Poor Responders: Young and Low BMI Improve Most

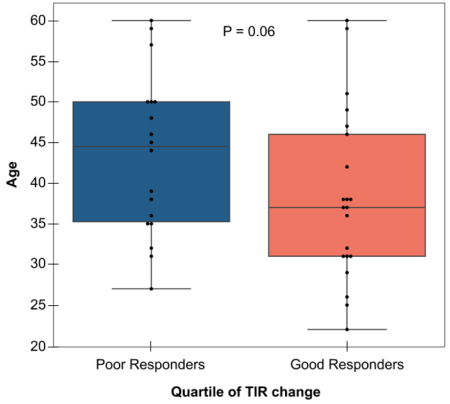


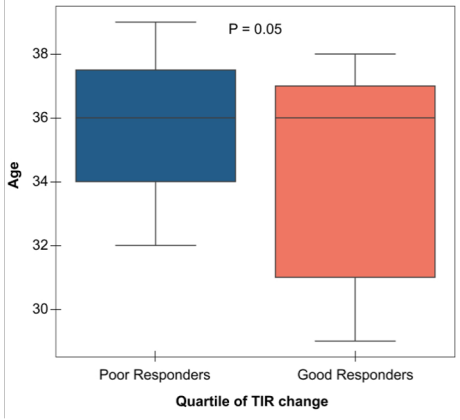

January.ai

Healthy

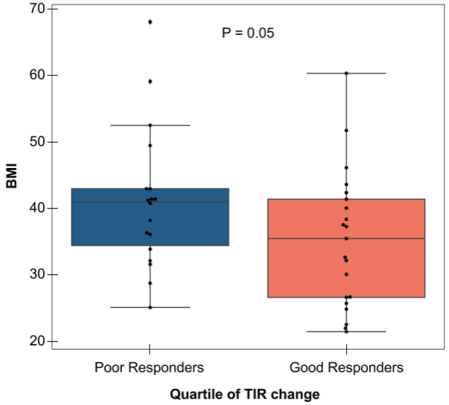
Type 2 Diabetes

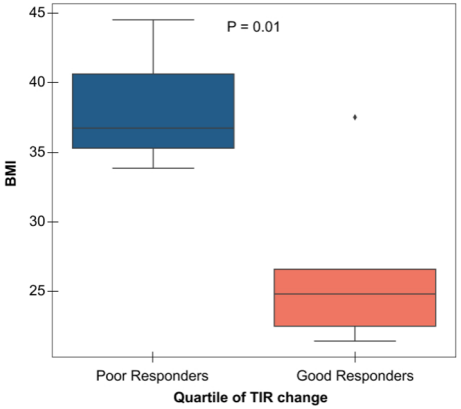
Age



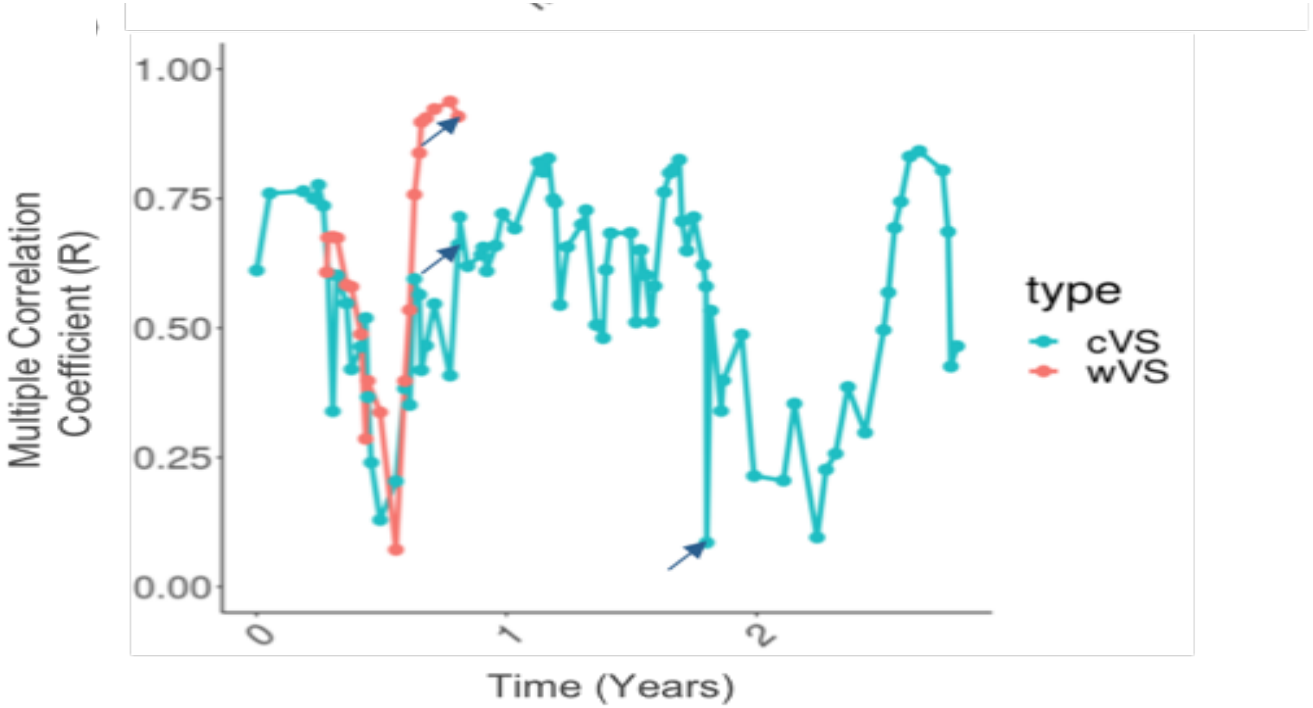




BMI



# Personal Monitoring of Health Using a SmartWatch




Dunn et al, 2021, Nat. Medicine, in press.

# Team

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# Acknowledgements


Exposome
Chao Jiang
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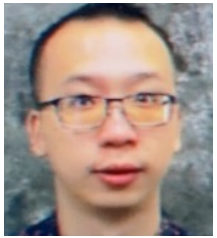
Xiyan Li

Wearables
Xiao Li
Jessie Dunn
Denis Salins
Sophia Miryam …
Heather Hall



Peng Gao, PhD
Postdoc

Allison Zhang, PhD
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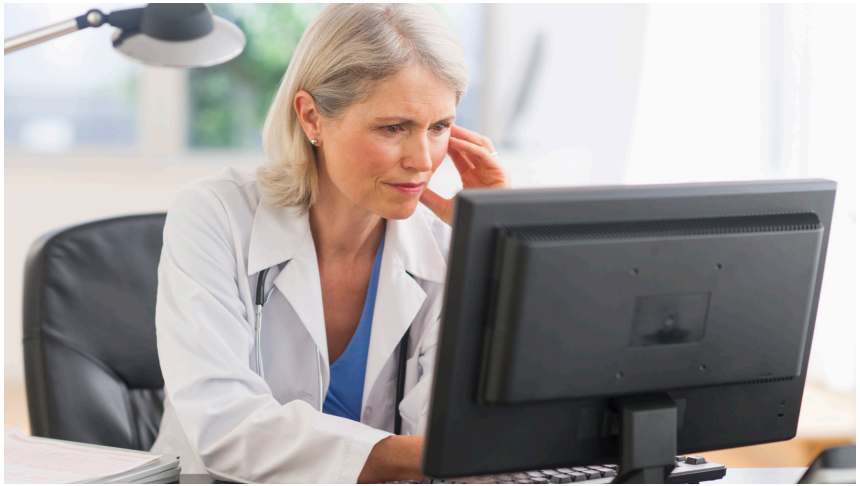
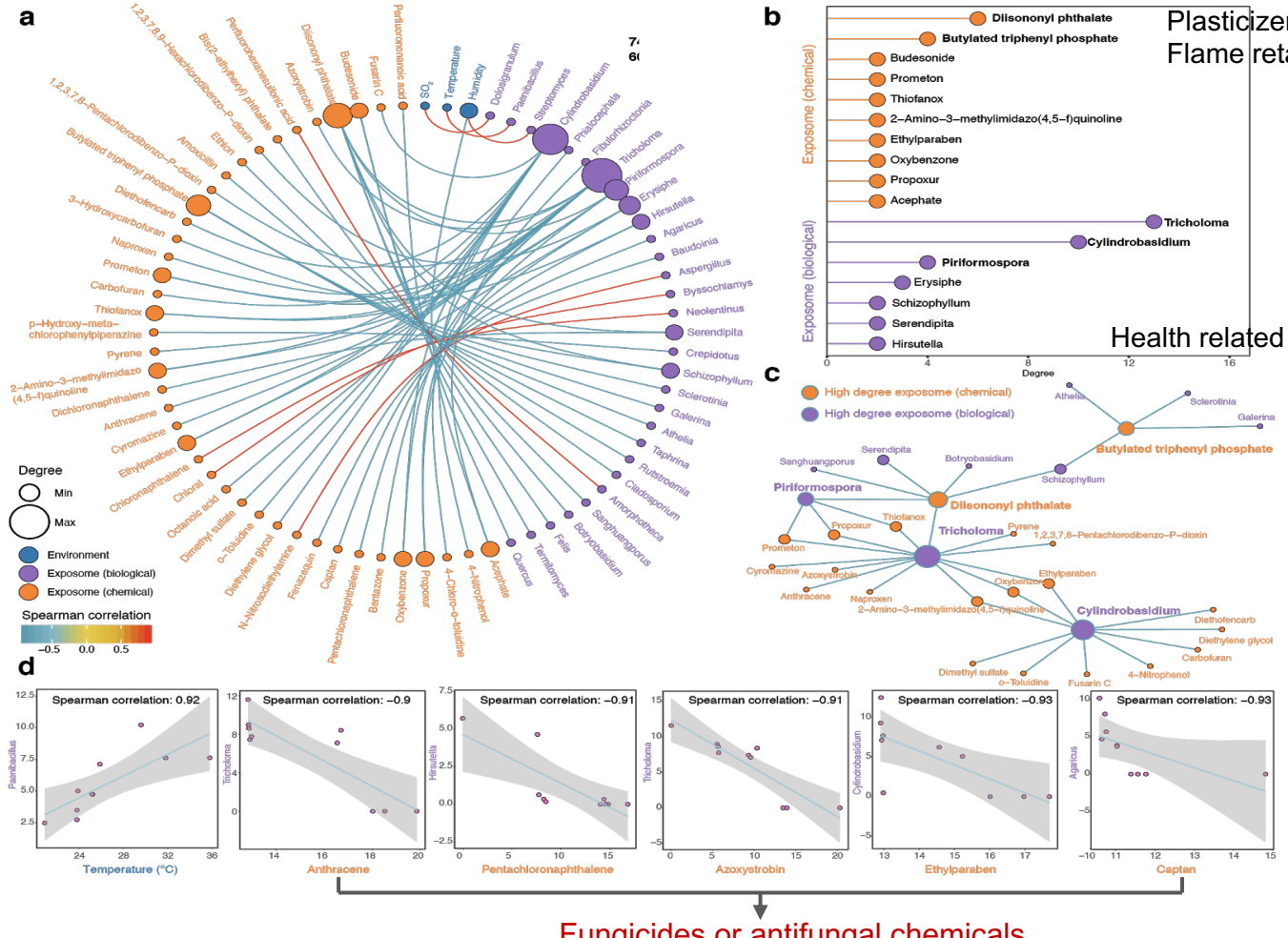
Postdoc

# Share Information With Physician



# Exposome Correlation Between Biologicals, Chemical, Environmental Factors

**74 Nodes**
**60 Edges**

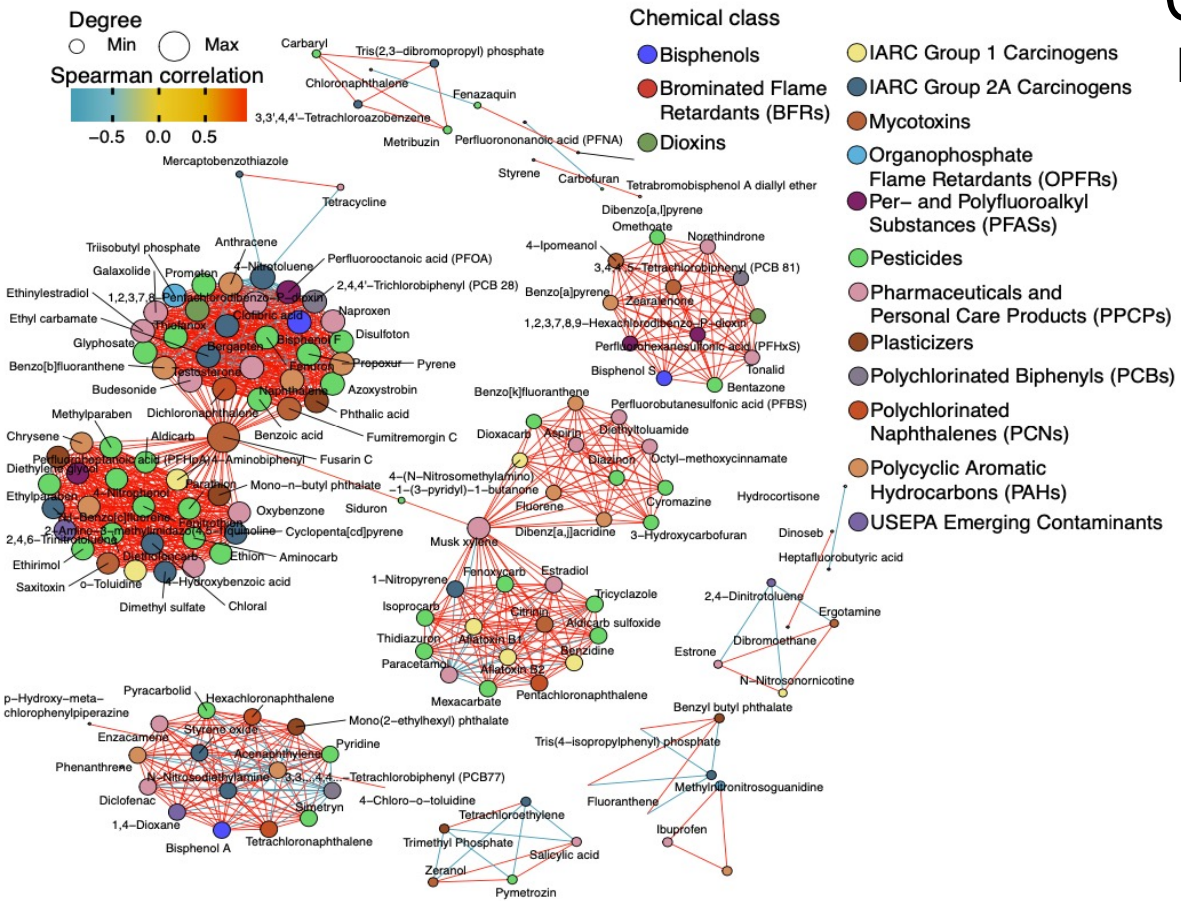



Fungicides or antifungal chemicals

# Chemical exposome

## Potentially 2796 chemicals

## 158 Annotated Chemicals

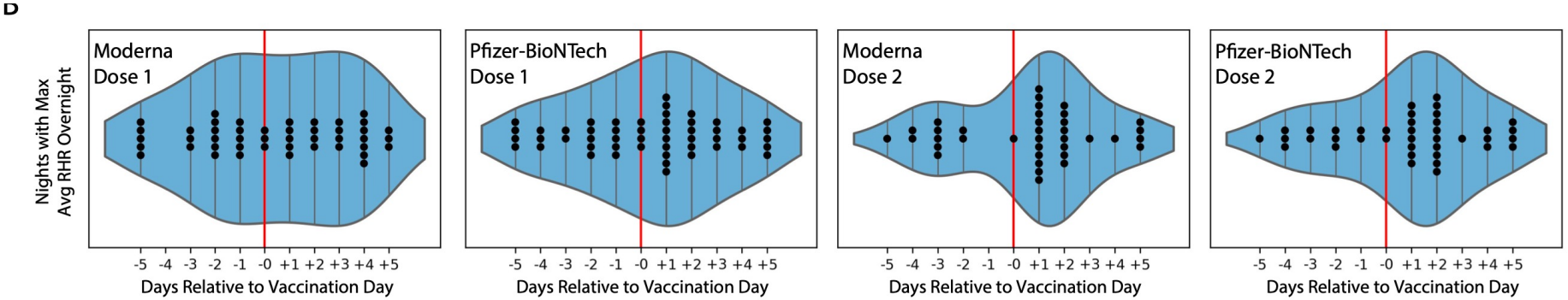


## Companies I Have CoFounded

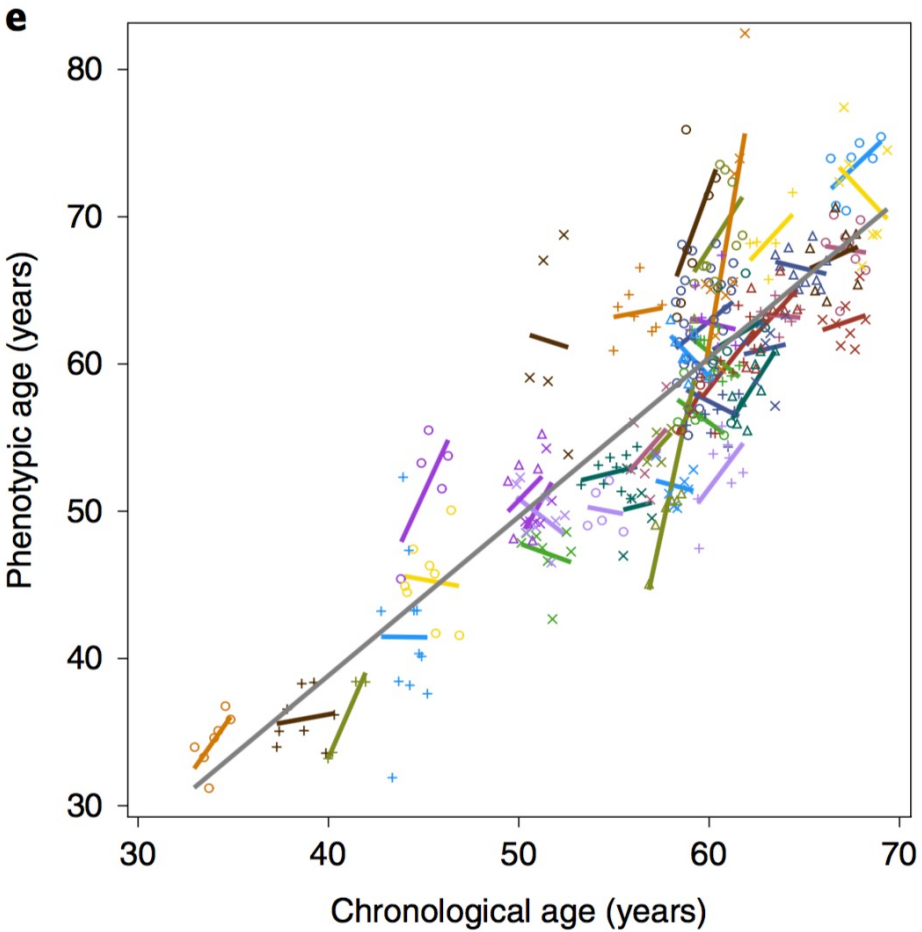
- Personalis:  Genomics Analysis
- Qbio:  Big Data and Health, including MRI
- January AI:  Metabolic Health
- Mirvie: Maternal Health
- Fodsel Inc: Preterm therapeutics
- SensOmics: Wearables
- Fitricine: Cancer nutrition

**+ others ….**

# Covid-19 vaccination effect on alerts



# Individuals Age At Different Rates




PLOS MEDICINE

**A new aging measure captures morbidity and mortality risk across diverse subpopulations from NHANES IV: A cohort study**

Zuyun Liu, Pei-Lun Kuo, Steve Horvath, Eileen Crimmins, Luigi Ferrucci, Morgan Levine

Published: December 31, 2018 • https://doi.org/10.1371/journal.pmed.1002718

*Phenotypic age:*

Chronological age and nine biomarkers, including albumin, creatinine, glucose, log (C-reactive protein), lymphocyte percent, mean cell volume, RDW, ALKP and white blood cell count

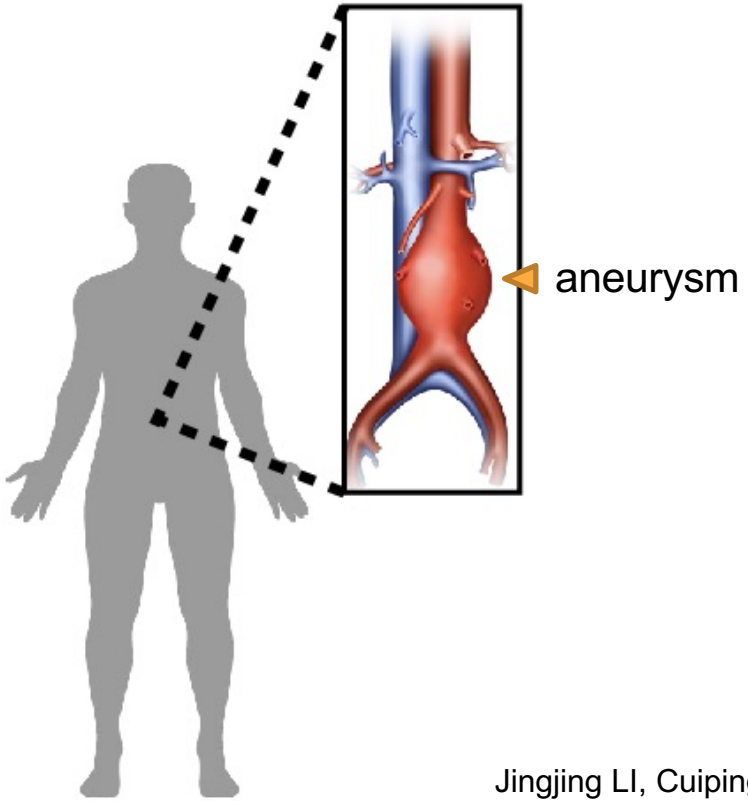
Ahadi, Zhou et al. Nat. Medicine 2020

# Polygenic Risk Score: Use 1000s to Millions of Common SNPs

| Disease | # SNPs |
|---|---|
| Coronary Artery Disease | 6.6M |
| Atrial Fibrillation | 6.7M |
| Type 2 Diabetes | 6.9M |
| Inflammatory Bowel Disease | 6.9M |
| Breast Cancer | 5.2K |

Khera et al. Nat Genet. 2018 50: 1219–1224

# Abdominal Aortic Aneurysm: High Prevalence and Mortality

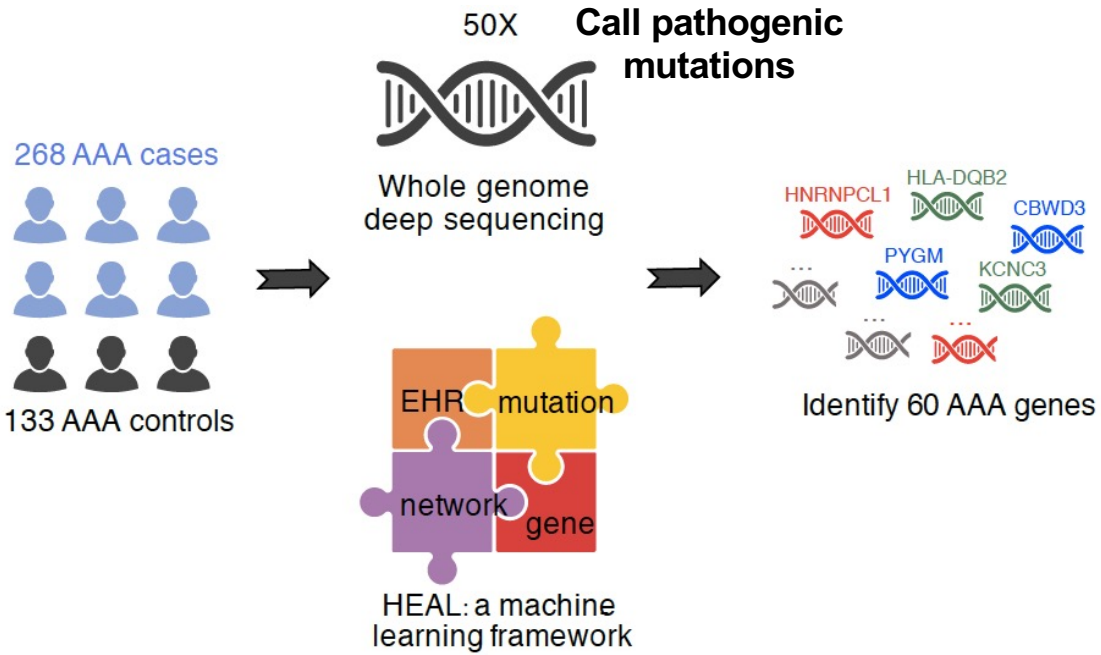



## Facts

1. affecting 10% of the aged population
2. the 13th leading cause of death (U.S.)
3. asymptotic as it grows
4. irreversible
5. >90% mortality rate upon rupture

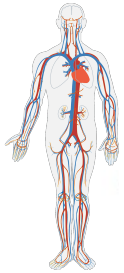
Jingjing LI, Cuiping Pan, Sai Zhang .. Phil Tsao, Cell 2018

# Identifying Genes Associated with AAA

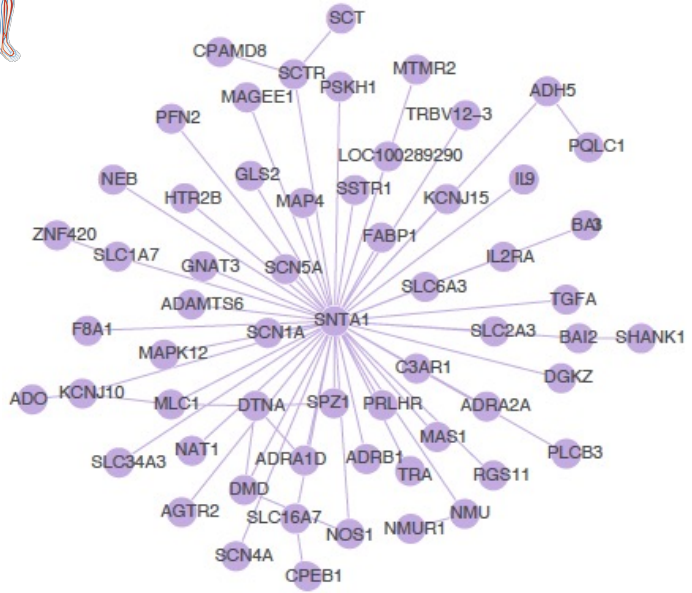



Jingjing LI, Cuiping Pan, Sai Zhang .. Phil Tsao, Cell 2018

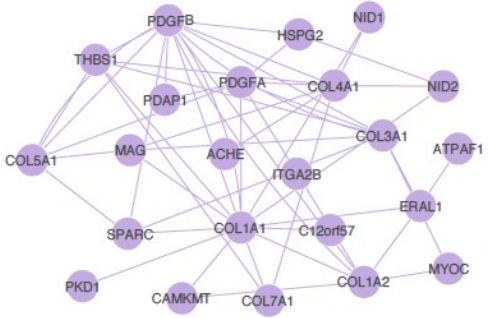
# Relevant Modules



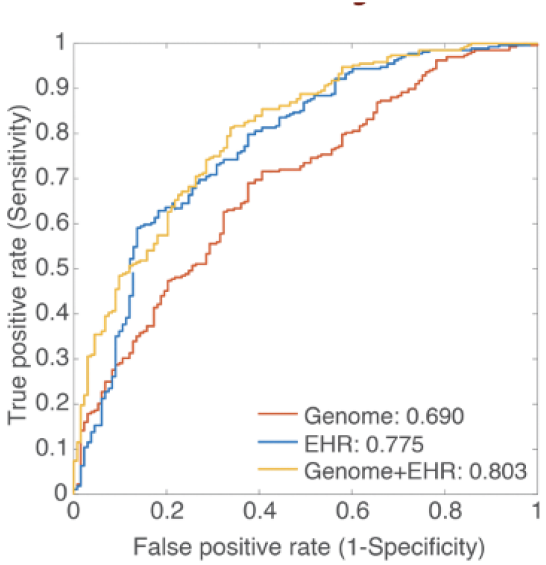
## Blood Circulation, Blood Pressure, Cardiomyopathy

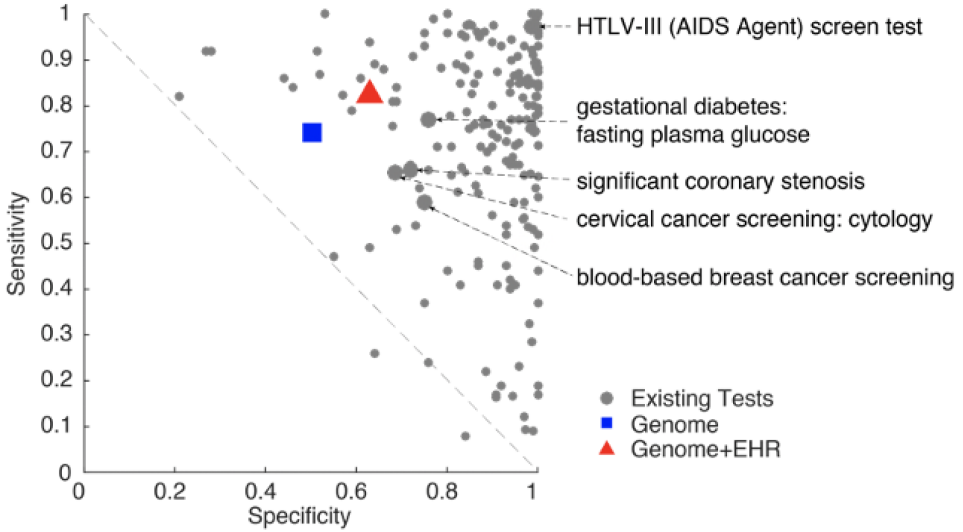



## Aneurysm



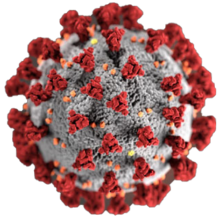
# HEAL accurately predicts AAA risk -> clinical utility



# The Host Genetics of ALS and COVID19 Severity Using ML

Sai Zhang, Johnathan Cooper-Knock



1. Combine GWAS signals with Open Regions in Motor Neurons:

   7 genes → 690 genes

2. Combine GWAS signals with open chromatin regions from lung:

   47 genes → 1370 genes

Sai Zhang, Johnathan Cooper-Knock .. Michael Snyder *Neuron* 2022

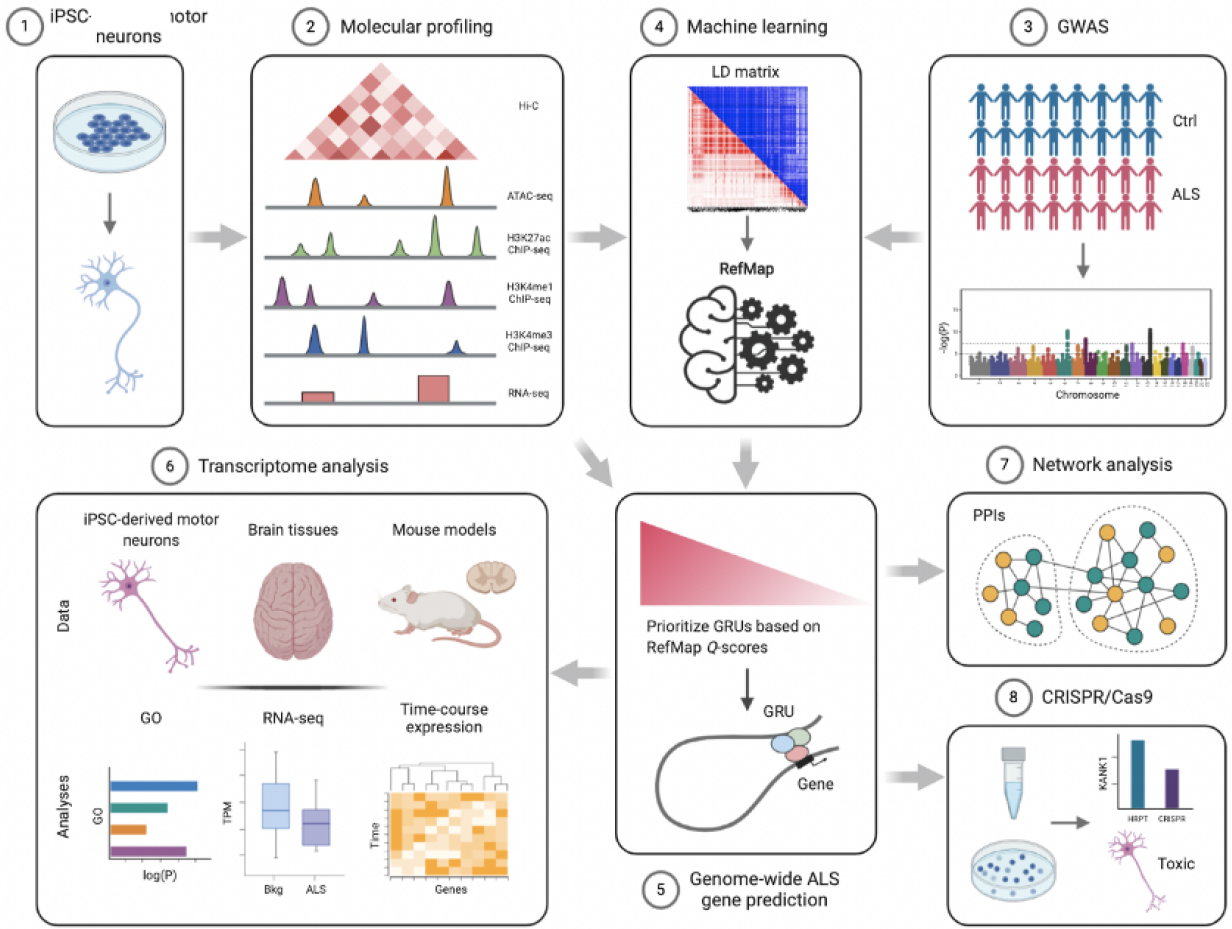
Zhang et al , *BioRixv 2021*

January AI slide

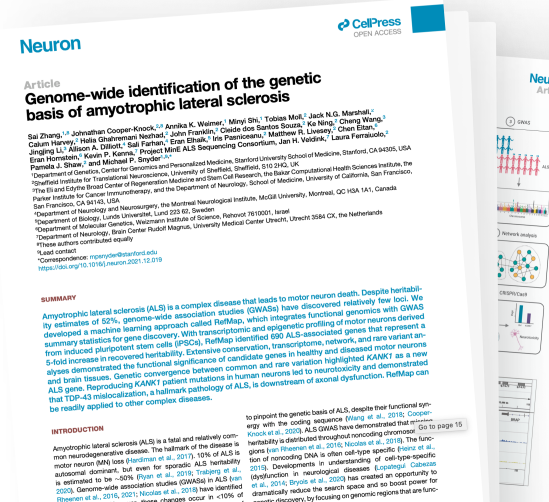
# Amyotrophic Lateral Sclerosis (ALS)

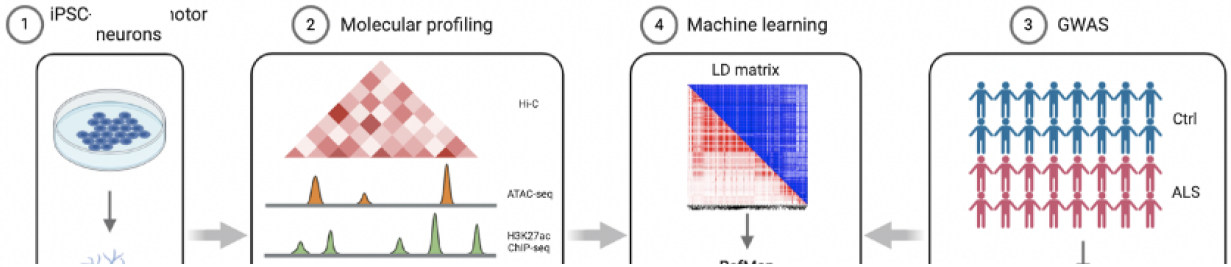
A neurodegenerative disease with motor neuron death leading to muscle weaken

- Estimated heritability of sporadic ALS = 61%
- Proportion of sporadic ALS patients with an identified genetic cause = <10%
- More ALS genes are missing




**RefMap**: A machine learning framework to discover novel disease genes



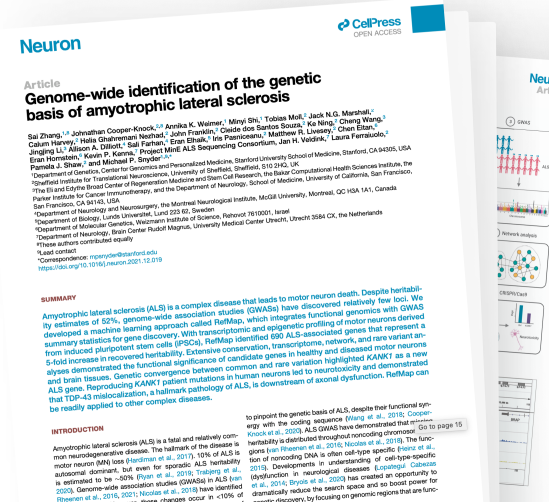



**RefMap**: A machine learning framework to discover novel disease genes

Found 690 Genes associated with ALS

→ 31% of heritability (5-fold inc.)

→ Showed motor neurons defects upstream of TDP-43



# Abdominal Aortic Aneurysm (AAA)

Article

Cell

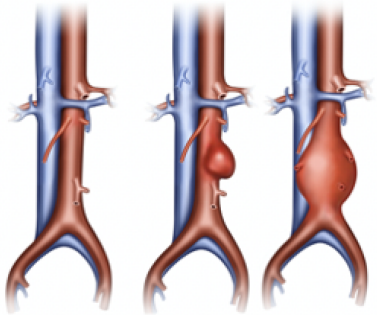
**Decoding the Genomics of Abdominal Aortic Aneurysm**

Jingjing Li,[1,2,6,7] Culping Pan,[1,3,6,7] Sai Zhang,[1,4,7] Joshua M. Spin,[3,4,5] Alicia Deng,[3,4,5] Lawrence L.K. Leung,[3,4,5] Ronald L. Dalman,[3,5] Philip S. Tsao,[1,4,5,*] and Michael Snyder[1,5,8,*]

[1]Department of Genetics, Center for Genomics and Personalized Medicine, Stanford University School of Medicine, Stanford, CA 94305, USA

## Clinical Facts

- Asymptomatic at onset - fast growing
- 90% mortality rate upon rupture
- The 10th leading cause of death in US
- **No early screening tool**

## Epidemiology

- **Heritability: 70%**
- Aged population >50 yo.
- Lifestyle matters
- High blood pressure
- Cholesterol etc