SomaLogic

Discovery and Validation of protein signatures for NAFLD risk and NASH status

February 2020

Stephen A Williams MD PhD

©2020 SomaLogic, Inc.

1

SomaLogic

©2019 SomaLogic, Inc.

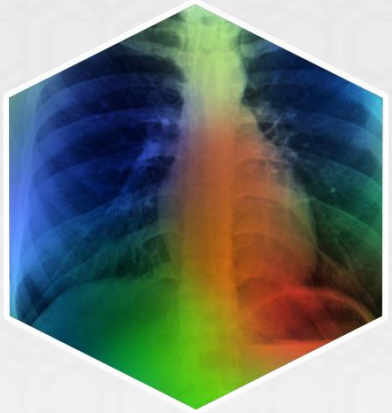
What will be the single most dominant source of information for disease prevention and patient care in 5-10 years?

wearables

or

Health records with AI

or

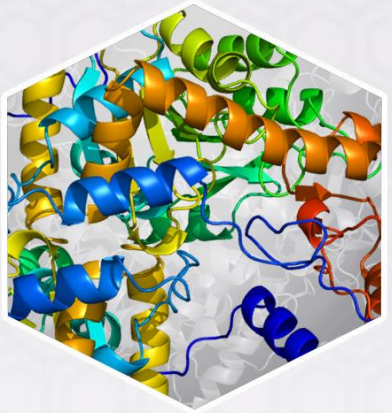


imaging

or

genetics

or



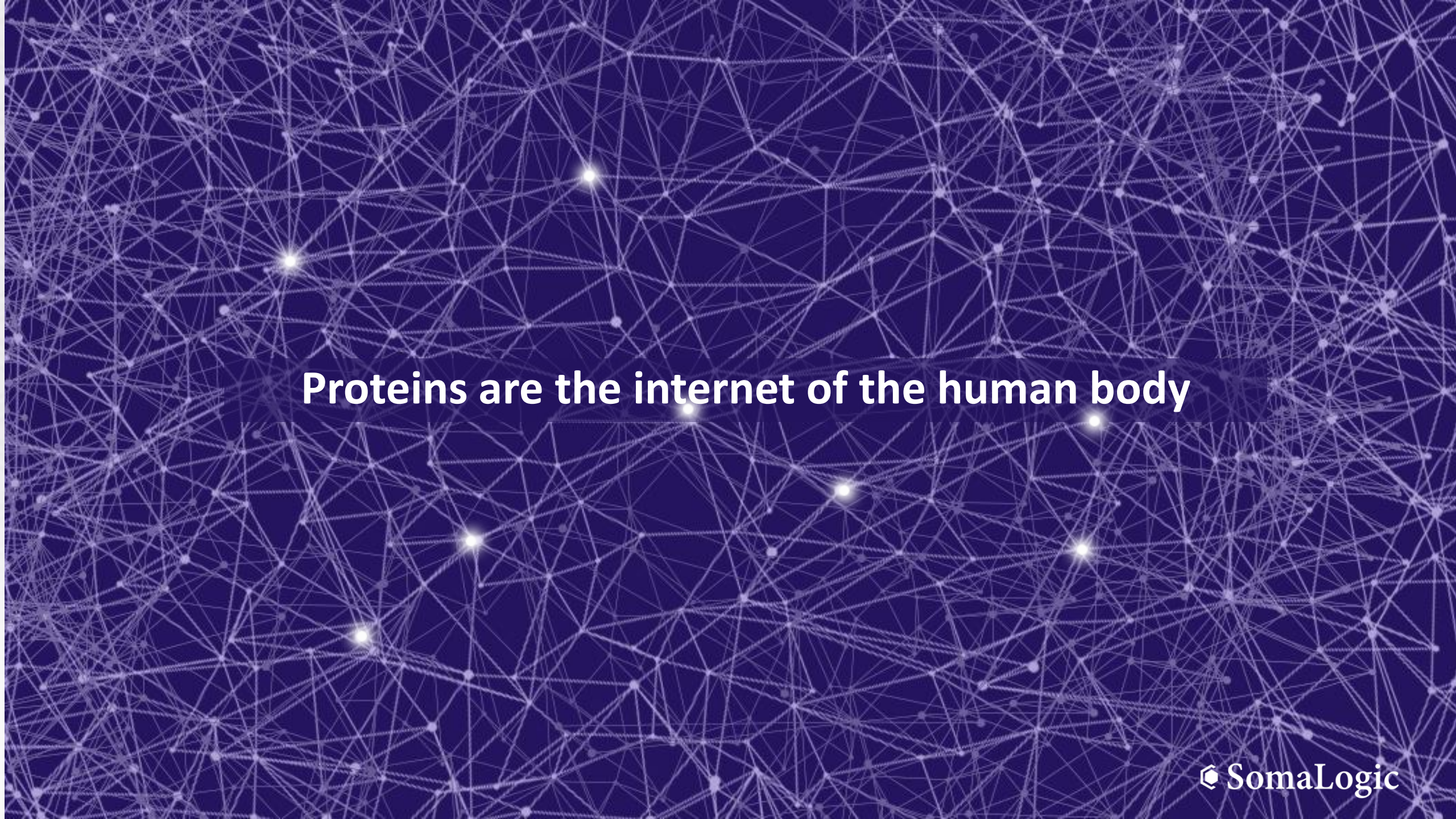
proteins

©2020 SomaLogic, Inc.

SomaLogic

Proteins mediate the effects of all known drugs

SomaLogic


Proteins are the internet of the human body
SomaLogic

But existing methods of interrogating proteins are archaic

= I T ’ S

= H A R D !

©2020 SomaLogic, Inc.

SomaLogic

Interrogate the body's internet:

BANDWIDTH

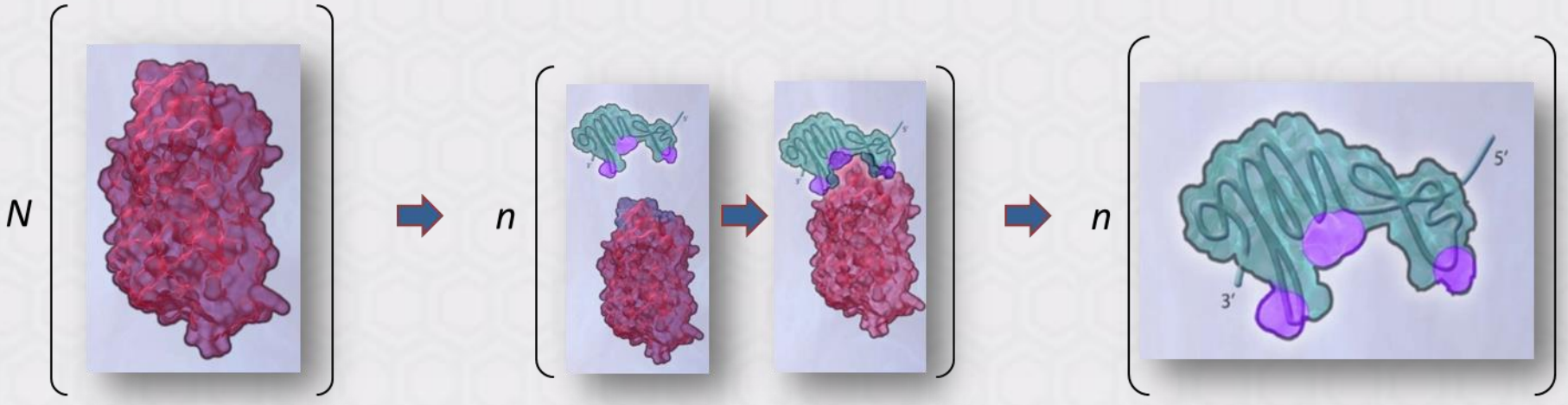
SomaScan platform

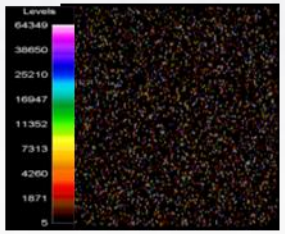
SEARCH ENGINE "APPS."

SomaSignal tests

©2020 SomaLogic, Inc.
SomaLogic

SomaScan principles





©2020 SomaLogic, Inc.

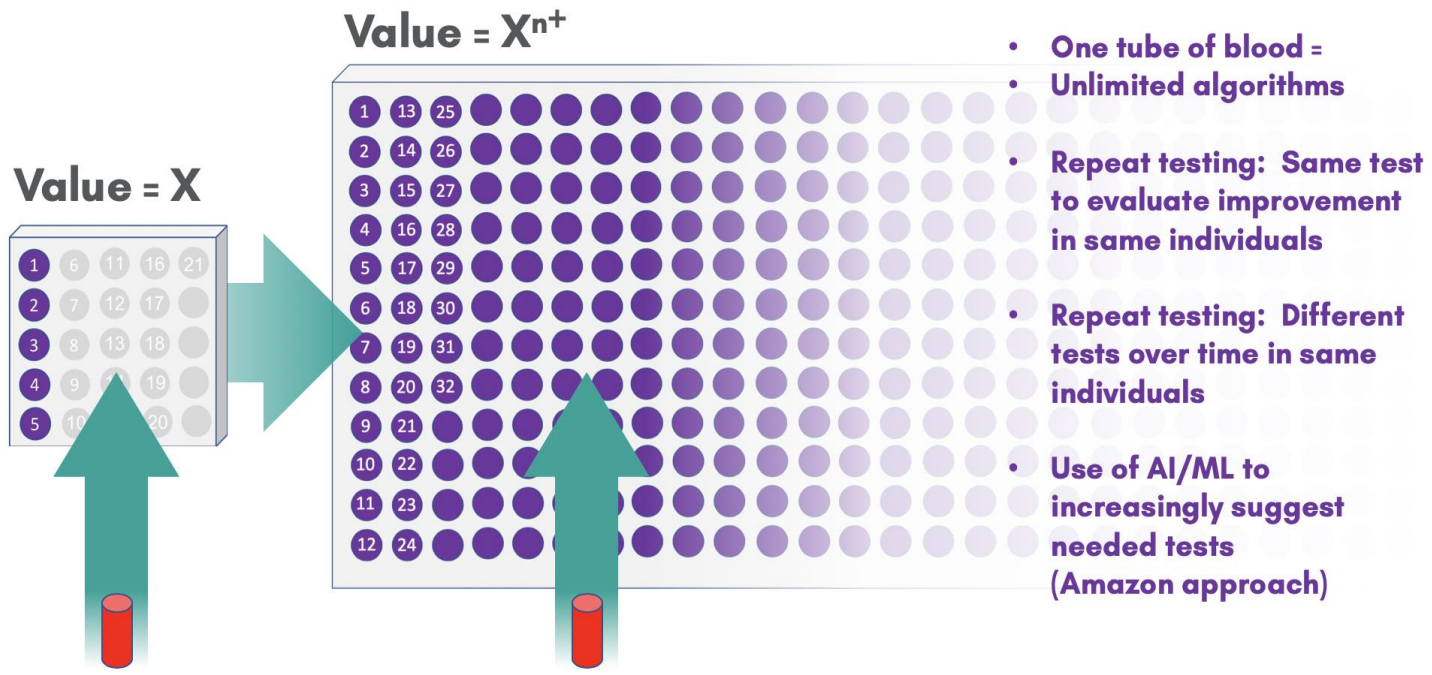
Scaling of Health “Apps.” on the SomaScan platform

“Medical devices as software”

Process for test development:

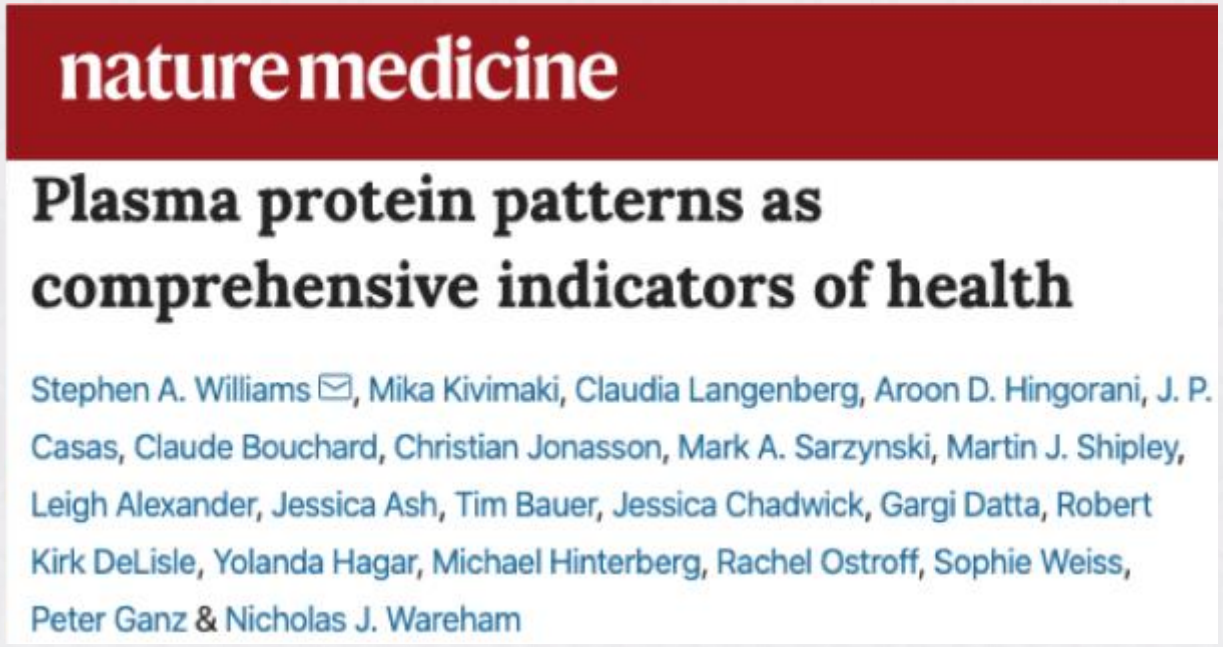
1. Select the best truth-standards
2. Get clinical samples and data
3. Document statistical plan: “virtual prospective studies” on retrospective samples
4. Assay the samples on SomaScan
5. Use machine learning to derive patterns of the truth standard
6. Refine and finalize the model
7. Validate on independent data
8. Embed as software “app” on the platform

SOMAsignals™ is a biotechnology product that scales like a digital platform



©2020 SomaLogic, Inc.
SomaLogic

One sample reveals insight into multiple health issues



- liver fat
- kidney function
- percent body fat
- visceral fat
- lean body mass
- cardiopulmonary fitness
- physical activity
- alcohol consumption
- cigarette smoking
- diabetes risk
- primary cardiovascular event risk

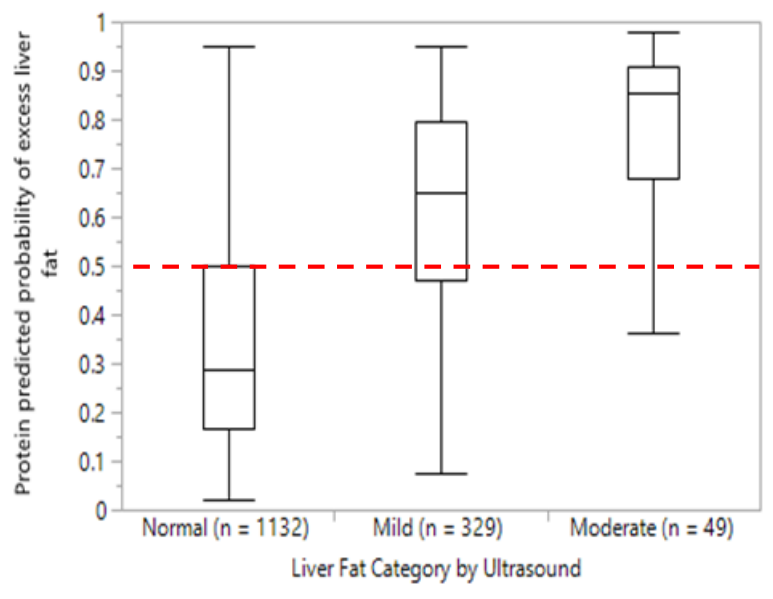
- SomaScan Platform measured ~5000 proteins in plasma samples from nearly **17,000 patients** and **85 million** measurements
- Protein-based models were as good or better than models based on traditional risk factors.
- Large-scale protein scanning could provide a comprehensive, **one-stop "liquid health check" for personalized, holistic health assessment.**

©2020 SomaLogic, Inc.
SomaLogic

Individualized risk factors & NAFLD (1)

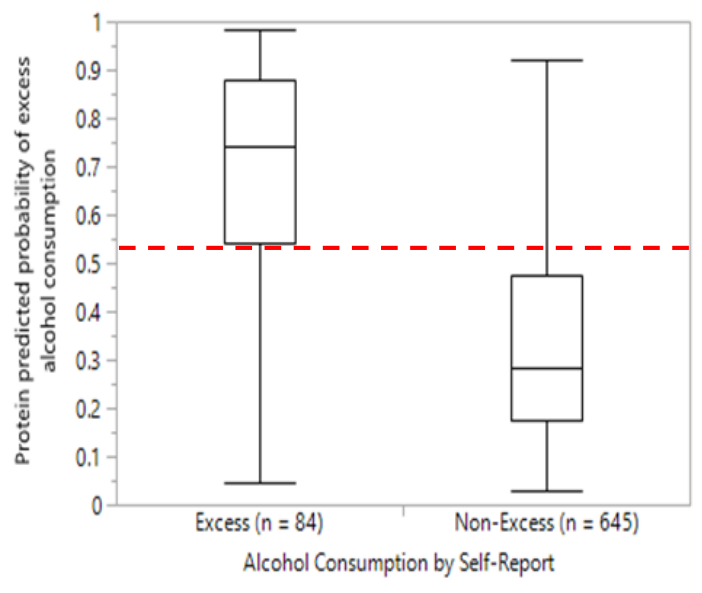
Protein predictions vs. truth standards (validation datasets)

Liver fat vs. ultrasound



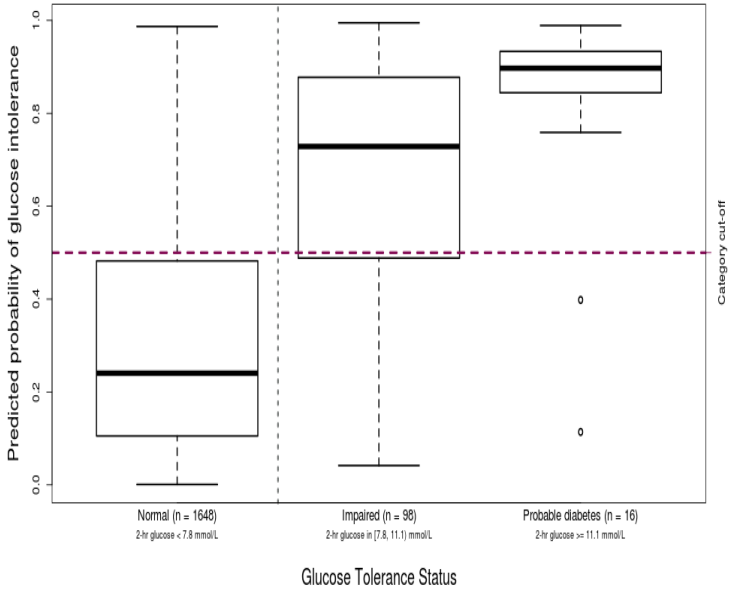
94 protein model

Alcohol > 7 drinks (US) or 14 units (UK) per week



33 protein model

Glucose tolerance



42 protein model

Normal/abnormal threshold

©2020 SomaLogic, Inc.

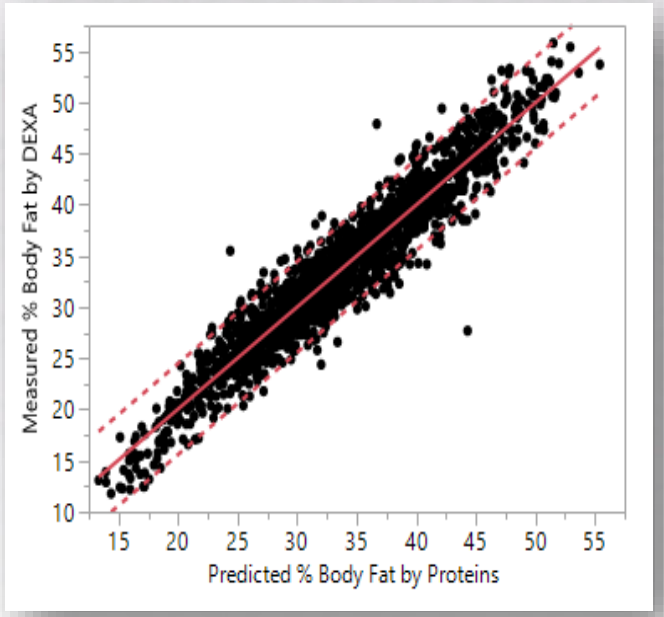
10

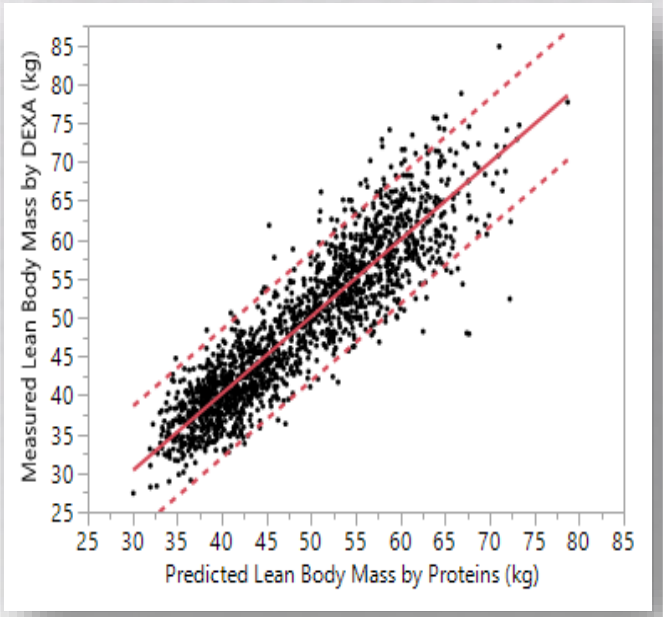
SomaLogic

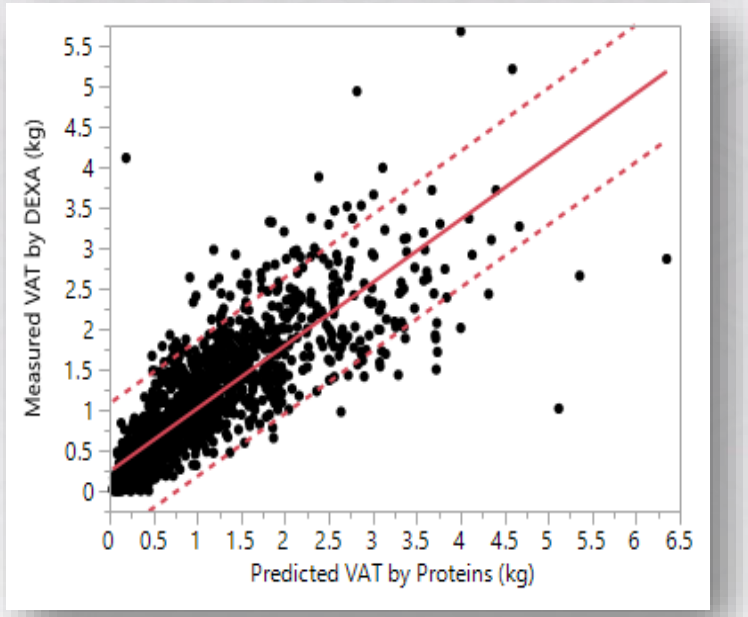
Individualized risk factors for NAFLD (2) Body Composition

Protein predictions vs. truth standards (validation datasets)

- **Key sources of data:**
  - UK cohort: 11,471 subjects with DEXA scan results
  - Validation results are shown: r squared 0.91, 0.82, 0.71 respectively
  - Protein models contain 219,115 and 96 proteins respectively







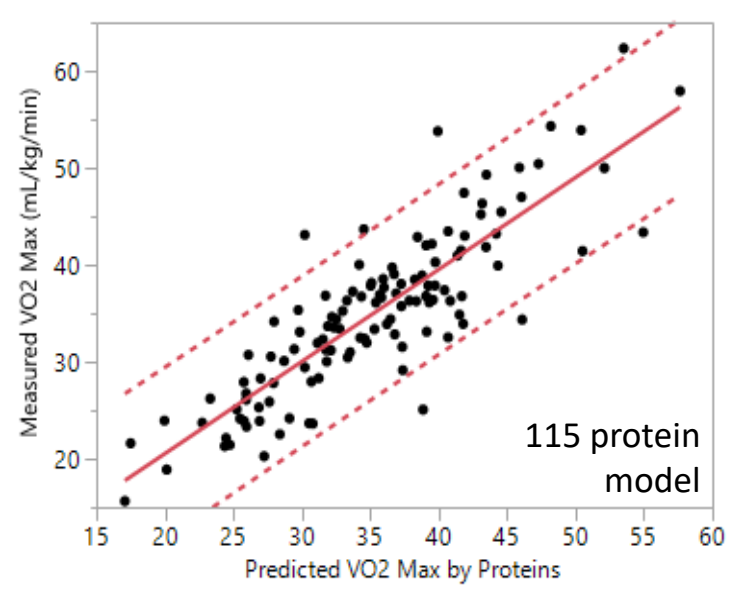
Charts show results in the validation fraction

©2020 SomaLogic, Inc.
SomaLogic

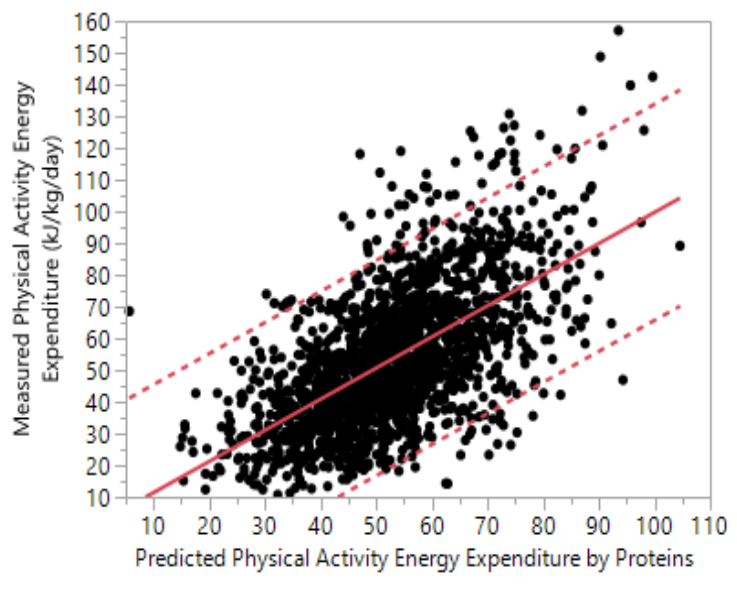
Individualized risk factors for NAFLD (3): Fitness, Activity

Protein predictions vs. truth standards (validation datasets)

Cardio-respiratory fitness vs. VO2 max



Weekly physical activity

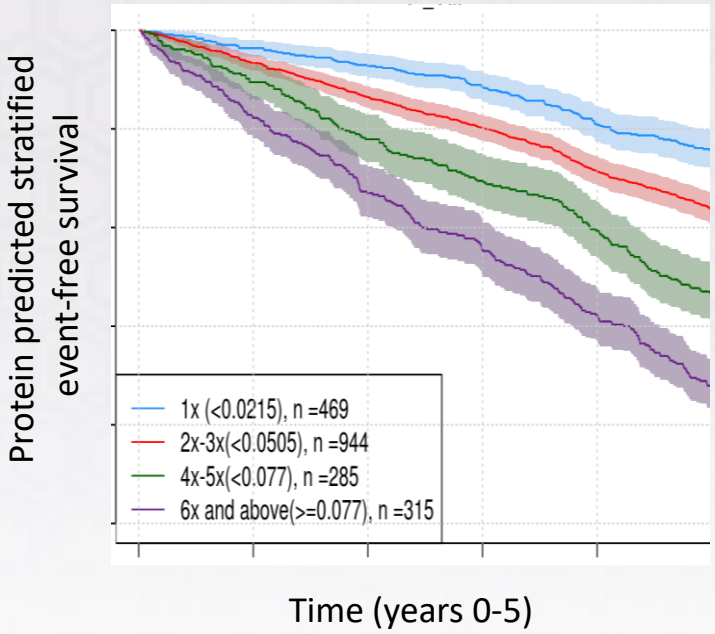


©2020 SomaLogic, Inc.
SomaLogic

Protein predictors of future cardiovascular events:

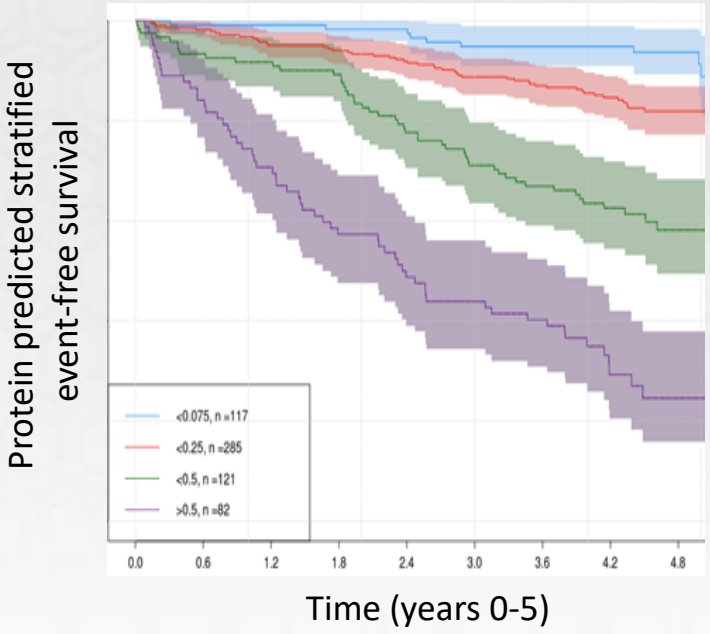
"Cardiovascular disease is the single most important cause of death in NAFLD and NASH"

Risk of Primary Heart attack, stroke, heart failure or death*



*For clarity, this view for CV primary risk is enriched for events ~10x above natural prevalence

Risk of Secondary Heart attack, stroke, heart failure or death



©2020 SomaLogic, Inc.

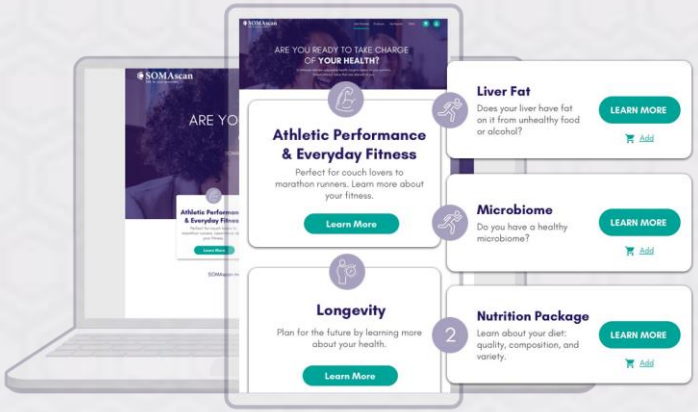
Moving into commercialization: First 10 tests are available in self-pay medical practices

Test report – 10 test

- Patient's personalized test results
- Explanation of disease states and potential next steps

Test overview booklet

- Overview of the SomaScan platform, the tests, and disease states



Digital interface

- Coming soon
- Interactive mobile / web interface where patients can view test results and learn more about tests, results and next steps
- Monitor progress over time

©2020 SomaLogic, Inc.
SomaLogic

Today's SomaSignal "Apps."

SomaLogic

Jacob Souvenir
Accession Number: A00007

Your Test Result Summary

Primary Cardiovascular Risk — 4 years
What is my risk of having a heart attack, stroke, or heart failure within the next 4 years?

Secondary Cardiovascular Risk — 4 years
What is my risk of having another issue with my heart or having a stroke in the next 4 years?

Liver Fat
Do I have excess fat in my liver?

Glucose Tolerance
If I have simple sugars, does my blood glucose spike to unhealthy levels?

Alcohol Impact
Is my body showing the effects of my weekly alcohol consumption?

Cardiorespiratory Fitness — VO_2 Max
What is my aerobic fitness level?

D0004229 Rev 1

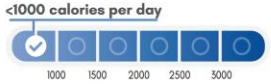
page 2 of 16

SomaLogic

Jacob Souvenir
Accession Number: A00007

Your Test Result Summary (continued)

Resting Energy Rate
How many calories does my body burn at rest when I am not doing physical activity?



Body Fat Percentage
What is my body fat percentage?

Visceral Fat
How much fat is around my organs?

Lean Body Mass
What is my lean body mass?

D0004229 Rev 1

page 3 of 16

©2020 SomaLogic, Inc.

SomaLogic

NASH: Objectives of collaboration with NASH CRN

- Aim 1: To develop and validate protein models predicting each component of the liver biopsy that are robust to the presence/absence of active pharmacologies and presence/absence of diabetes:
  - Steatosis (0 vs. 1, 2 or 3)
  - Inflammation (0 or 1 vs. 2 or 3)
  - Hepatocyte ballooning (0 vs. 1 or 2)
  - Fibrosis (0 or 1a, 1b, 1c vs. 2, 3 or 4)
- Aim 2: To determine the models' ability to measure longitudinal change during therapy
- Aim 3: To develop protein models that are prognostic of future change

- Current status:
  - ~3500 samples from 636 participants have been SomaScanned (~5000 proteins, 17,500,000 measurements)
  - Bioinformatics, **model development and validation is complete** and under review by the NASH CRN; representative Joel Lavine, U. Columbia
  - Summer 2020: RUO application to batched sample sets with serum
  - End 2020: CAP/CLIA application to individual patients

©2020 SomaLogic, Inc.

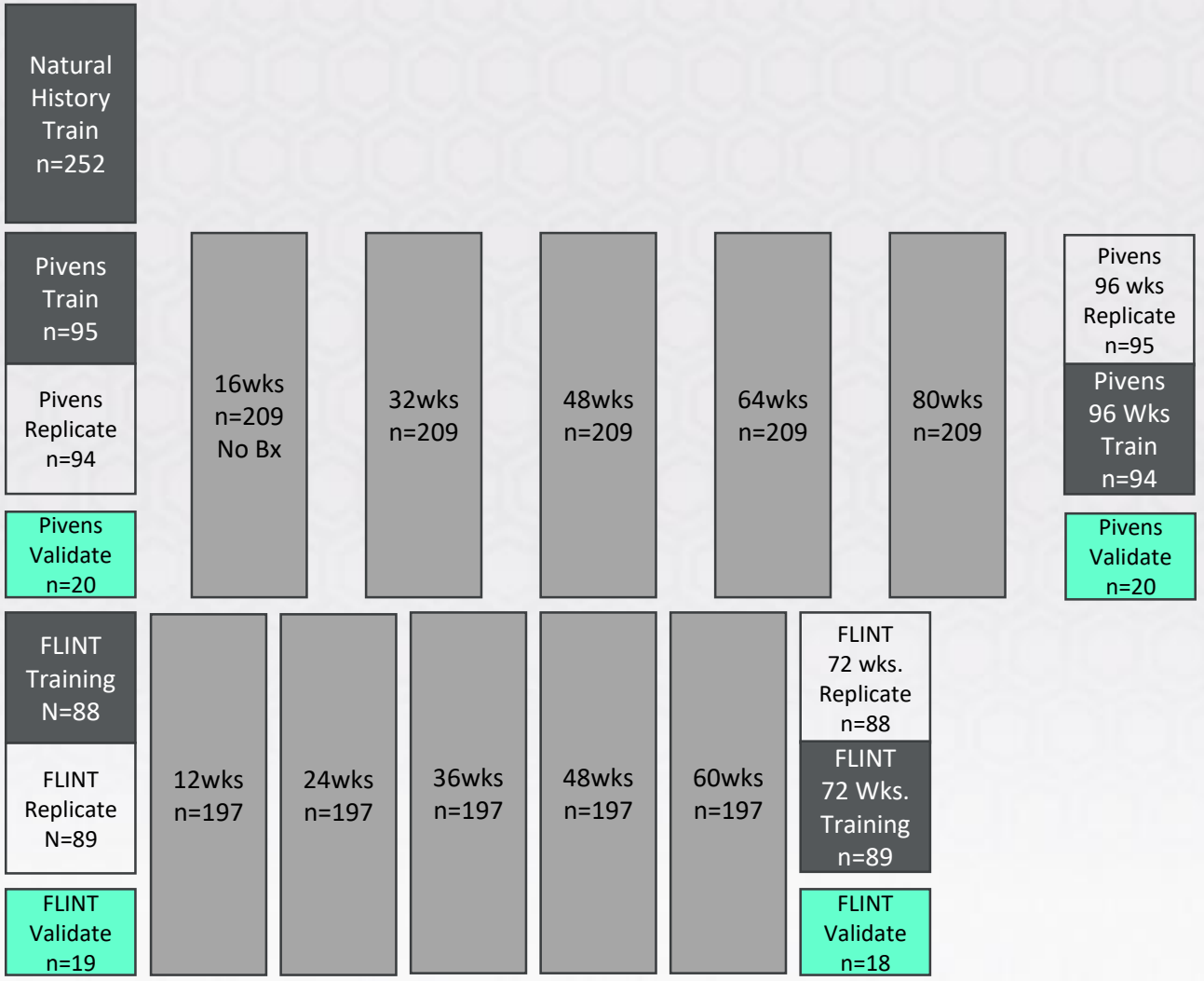
NASH CRN Program Design; 5000-plex assay; Serum

Key

Dark blue = training with Bx* results
White = replication with Bx results
Light blue = validation with Bx results
Gray = monitoring without Bx results

Pivens
Placebo vs. piaglitazone vs. vitamin E

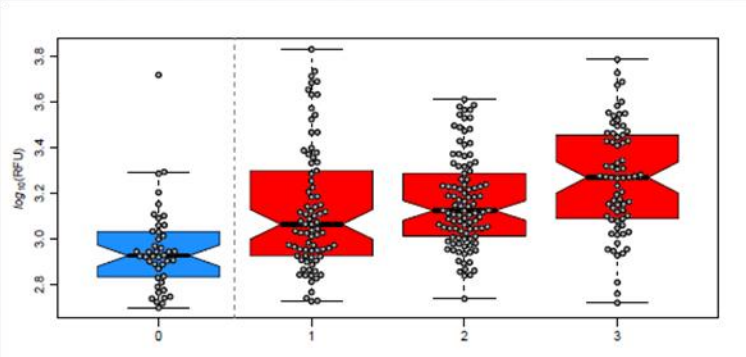
FLINT
Placebo vs. obeticholic acid



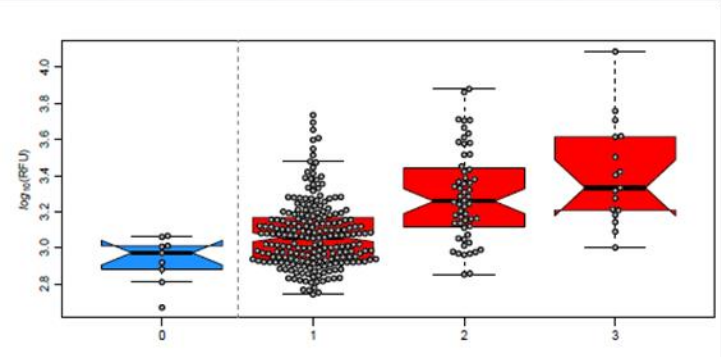
*Bx = group consensus reads by NASH CRN expert pathologists

©2020 SomaLogic, Inc.

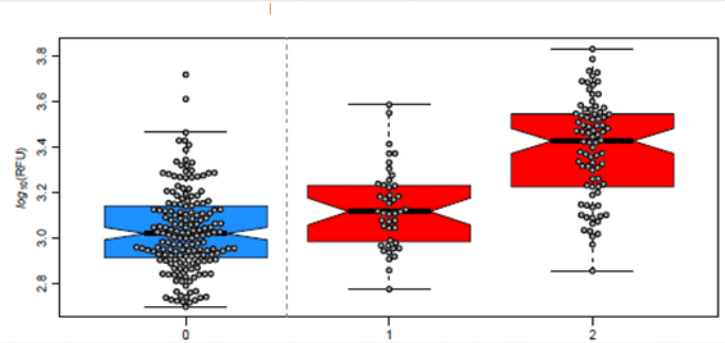
Prior/public results on natural history study (1129 plex assay)



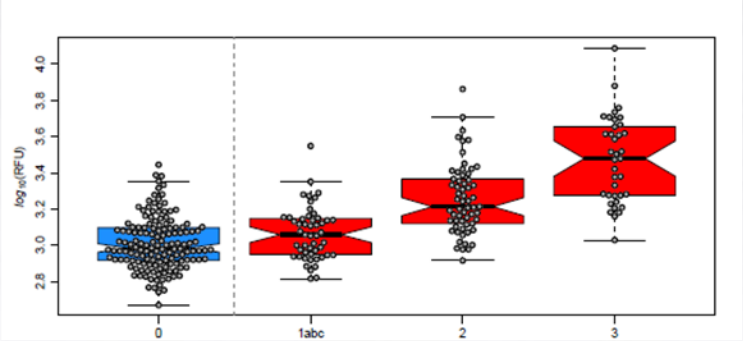
Steatosis proteins



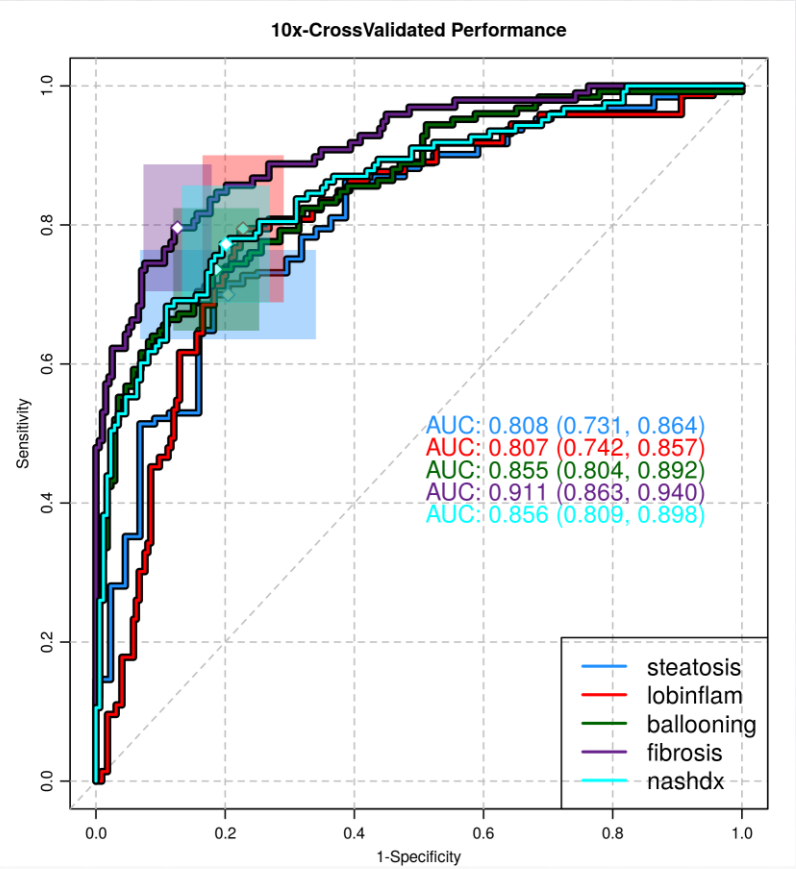
Inflammation proteins



Hepatocyte Ballooning



Fibrosis proteins



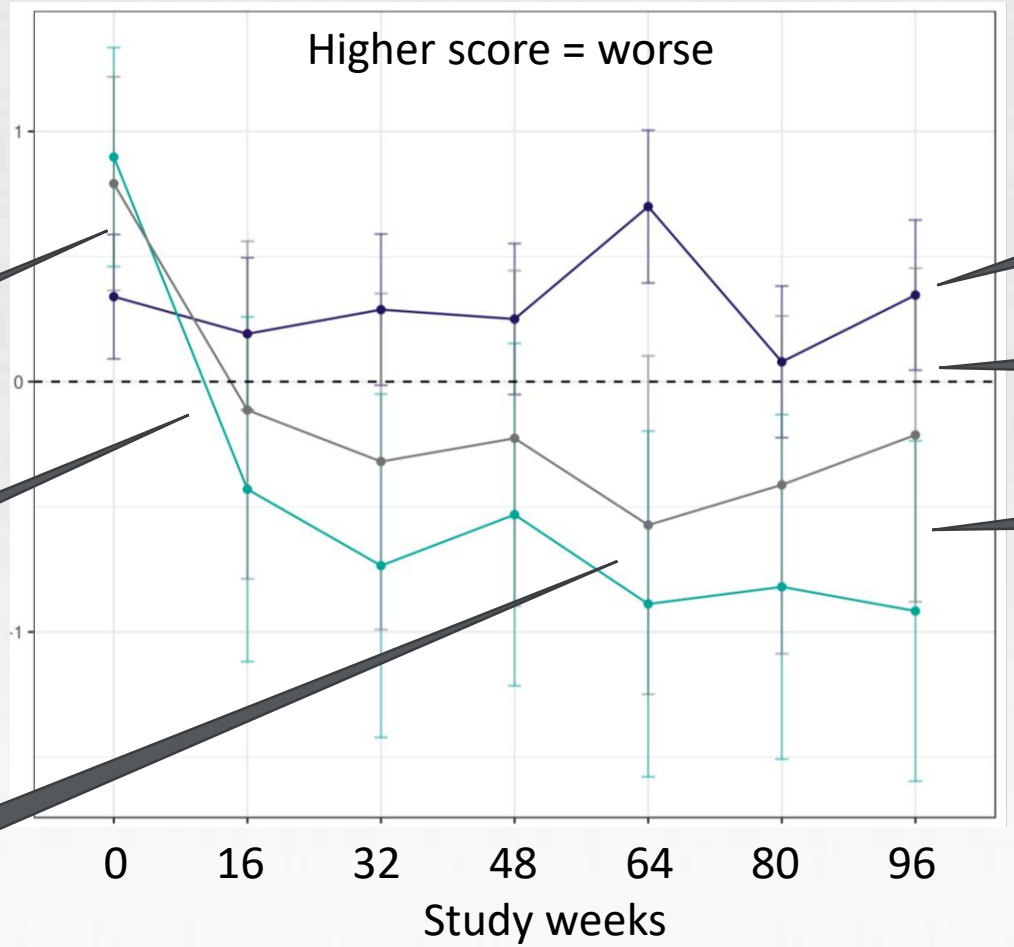
Multi-protein model results (AUC)

©2020 SomaLogic, Inc.
18
SomaLogic

What does longitudinal noninvasive monitoring look like?
e.g. tracking continuous model outputs (hypothetical data)

Dichotomized models have continuous probability outputs for crossing a threshold:

- Steatosis (0 vs. 1, 2 or 3)
- Inflammation (0 or 1 vs. 2 or 3)
- Hepatocyte ballooning (0 vs. 1 or 2)
- Fibrosis (0 or 1a, 1b, 1c vs. 2, 3 or 4)



Meets eligibility for the trial?

Early interim analysis?

Time to maximum drug effect; plateau reached?

Stability of placebo group?

Active vs. placebo differences

Drug or dose A vs. Drug B differences

Available mid 2020

©2020 SomaLogic, Inc.

SomaLogic

Robust Commercial Product Pipeline of 100+ Tests

Any test, or combination of all available tests can be run on any patient from one biological sample

Launched (Q4:2019)

Preventative Medical

Primary CV risk – 4 year
Secondary CV risk – 4 year
Liver fat
Glucose tolerance

Health/Wellness

Resting energy rate
Cardiorespiratory fitness/VO_2 max
Alcohol impact
Body fat percentage
Visceral fat
Lean body mass

Available 2020-2021

Disease Management

NASH: 4 liver biopsy components
Cancer susceptibility (top 4)
Kidney disease prognosis
Congestive heart failure prognosis
Congestive heart failure type
Rule-out symptomatic coronary heart disease
Statin adherence

Preventative Medical

eGFR (kidney function)
Predict type II diabetes diagnosis with complications
GLP-1 agonist response
Coronary artery calcium surrogate

Health/Wellness

Healthspan
Lifespan
Sleep quality
Alzheimer's/dementia risk
Cognitive function
Biologic/functional age
Social deprivation
Smoking status
Physical activity
Body weight trajectory
Bone mineral mass
Insulin sensitivity

Available 2022+

Disease Management

CHF therapy sensitivity
Cancer early detection
COPD risk/risk of progression
Pulmonary function

Preventative Medical

CV risk (all-comers multiple subtypes)
Cancer risk (top 15)
Functional status/ability w/aging

Health/Wellness

Circadian cycle
Reproductive health
Cognitive trajectory
Depression/mood w/aging
Frailty
Grip strength w/aging
Mental stress
Inflammatory load
Microbiome diversity
Diet change/hypertension correlation
Joint health

©2020 SomaLogic, Inc.

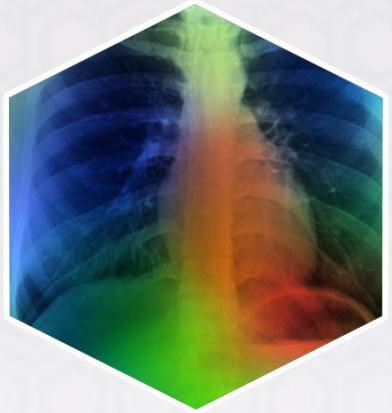
What will be the single most dominant source of information for disease prevention and patient care in 5-10 years?

wearables

or

Health records with AI

or

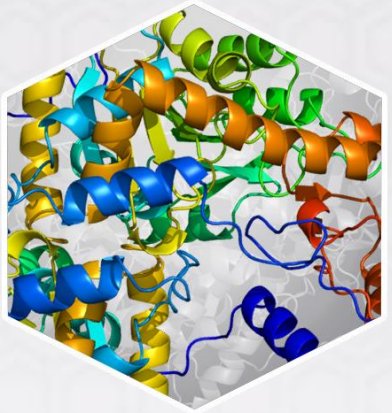


imaging

or

genetics

or



proteins

©2020 SomaLogic, Inc.

SomaLogic