An Environmental Biodynamics Approach to Develop Biomarkers of Autism Spectrum Disorder

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Mount Sinai

Conflict of Interest

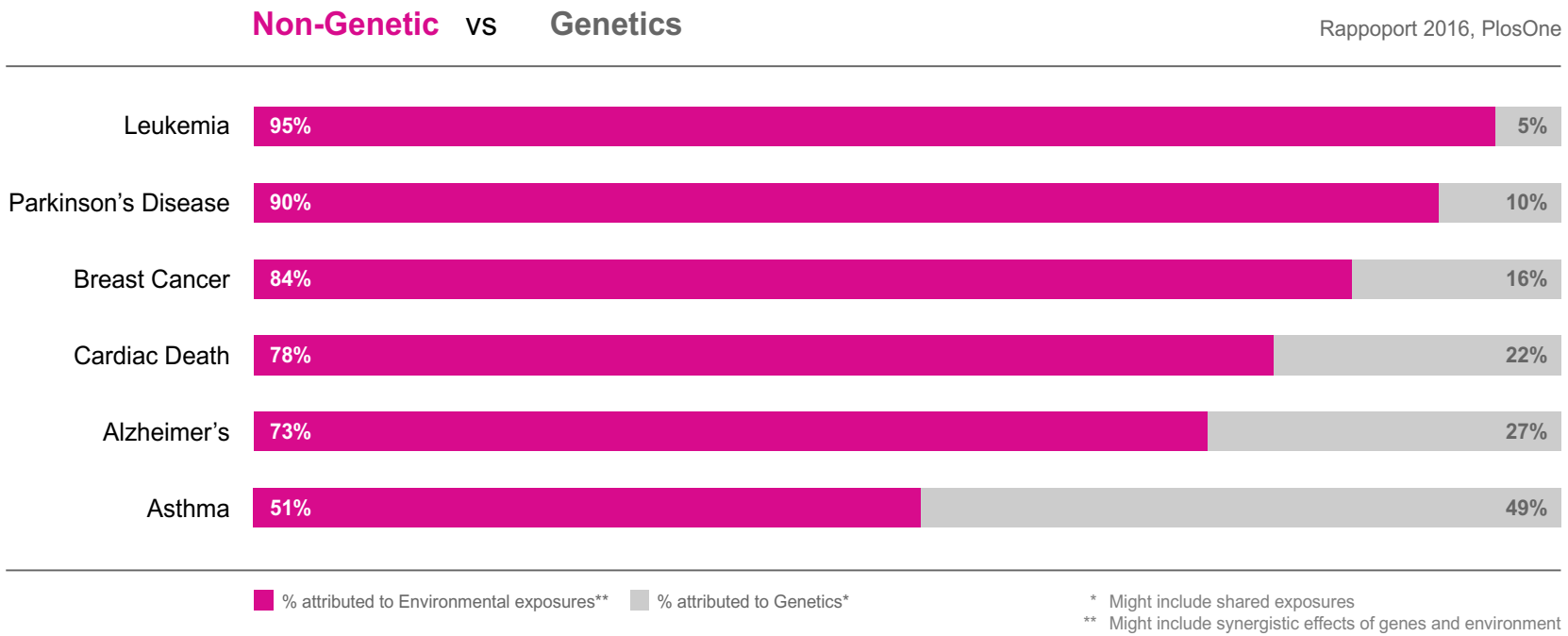
Manish Arora's conflict of interests are listed below and are managed by the Icahn School of Medicine at Mount Sinai in keeping with institutional guidelines.

- Mount Sinai holds patents for technology to be described in this presentation. Dr. Arora is listed as inventor

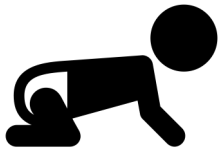
- Mount Sinai undertakes technology transfers for the technology discussed in this presentation. Dr. Arora is listed as PI on these technology transfers

- Mount Sinai partners with private, academic and not-for-profit groups to undertake commercial/for-profit endeavors (e.g. private labs, start-ups, etc). Dr. Arora is listed as inventor/co-founder of Linus Biotechnology Inc.

What role does the environment play in precision medicine?



Precision Environmental Medicine



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- SES
- Lifestyle
- Environmental exposures (in the broadest terms)
- Genetic profile
- Etc…..

?

Actionable information?

- Accurate prediction of disease risk in future (e.g. what is their risk of autism?)
- Which biochemical pathways should be targets for treatment development?
- Prioritize prevention
- Etc….

The environment is dynamic at different scales of time

Environmental Biodynamics

“Gene x Environment” paradigm is incomplete

$$\text{Health} = G \times E$$

“Complex systems cannot interact directly or exist in isolation”
- Curtin, Arora et al. 2021

Environmental Biodynamics

Health = G x **Time** x E

BioEssays

Hypothesis | Open Access

Biodynamic Interfaces Are Essential for Human–Environment Interactions

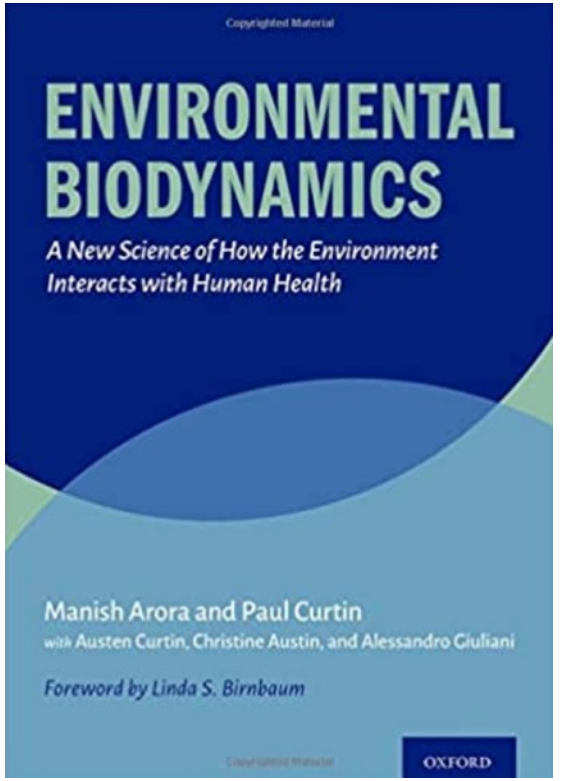
Manish Arora, Alessandro Giuliani, Paul Curtin

BioEssays

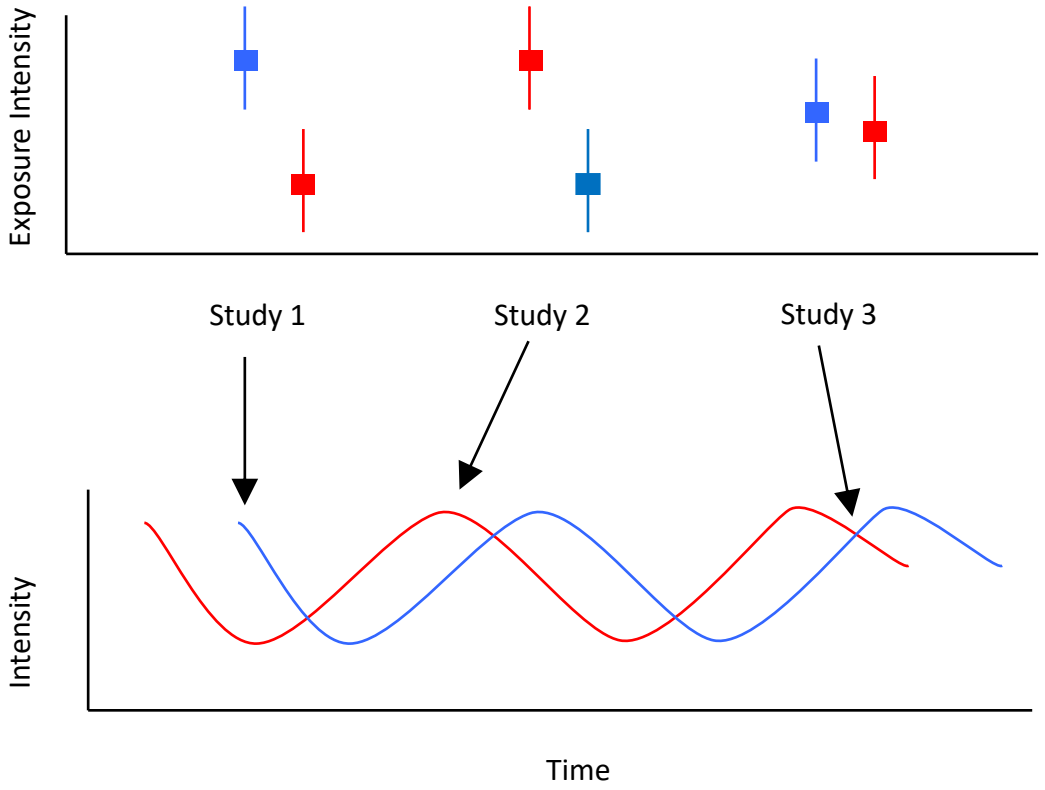
Idea to watch

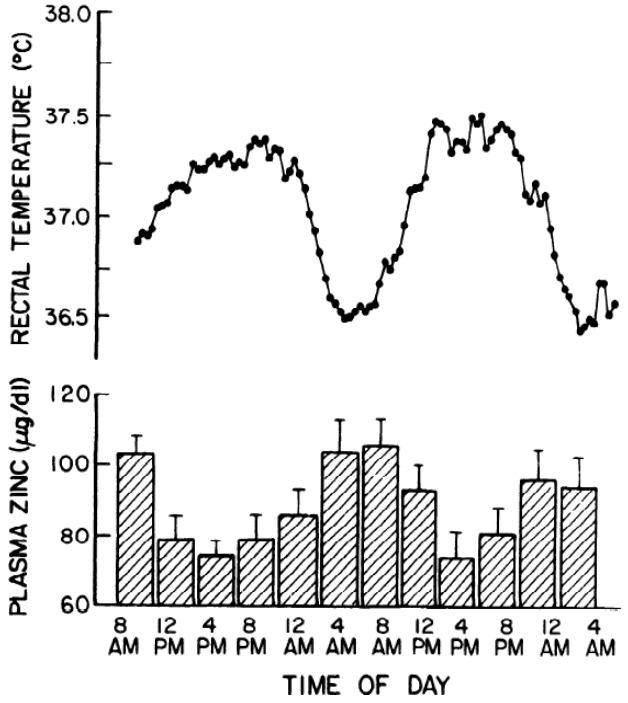
Environmental Biodynamics: A Bold New Frontier

Erin N. Haynes



Ignoring biodynamic interfaces





Scales et al. 1985

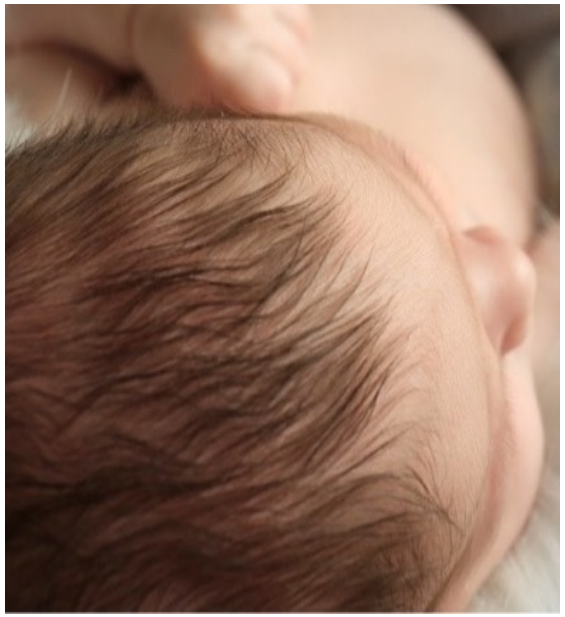
The challenge of measuring past exposure

Exposure timing…..retrospectively?!

Growth rings in a tree

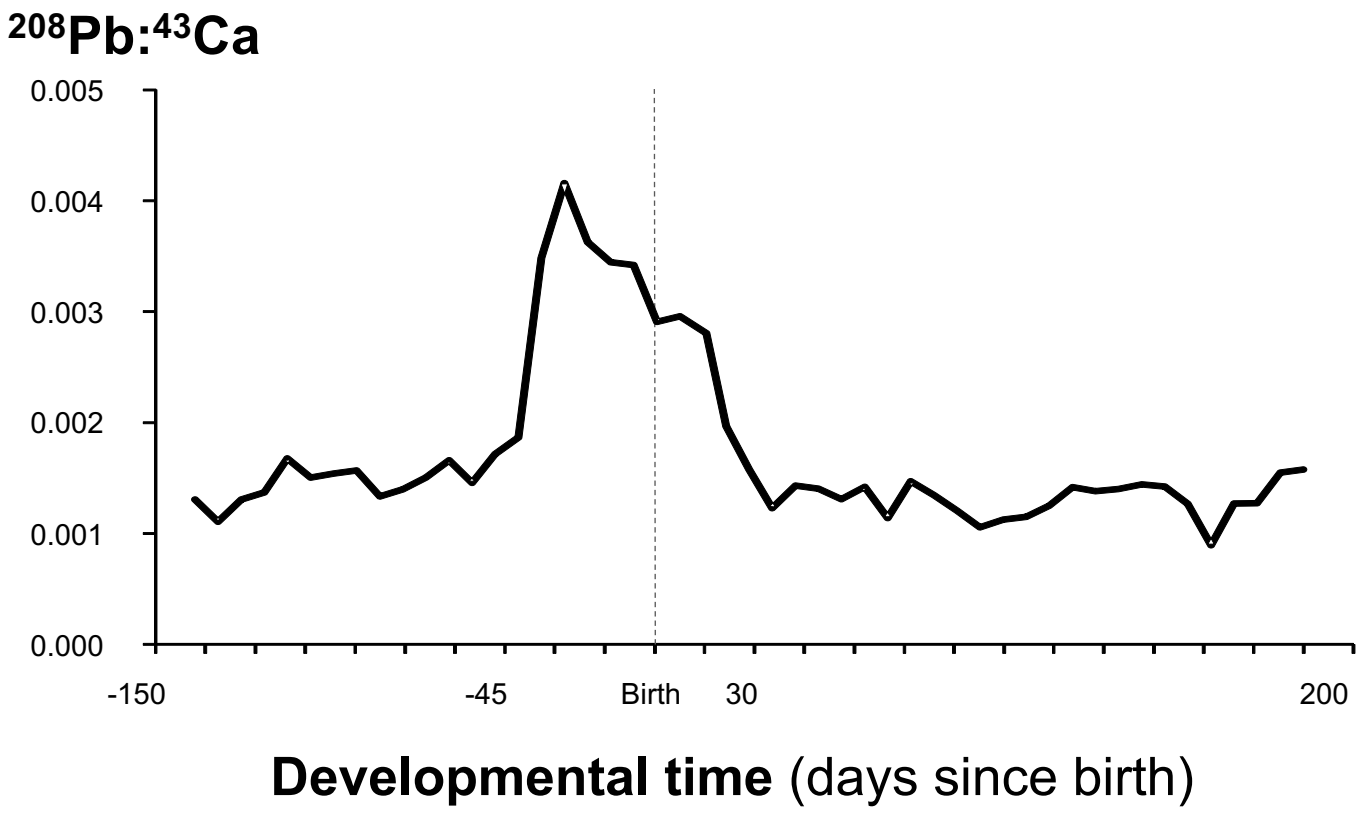
Growth rings in teeth

Growth rings in hair



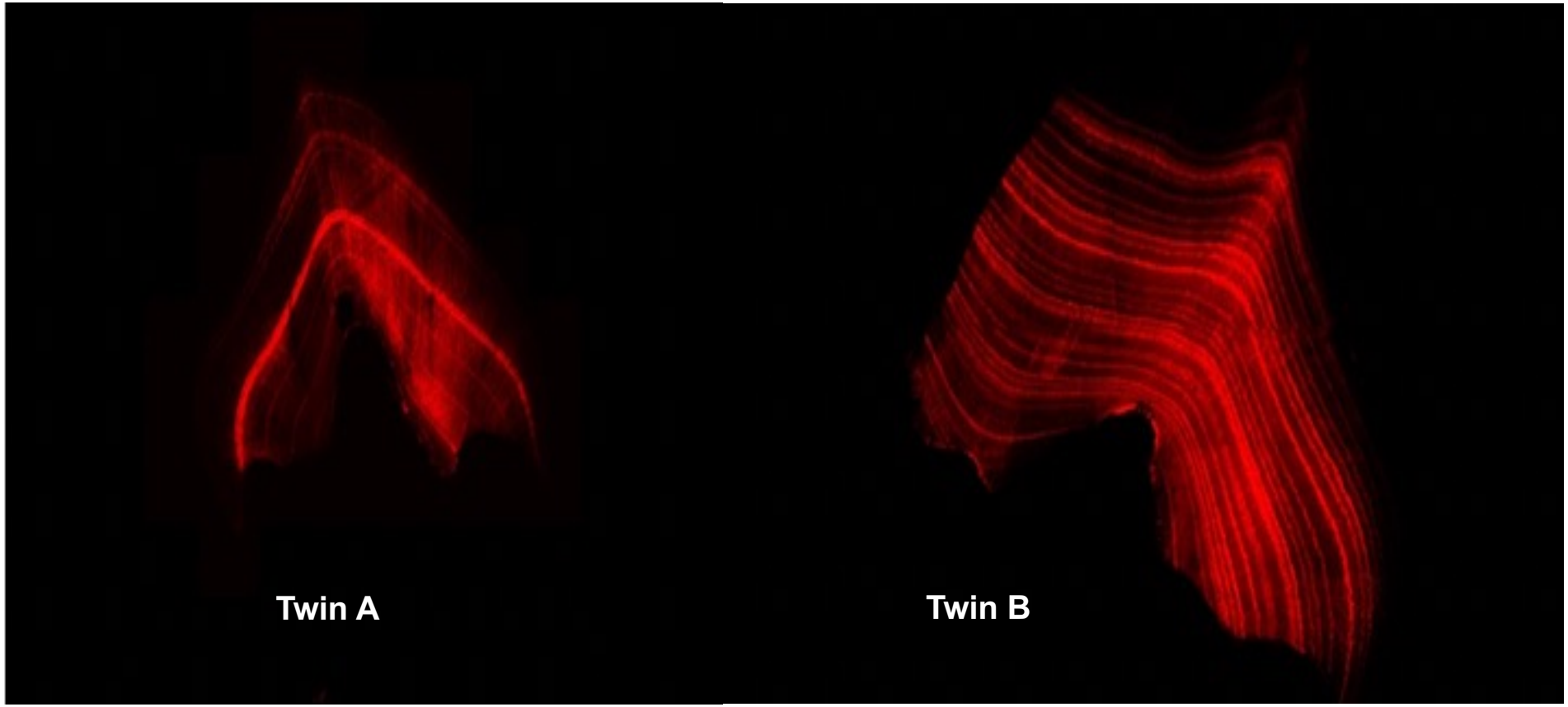
Images:
-Dr. Grissino-Mayer
-wikipedia.org

Example: metals



Arora et al. PLoS One 2014

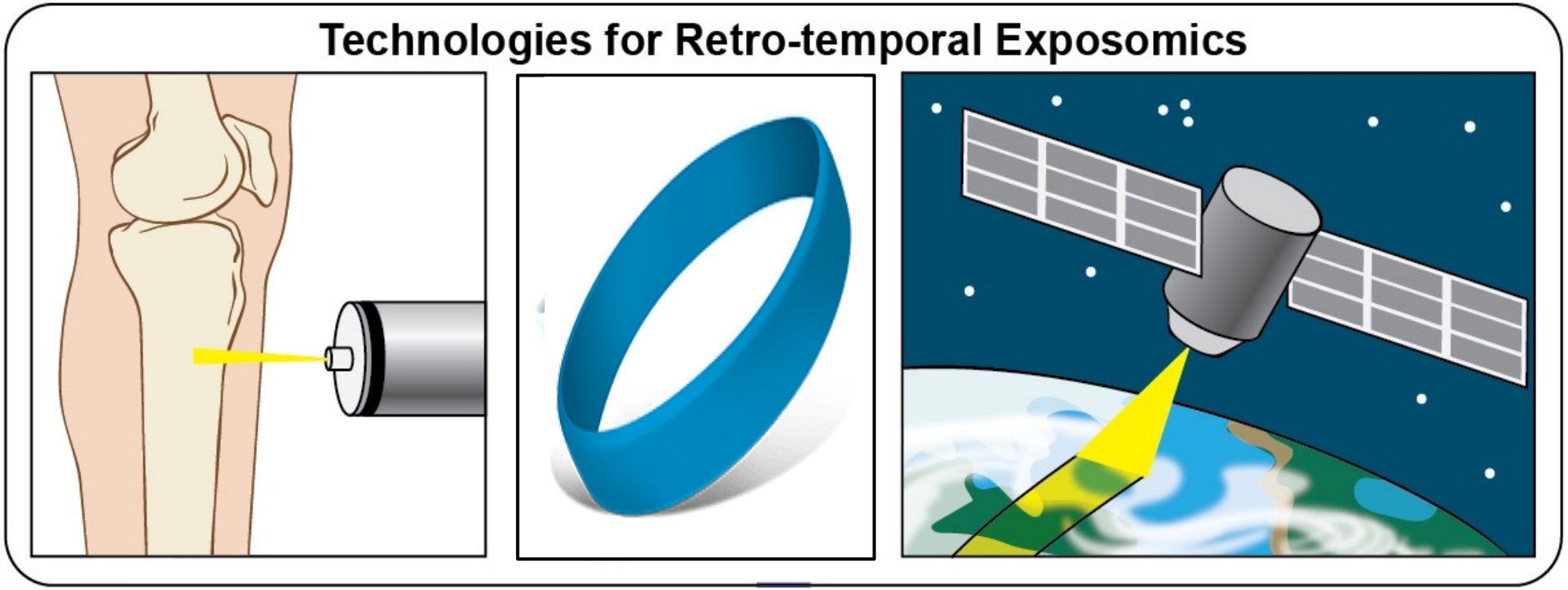
Example: inflammation



C Reactive Protein

Source: unpublished data. Acknowledgment: Drs. Sven Bolte, D. Dumitru, E. Baldwin, R Coenen, C. Austin, P. Curtin

Other technologies

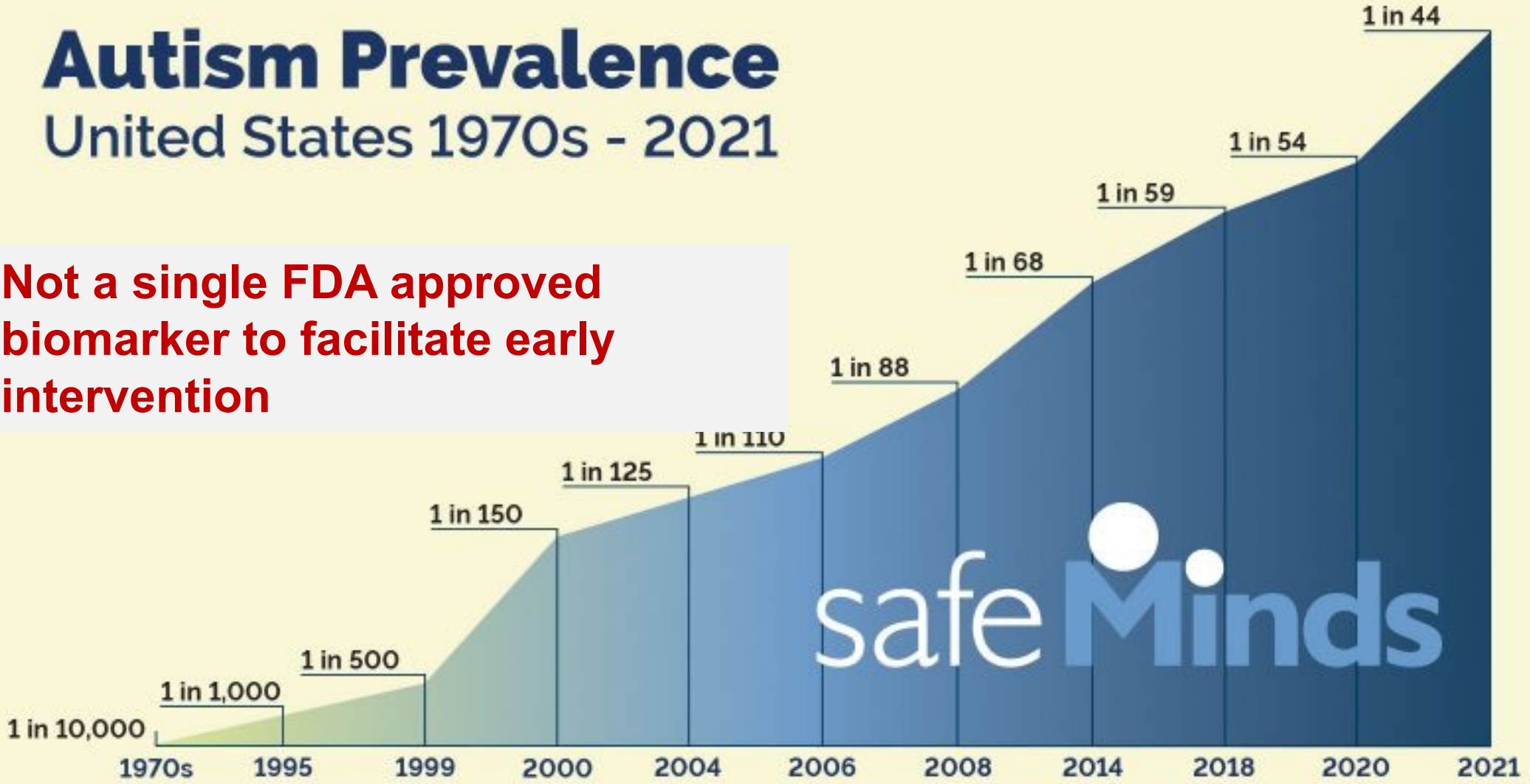


Autism Biomarker at Birth

Autism Prevalence

United States 1970s - 2021

Not a single FDA approved biomarker to facilitate early intervention



Can genomic testing predict risk of autism?

The Washington Post

June 30, 2017

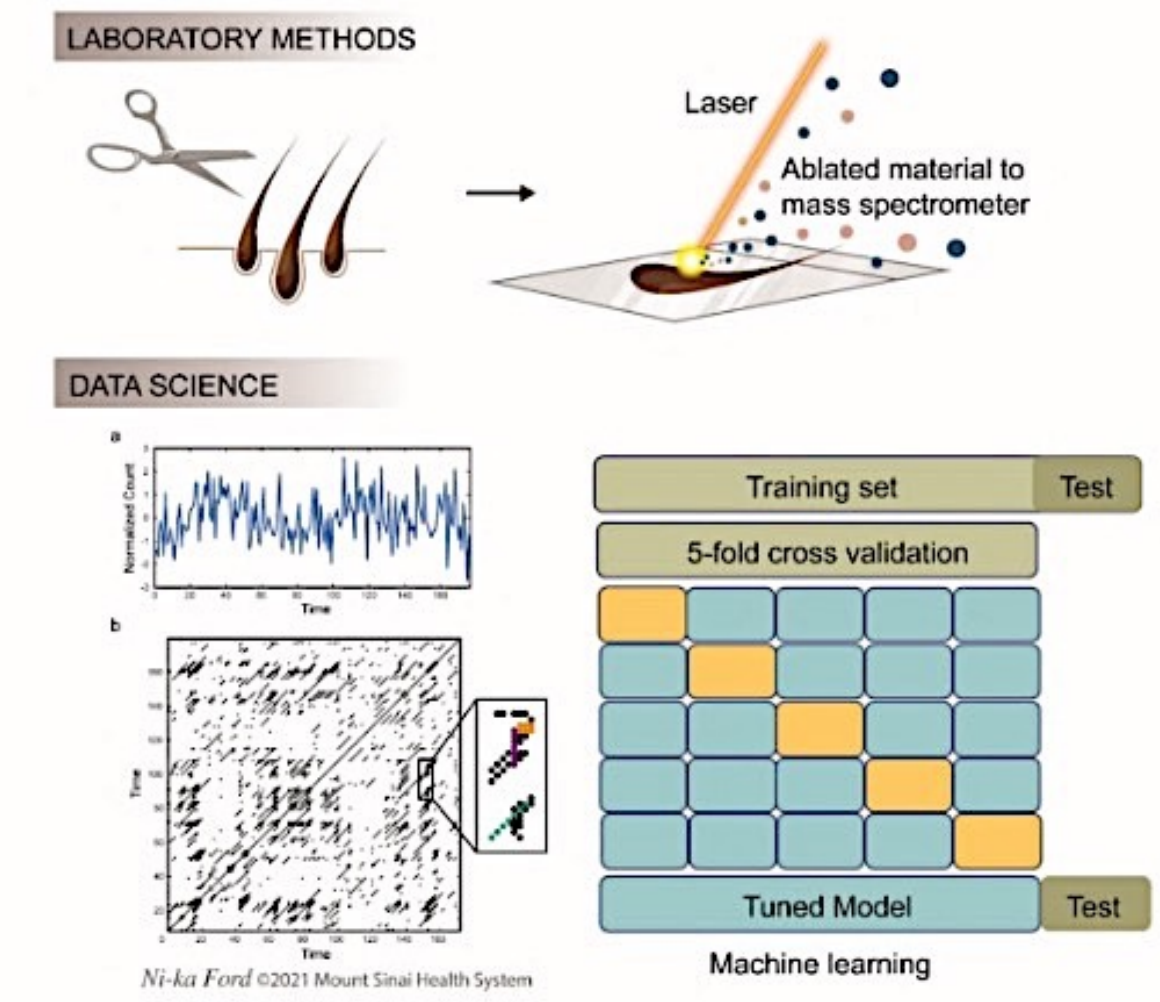
Is there a way to test for mutations before a child is born?

Clinicians routinely screen the chromosomes of a developing baby to identify large chromosomal abnormalities, including CNVs. There are prenatal genetic tests for some syndromes associated with autism, such as fragile X syndrome. But even if a developing baby has these rare mutations, there is no way to know for sure whether he will later be diagnosed with autism.

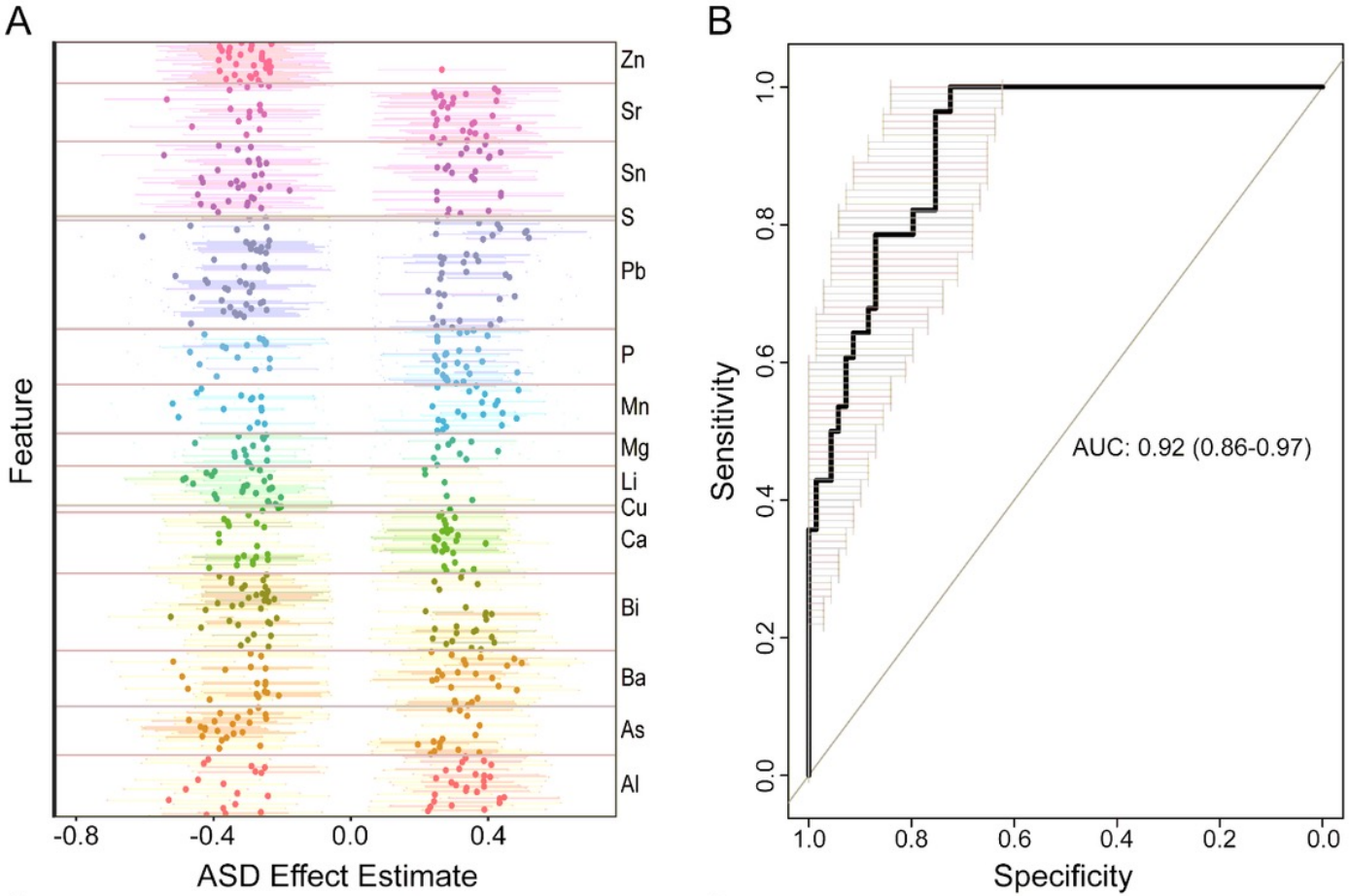
Methods

- Three studies in Japan, Sweden and USA
- Total N = 486 participants
- DSM-V standard clinical diagnosis

Methods


LABORATORY METHODS
Laser
Ablated material to
mass spectrometer
DATA SCIENCE
Training set
Test
5-fold cross validation
Tuned Model
Test
Machine learning
Ni-ka Ford ©2021 Mount Sinai Health System

Autism biomarker (under review)



Performance at optimal threshold:

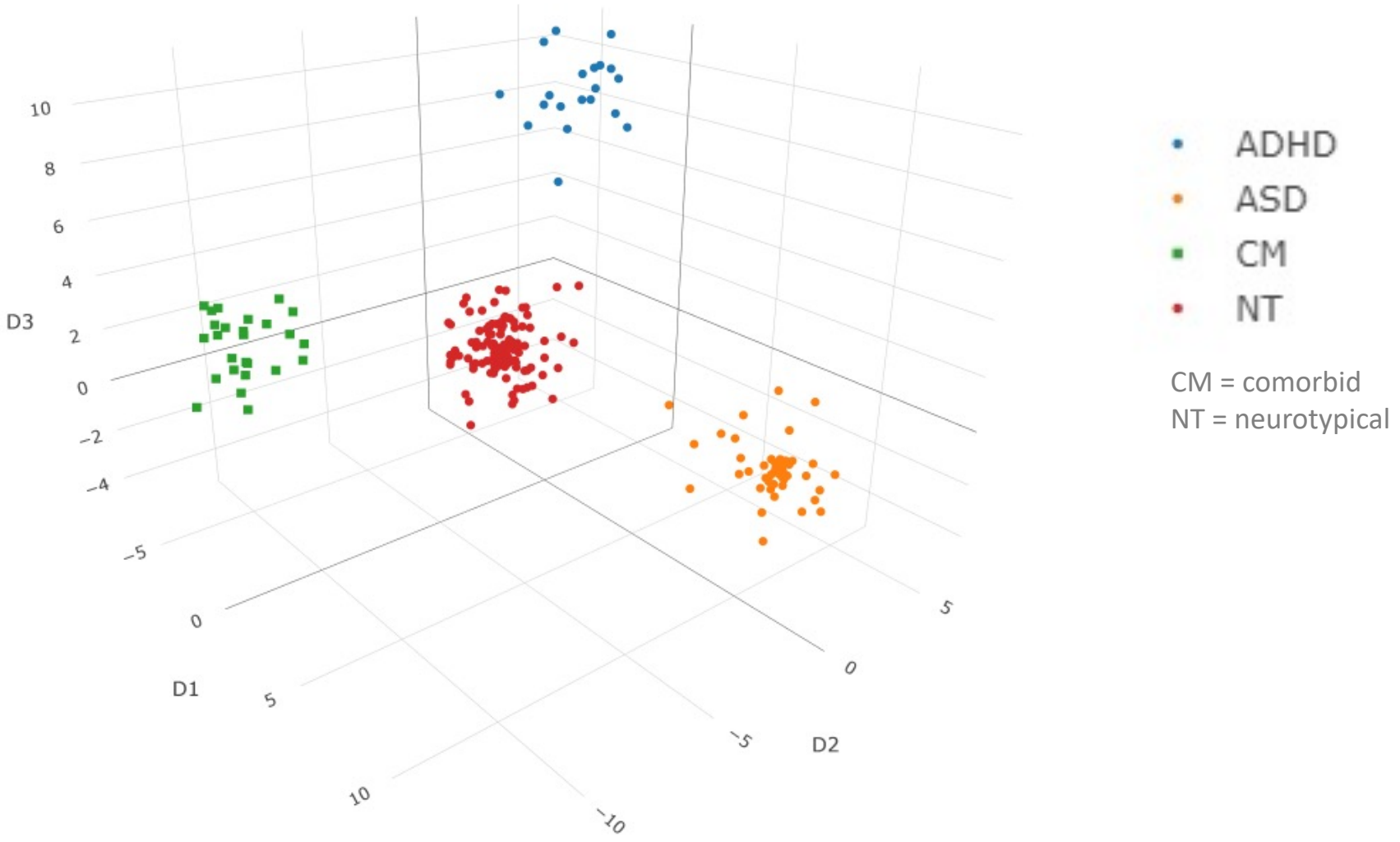
- 0.964 Sensitivity
- 0.754 Specificity

Received FDA Breakthrough Designation as an aid in diagnosis

Molecular phenotyping

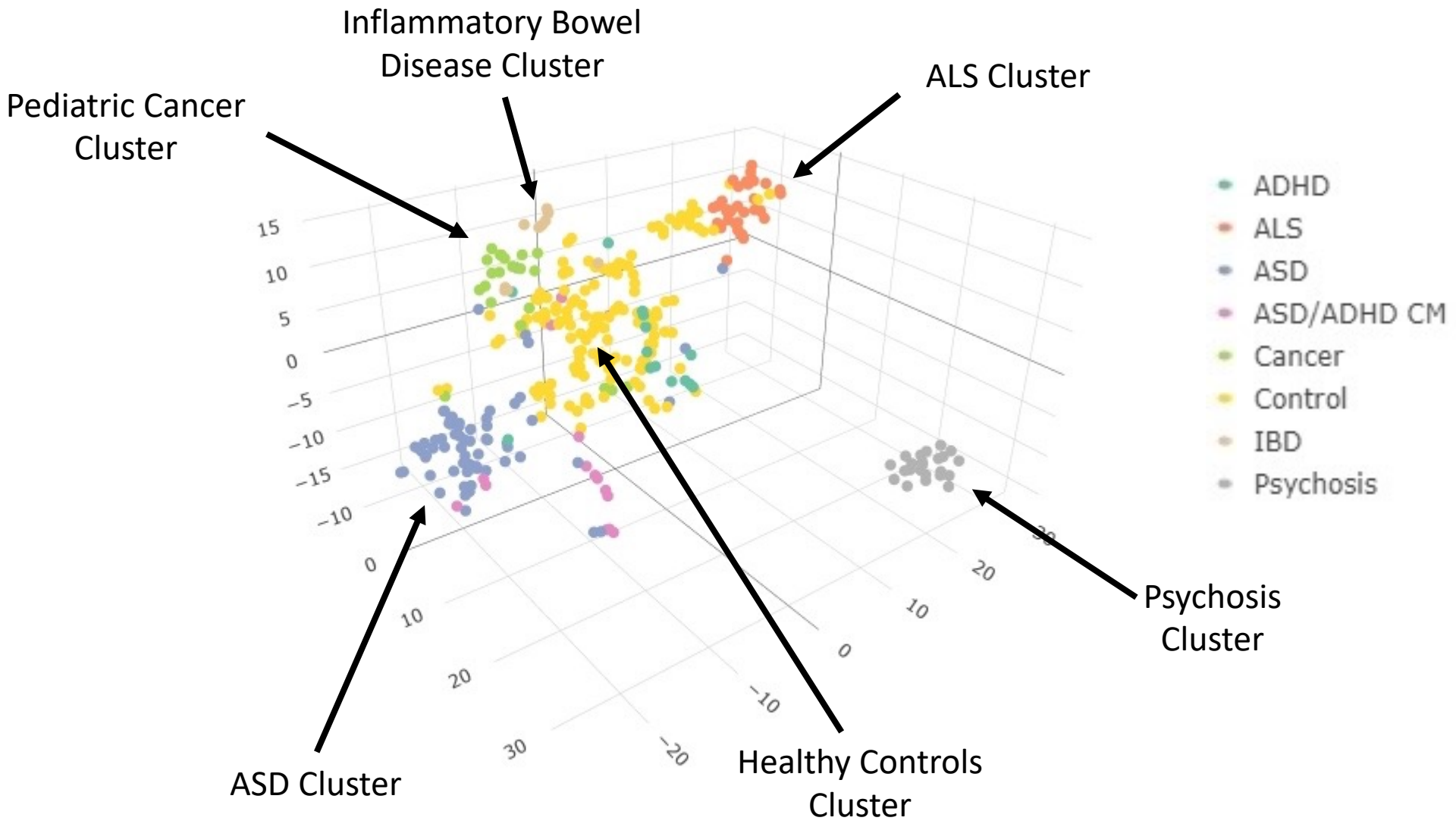
Clusters in 130 Features yield Robust Phenotypic Signatures

These can be leveraged for **predictive** or **retrospective** sub-typing



CM = comorbid
NT = neurotypical

Other disorders



Summary

- The environment is highly dynamic
- Measuring more and more exposures is not enough; we must focus on the time dimension
- Precision environmental medicine is an urgent need

Acknowledgment

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Thank you