Translational Exposomics for Advancement of Precision Health

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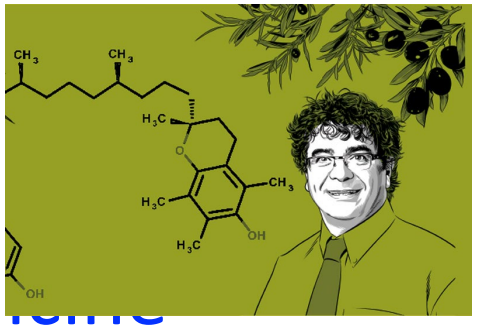
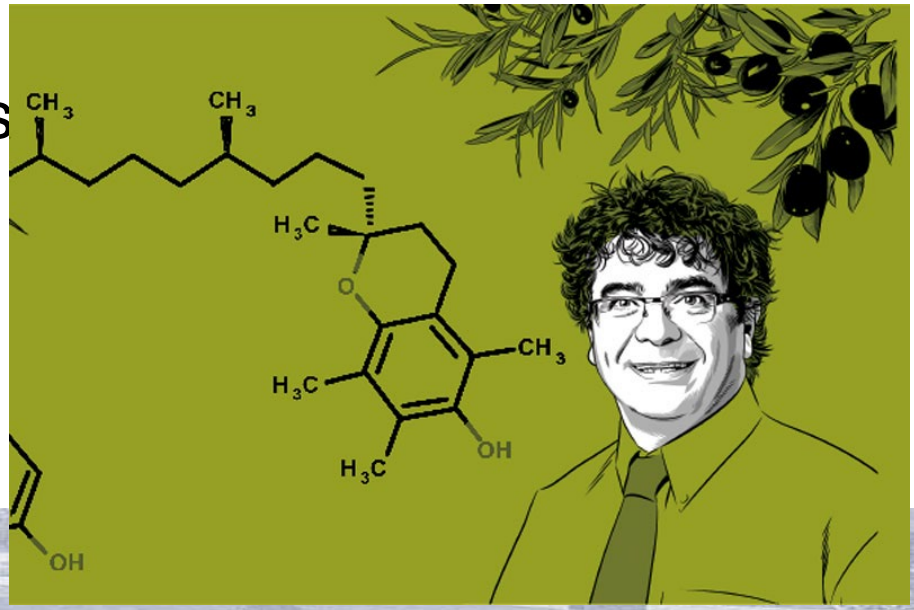


Outline

- Exposome and Exposomics
- Translational Exposomics
- Precision Environmental Health to Precision Medicine
- Exposomics for the Alzheimer's Disease
- Climate Change as a Global Exposome Factor
- Role of Glutathione in Liver Disease and Diabetes



Genetic Factors Are Not the Major Cause of Disease

PLOS ONE

RESEARCH ARTICLE

Genetic Factors Are Not the Major Causes of Chronic Diseases

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Abstract

The risk of acquiring a chronic disease is influenced by a person's genetics (G) and exposures received during life (the 'exposome', E) plus their interactions (G×E). Yet, investigators use genome-wide association studies (GWAS) to characterize G while relying on self-reported information to classify E. If E and G×E dominate disease risks, this imbalance obscures important causal factors. To estimate proportions of disease risk attributable to G (plus shared exposures), published data from Western European monozygotic (MZ) twins were used to estimate population attributable fractions (PAFs) for 28 chronic diseases. Genetic PAFs ranged from 3.4% for leukemia to 48.6% for asthma with a median value of 18.5%. Cancers had the lowest PAFs (median = 8.26%) while neurological (median = 26.1%) and lung (median = 33.6%) diseases had the highest PAFs. These PAFs were then linked with Western European mortality statistics to estimate deaths attributable to G for heart disease and nine cancer types. Of 1.53 million Western European deaths in 2000, 0.25 million (16.4%) could be attributed to genetics plus shared exposures. Given the modest influences of G-related factors on the risks of chronic diseases in MZ twins, the disparity in coverage of G and E in etiological research is problematic. To discover causes of disease, GWAS should be complemented with exposome-wide association studies (EWAS) that profile chemicals in biospecimens from incident disease cases and matched controls.

Citation: Rappaport SM (2016) Genetic Factors Are Not the Major Causes of Chronic Diseases. PLoS ONE 11(4): e0154387. doi:10.1371/journal.pone.0154387

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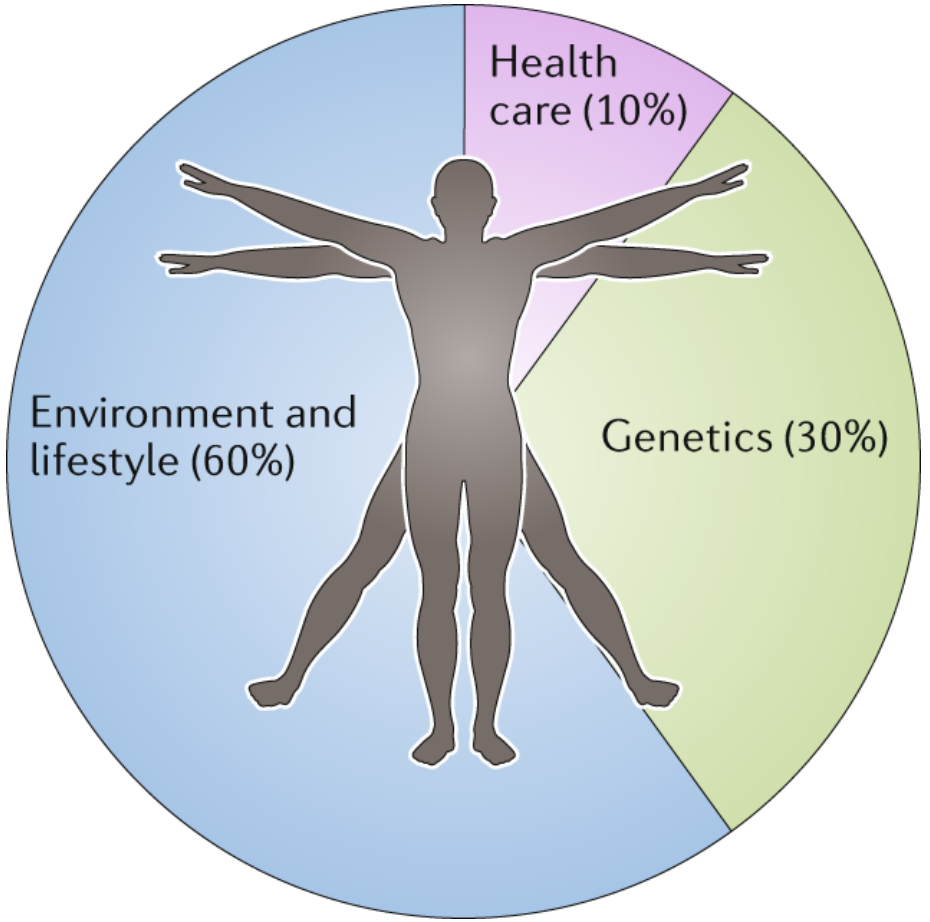
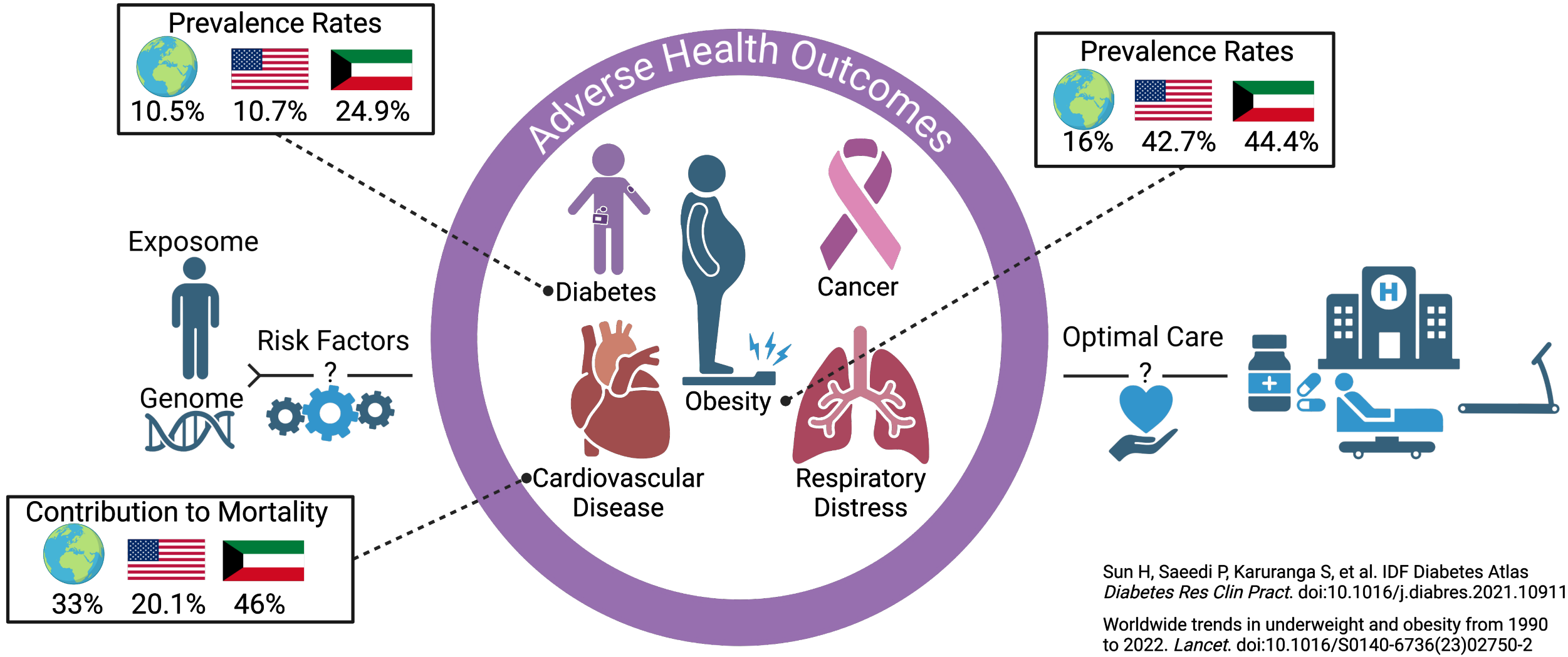


Nature Rev Clin Oncol 17:183–194, 2020

Disease Prevalence



Sun H, Saeedi P, Karuranga S, et al. IDF Diabetes Atlas *Diabetes Res Clin Pract*. doi:10.1016/j.diabres.2021.109119

Worldwide trends in underweight and obesity from 1990 to 2022. *Lancet*. doi:10.1016/S0140-6736(23)02750-2

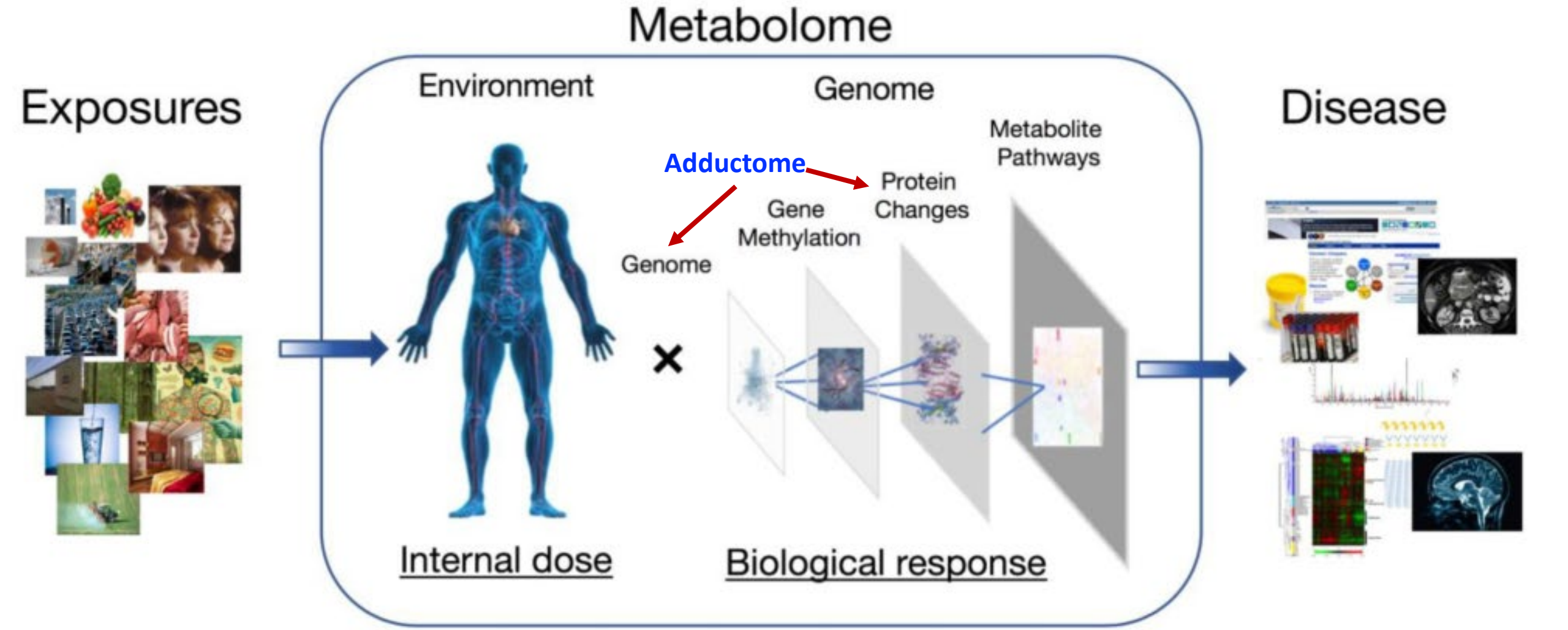
Di Cesare M, Perel P, Taylor S, et al. The Heart of the World. *Glob Heart*. 2024;19(1):11. doi:10.5334/gh.1288

Introduction to Exposome

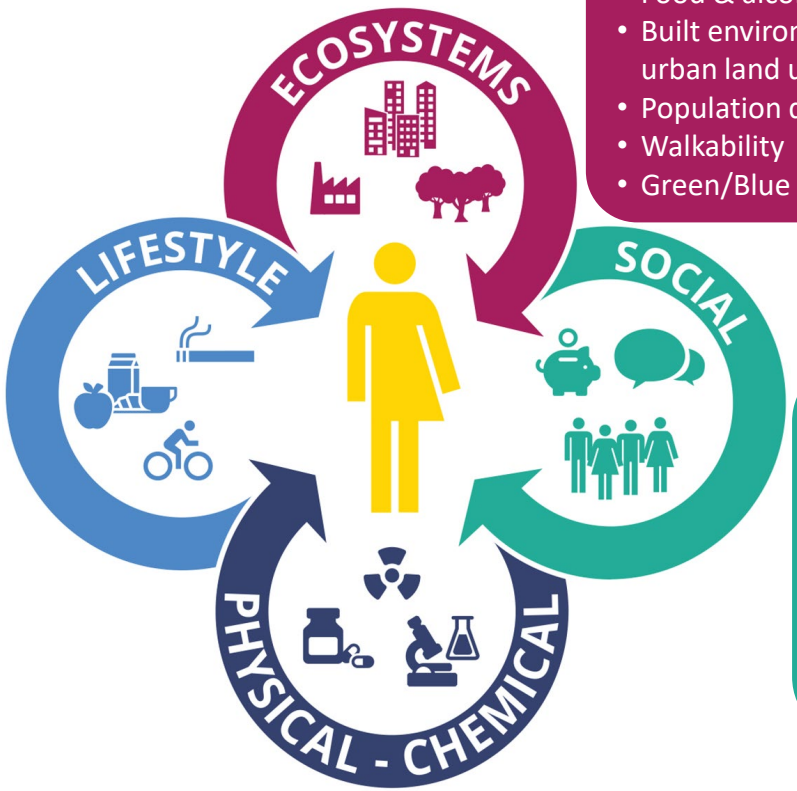
- Introduced by Dr. Christopher Wild (International Agency for Research on Cancer) in 2005 to emphasize the critical role of environmental exposures in disease etiology.
- Evolved to incorporate advanced technologies and comprehensive methodologies for assessing exposures throughout an individual's lifetime.

The human exposome encompasses exposures to environmental factors **throughout life**, starting from conception and pregnancy.

Exposome: from Exposures to Disease



The Exposome Concept



ECOSYSTEMS
- Food & alcohol outlets
- Built environment, urban land uses
- Population density
- Walkability
- Green/Blue space

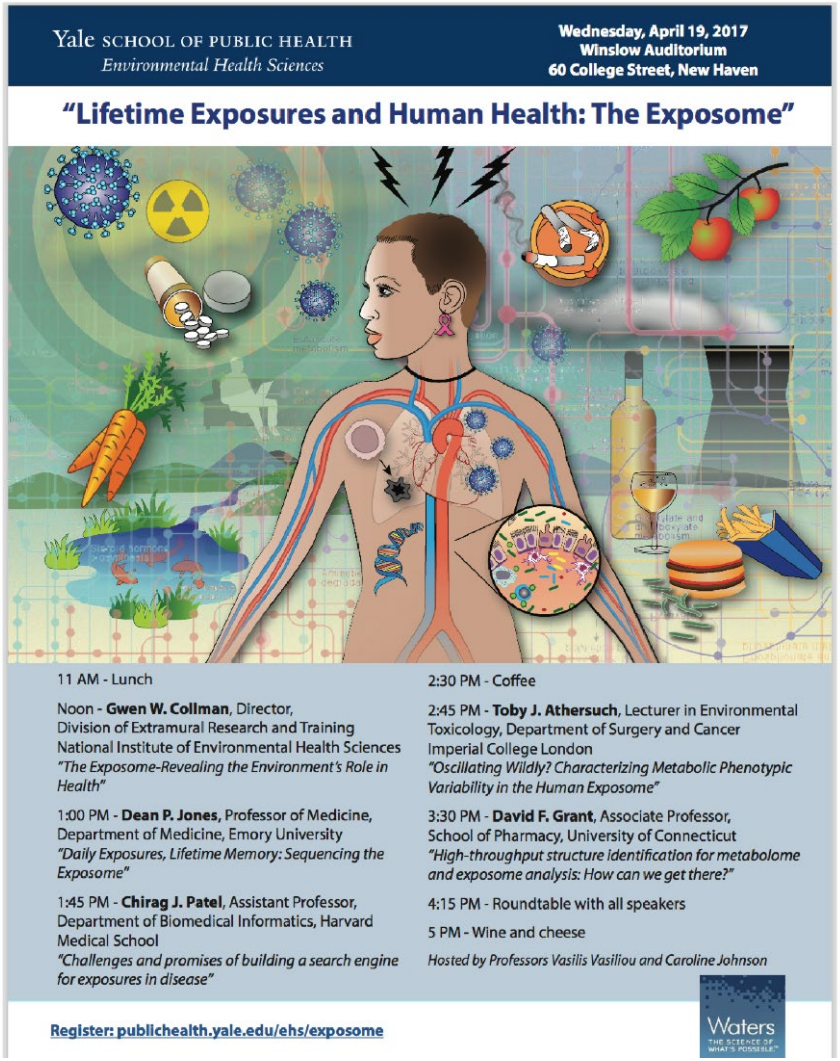
LIFESTYLE
- Physical activity
- Sleep behavior
- Diet
- Drug use
- Smoking
- Alcohol use

SOCIAL
- Household income
- Inequality
- Social capital
- Social networks
- Cultural norms
- Cultural capital
- Psychological & mental stress

PHYSICAL - CHEMICAL
- Temperature/humidity
- Electromagnetic fields
- Ambient light
- Odor & noise
- Point, line sources
- Air pollution
- Agricultural activities, livestock
- Pollen/mold/fungus
- Pesticides
- Fragrance products
- Flame retardants
- POPs
- Plastics & plasticizers
- Food contaminants
- Soil contamination
- Drinking water contamination
- Groundwater contamination
- Surface water contamination
- Occupational exposures

Vermeulen et al., Science, 2020

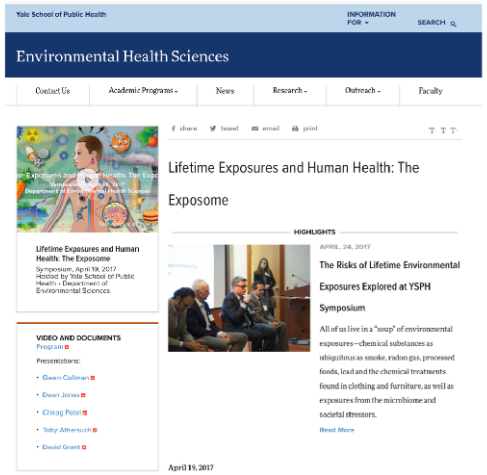
One of the First Exposome Conferences was Held at Yale in 2017




Johnson et al. Human Genomics (2017) 11:32
DOI 10.1186/s40246-017-0128-0
Human Genomics
MEETING REPORT
Open Access

Yale school of public health symposium on lifetime exposures and human health: the exposome; summary and future reflections

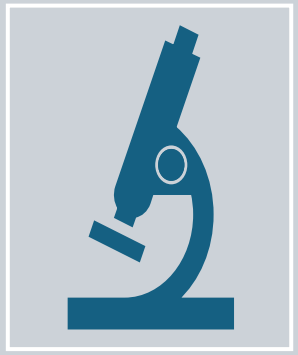
Caroline H. Johnson[1*], Toby J. Athersuch[2,3], Gwen W. Collman[4], Suraj Dhungana[5], David F. Grant[6], Dean P. Jones[7], Chirag J. Patel[8] and Vasilis Vasiliou[1*]



Available at

http://publichealth.yale.edu/ehs/exposome/

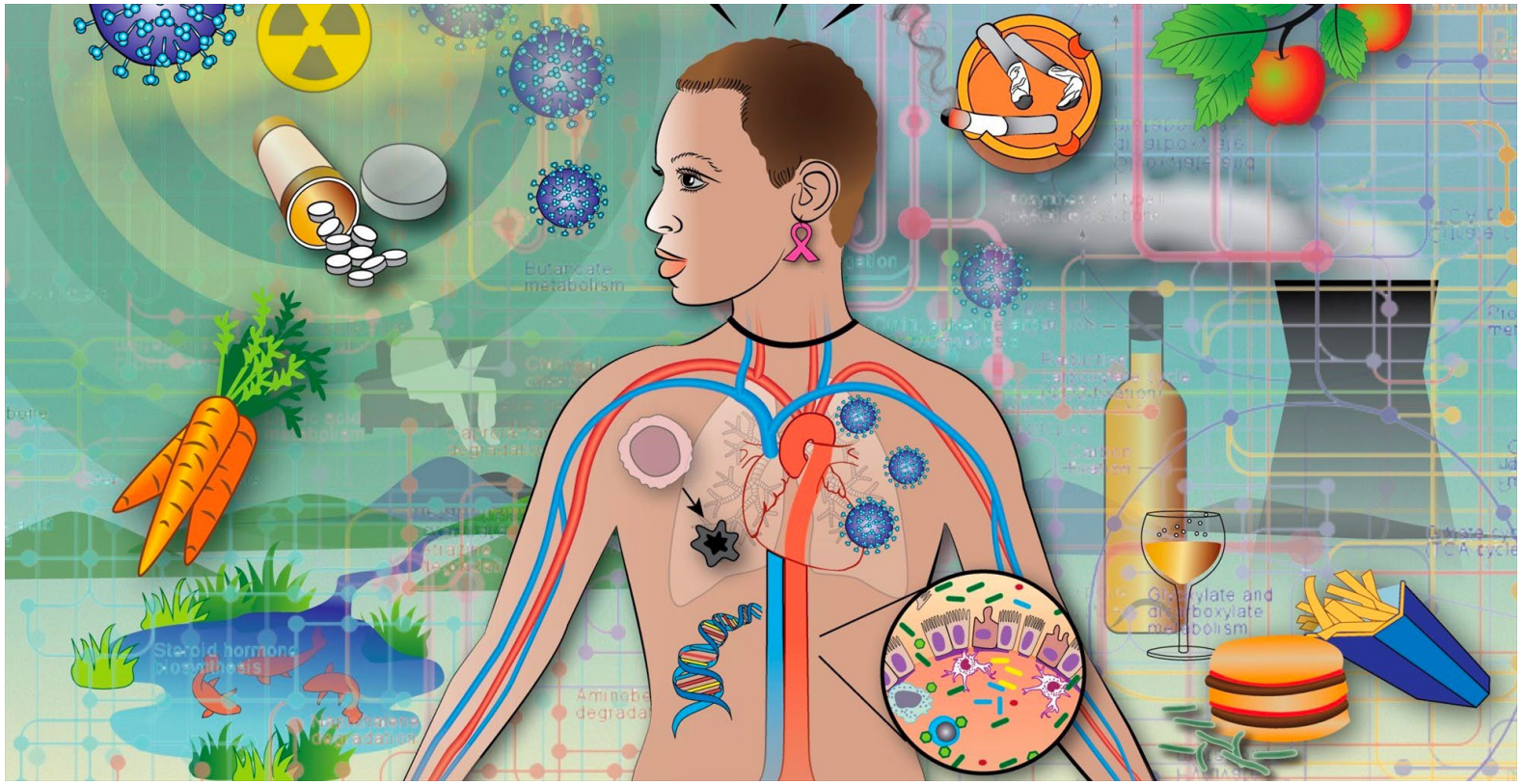
Defining Exposomics

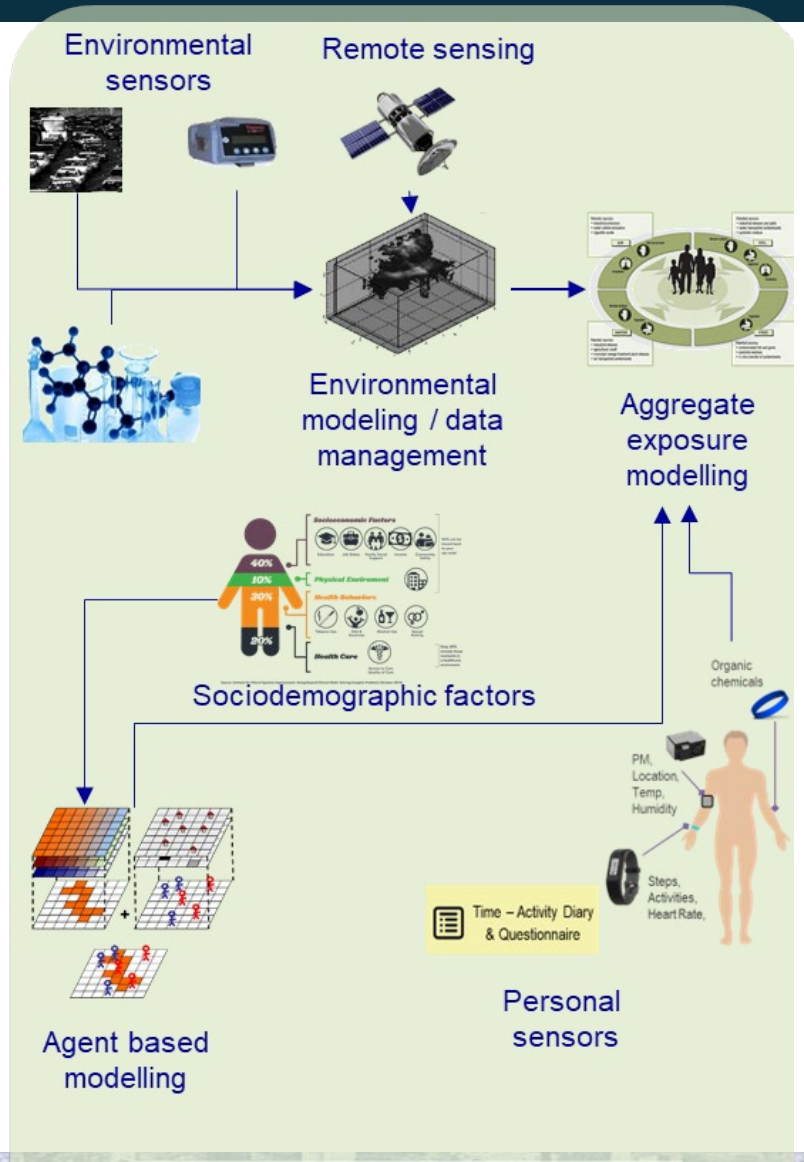


A multidisciplinary approach that combines advanced analytical techniques, bioinformatics, and epidemiological methods to comprehensively assess environmental exposures and their interactions with biological systems over time.

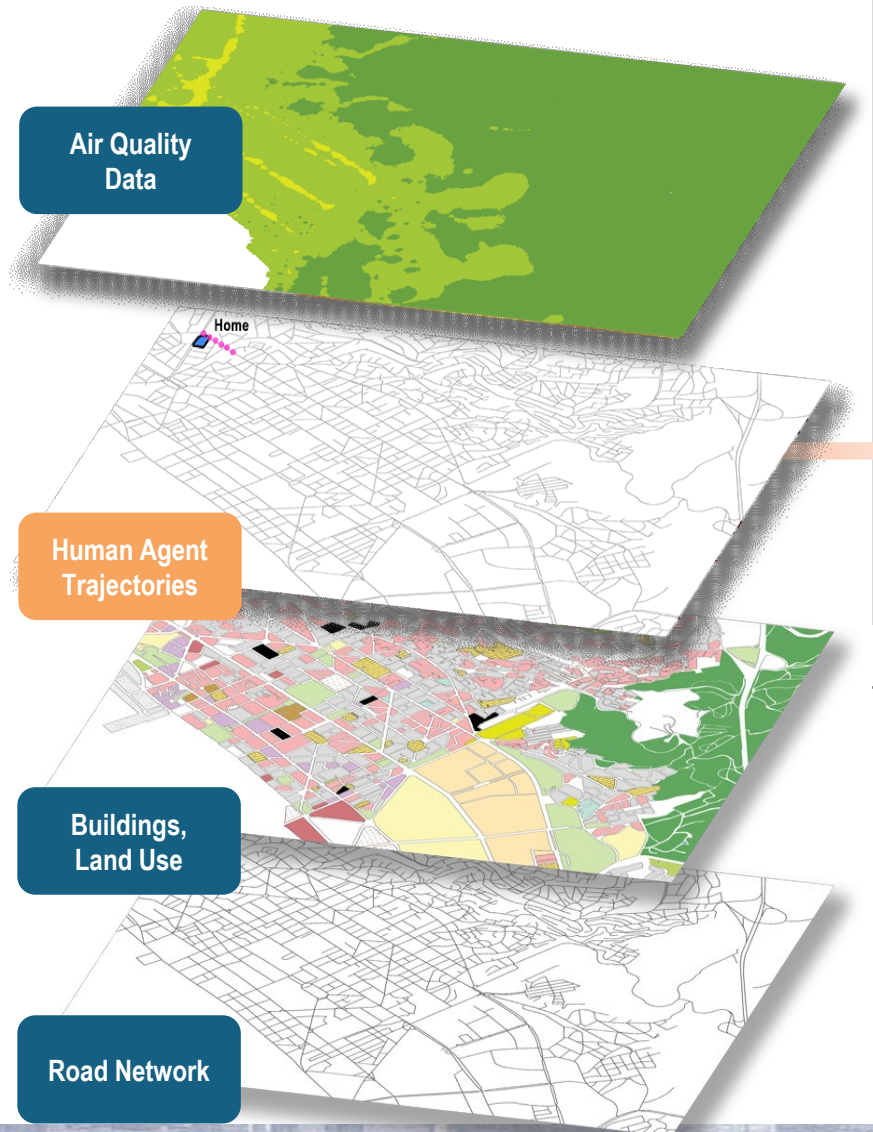
Omics technologies, including genomics, proteomics, and metabolomics, are pivotal in exposome research as they enable the detailed analysis of genes, proteins, and metabolites to understand how environmental exposures affect biological processes and health outcomes.

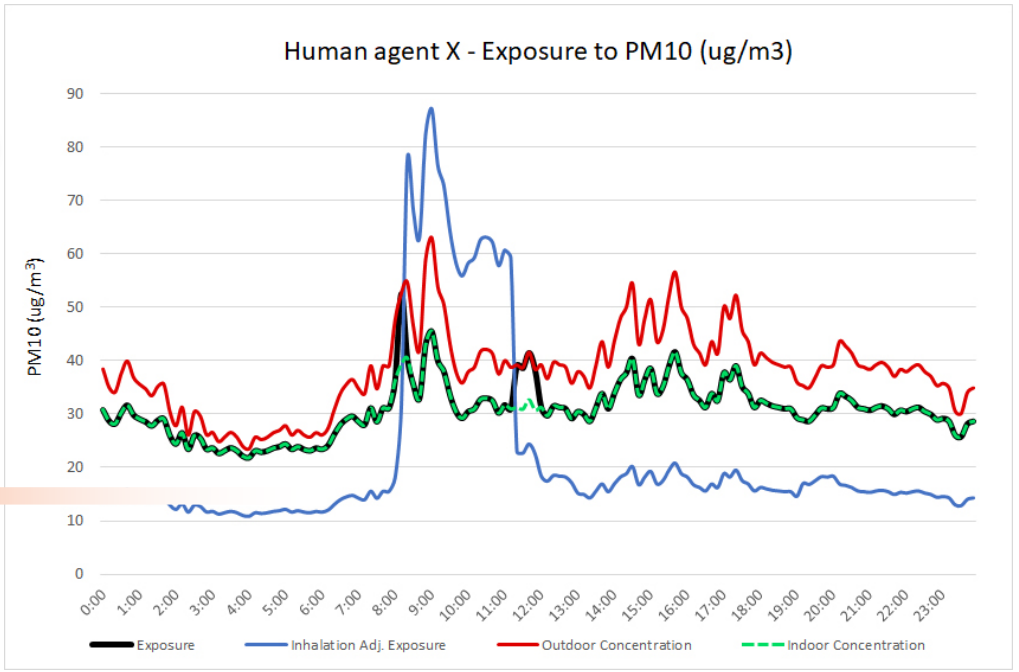
Environmental Data



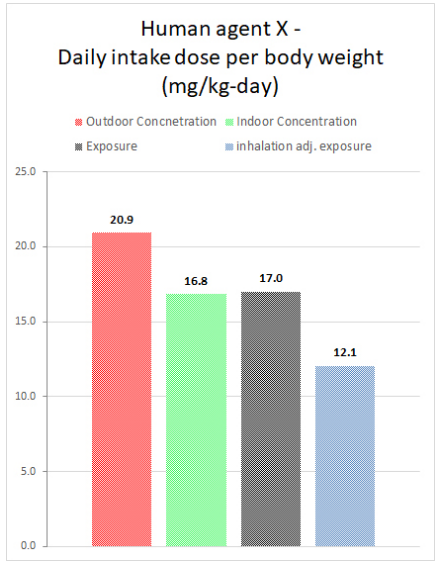


Space-Time Exposure and Mapping Exposures

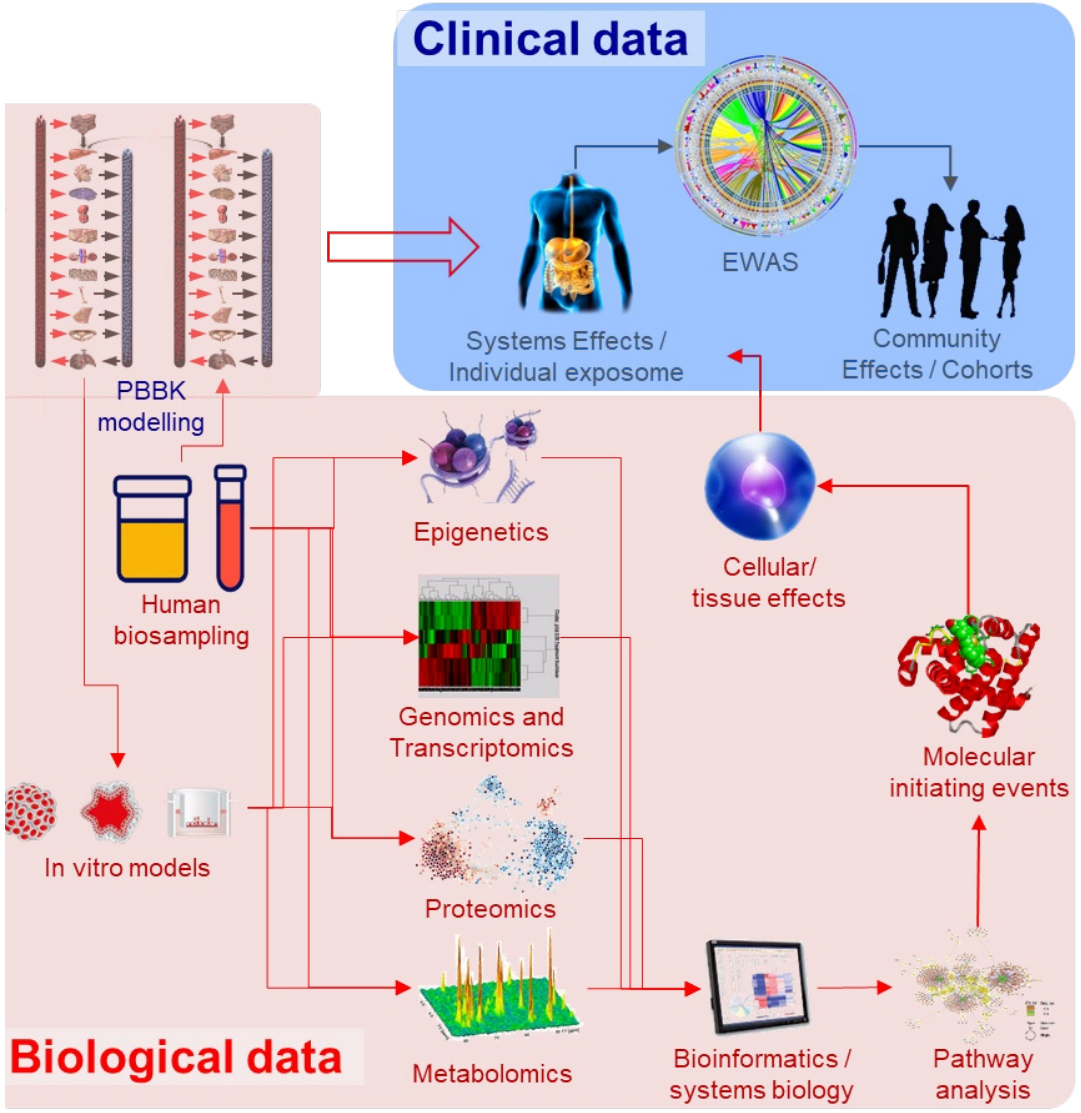




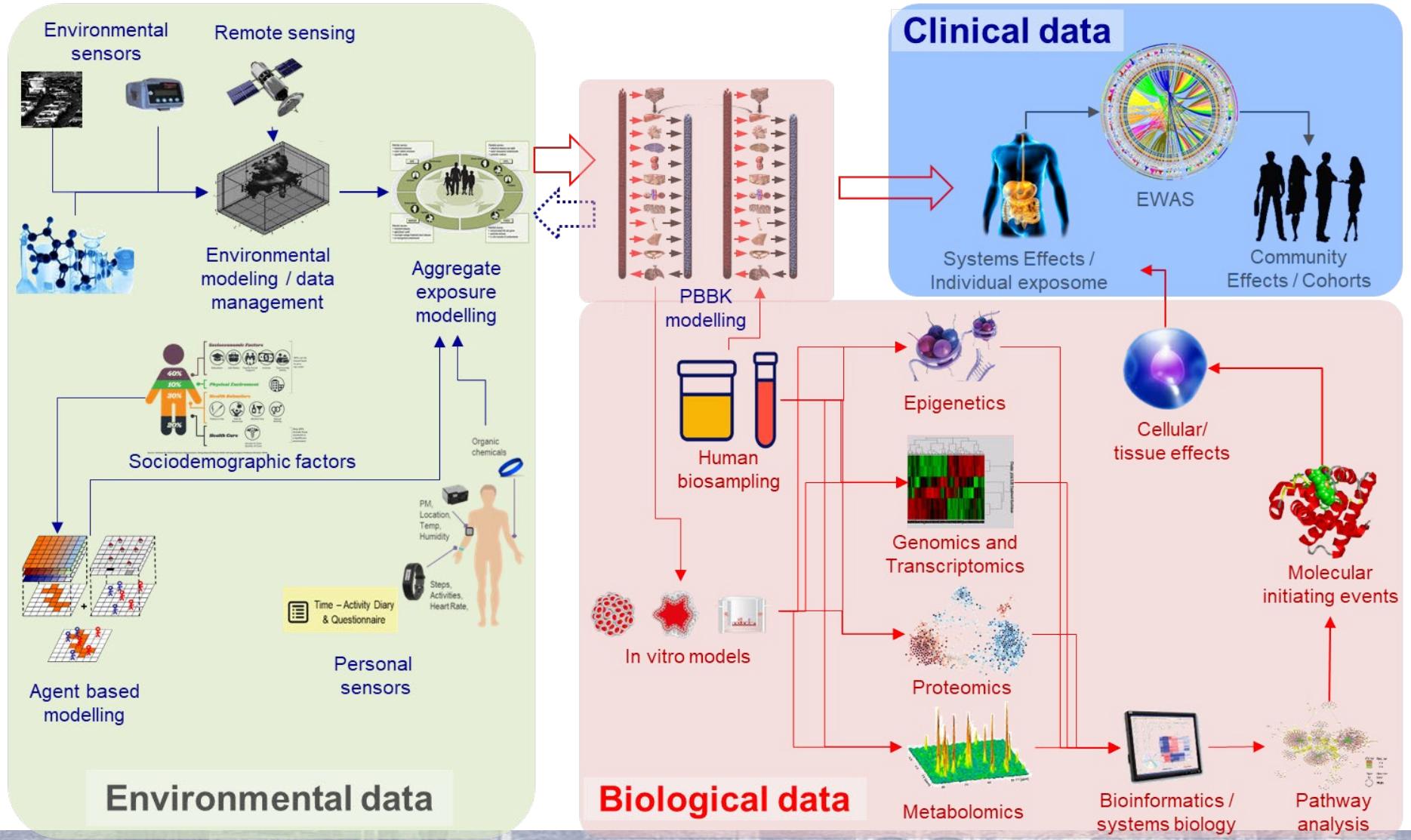
Time	Activity	Place	Vehicle
0:00	sleep	home	
8:10	commute	road	car
8:20	paidwork	work	
11:20	commute	road	car
12:00	eatdrink	home	
13:00	tvradio	home	
18:30	selfcare	home	
19:10	clean	home	
20:10	selfcare	home	
20:50	tvradio	home	



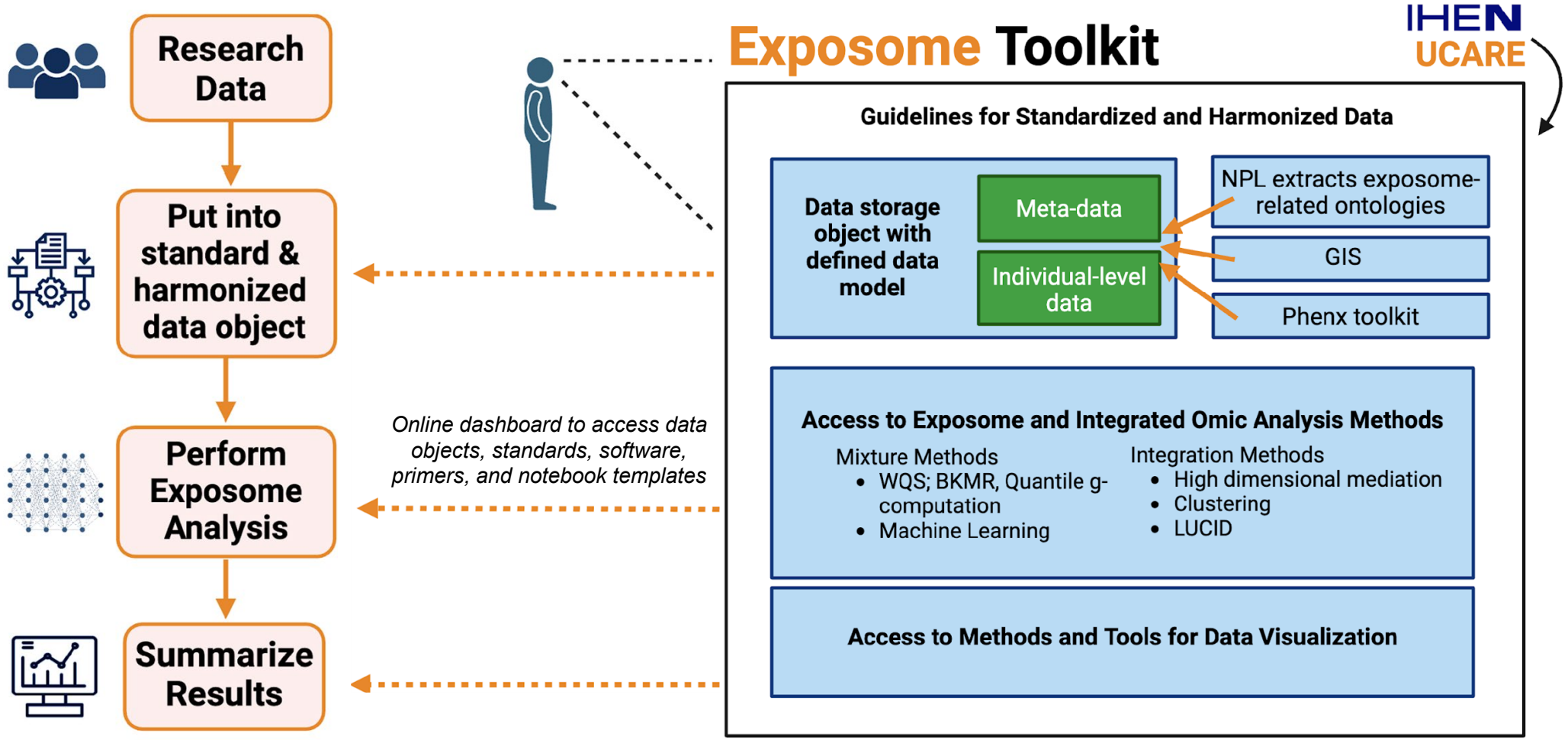
Exposomics in Biological Samples



Translational Exposomics



Computational Approaches in Exposomics



FAIR: **F**indability, **A**ccessibility, **I**nteroperability, and **R**eusability
CARE: **C**ollective Benefit, **A**uthority to **C**ontrol, **R**esponsibility, and **E**thics

UCARE Coordinating Center

US **C**enter for **A**ccelerating **R**esearch in **E**xposome and Translational Precision Environmental Health

Yale SCHOOL OF PUBLIC HEALTH
Environmental Health Sciences

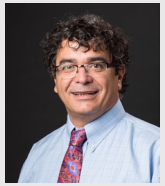
Icahn School of Medicine at Mount Sinai

Keck School of Medicine of USC

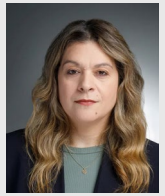
UNC GILLINGS SCHOOL OF GLOBAL PUBLIC HEALTH

Stanford University

Expertise of the UCARE Leadership

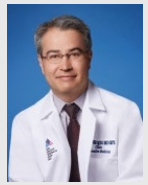






YSPH: Vasilis Vasiliou, Kei-Hoi Cheung, Krystal Pollitt, Caroline Johnson, Georgia Charkoftaki, Nicole Deziel, Zeyan Liew
Expertise: environmental toxicology, exposome, metabolomics, community engagement

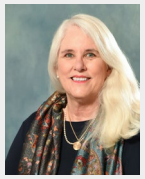
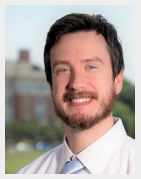


ISMMS: Dania Valvi, Vishal Midya, Youssef Oulhote, Bob Wright
Expertise: exposomics, environmental epidemiology, G*E interactions, machine-learning applications, exposome research in LMIC
Connection with other Consortia: HHEAR, EHEN, IHEN




USC: Lida Chatzi, David Conti, Jesse Goodrich, Max Aung
Expertise: translational exposome research, environmental epidemiology, multi-omics approaches, community engagement
Connection with other consortia: EHEN, IHEN, MOHD

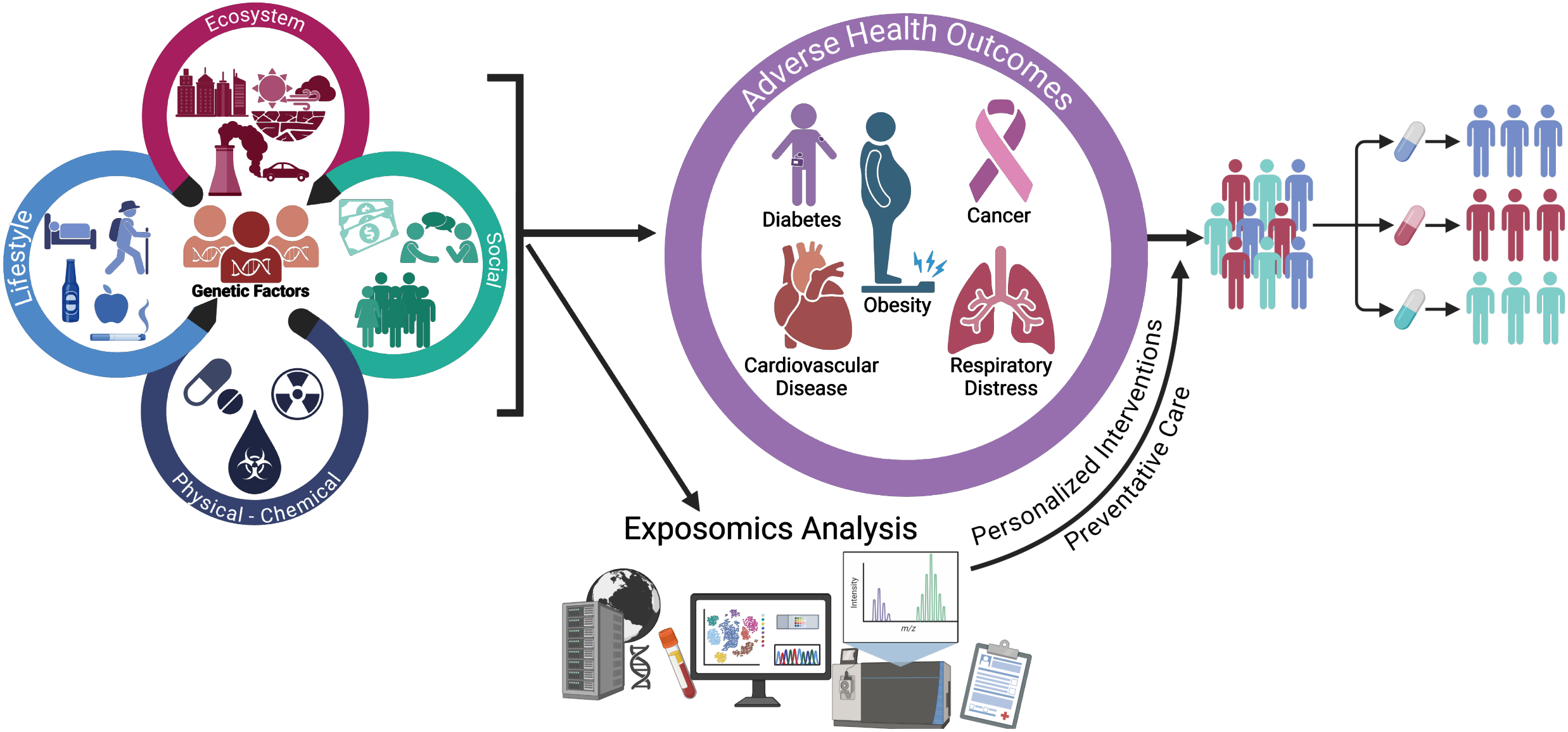



UNC: Susan Sumner, Blake Rushing, Wimal Pathmasiri, Susan McRitchie
Expertise: precision nutrition, toxicology, exposomics, metabolomics, metabolite identification, proteomics, microbiome, biostatistics, software development
Connection with other Consortia: HHEAR, CHEAR, ECHO, CURE, NPH

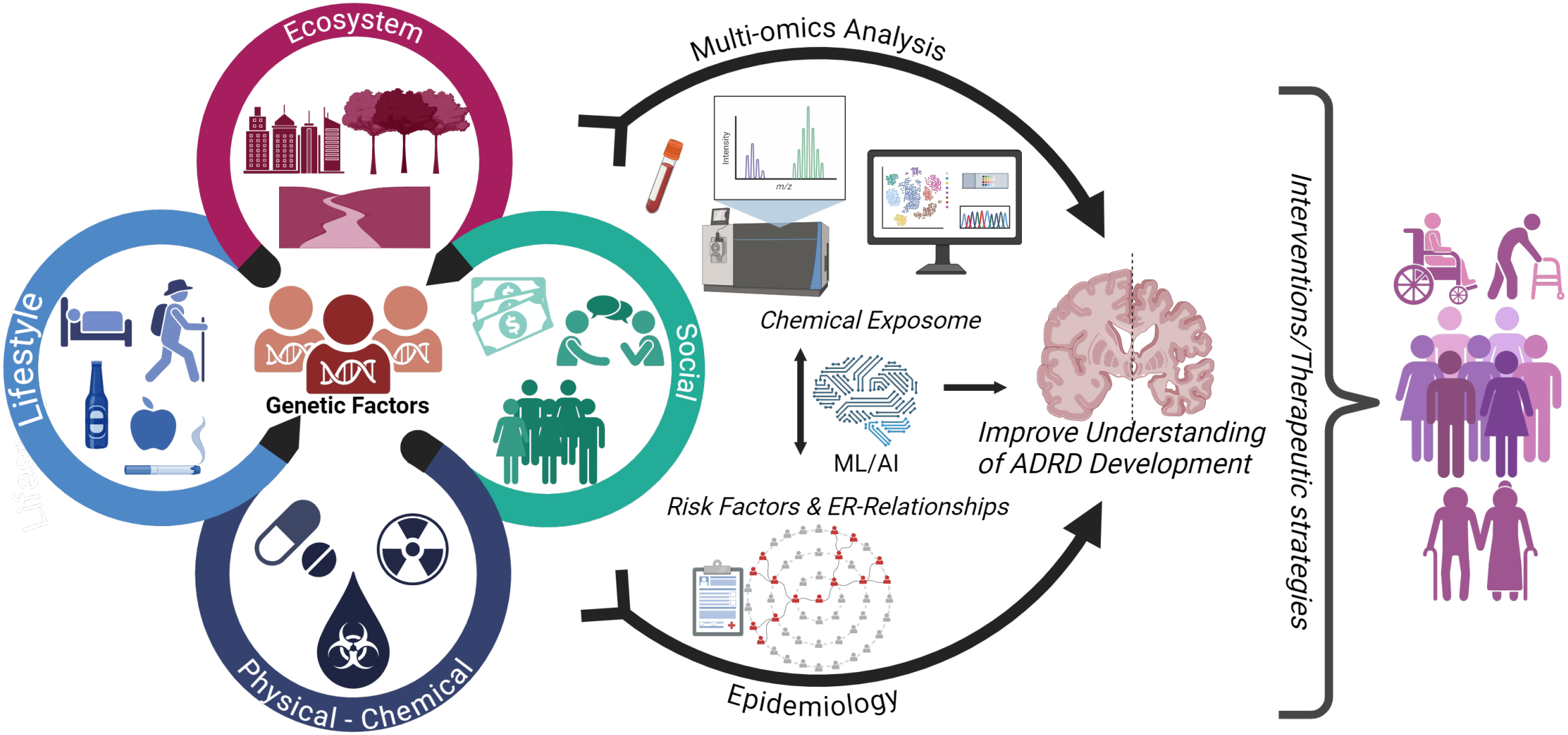

Stanford U.: Michael Snyder, Jennifer Li Pook Than
Expertise: functional genomics, GIS, personalized medicine, environmental justice

Precision Environmental Health

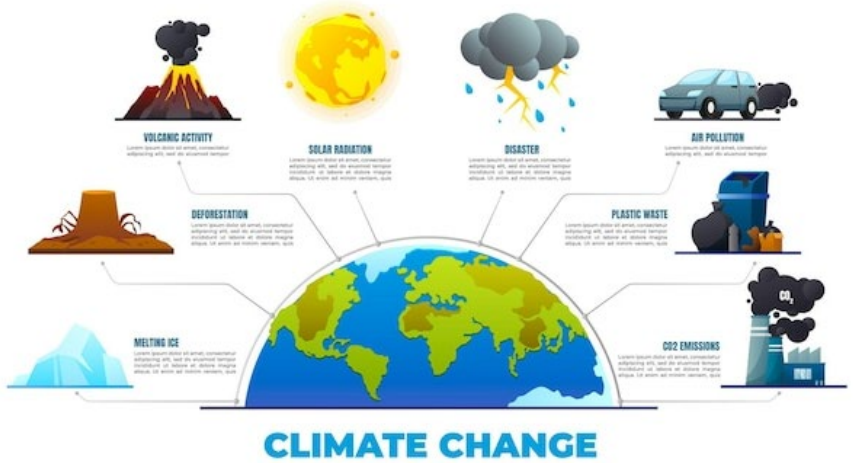
Precision Medicine

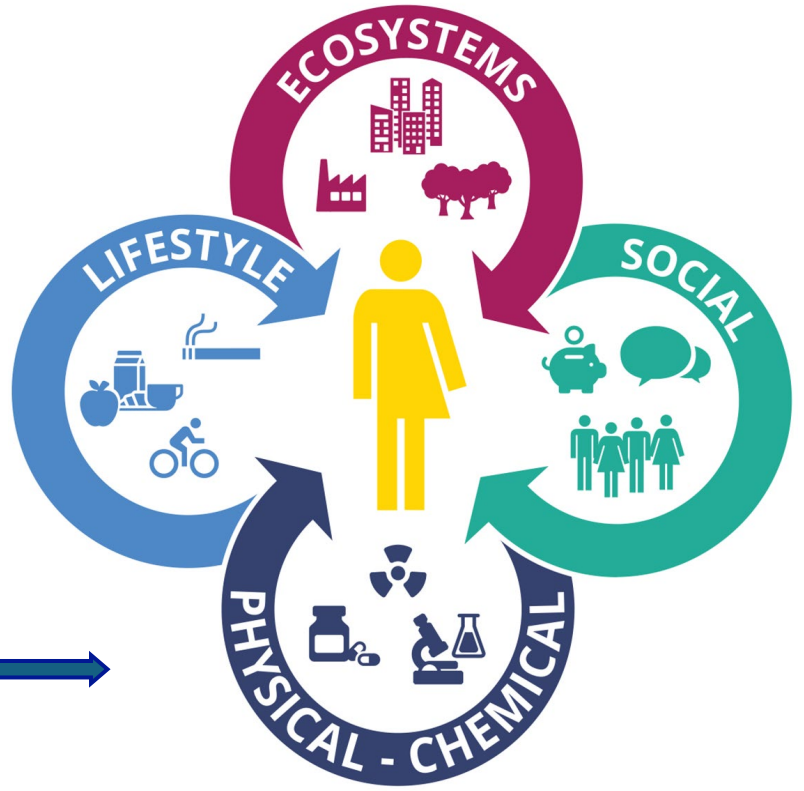


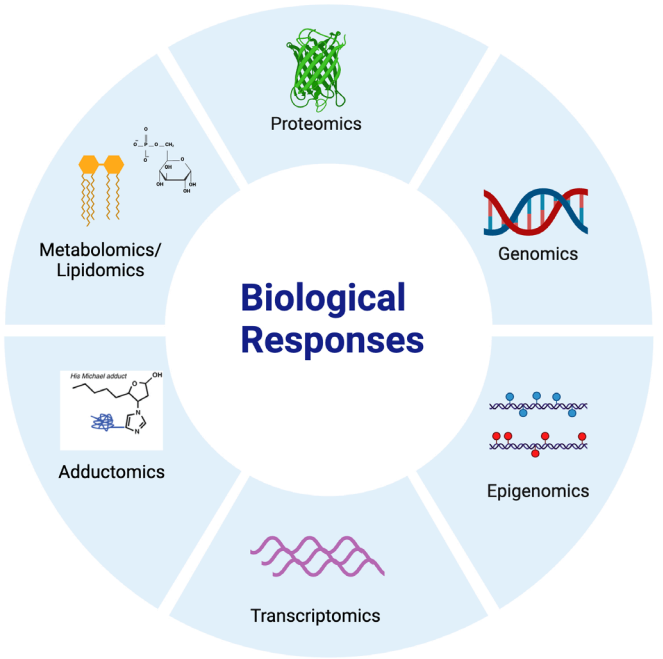
Exposomics for Alzheimer's Disease



Climate Change as a Global Exposome Factor



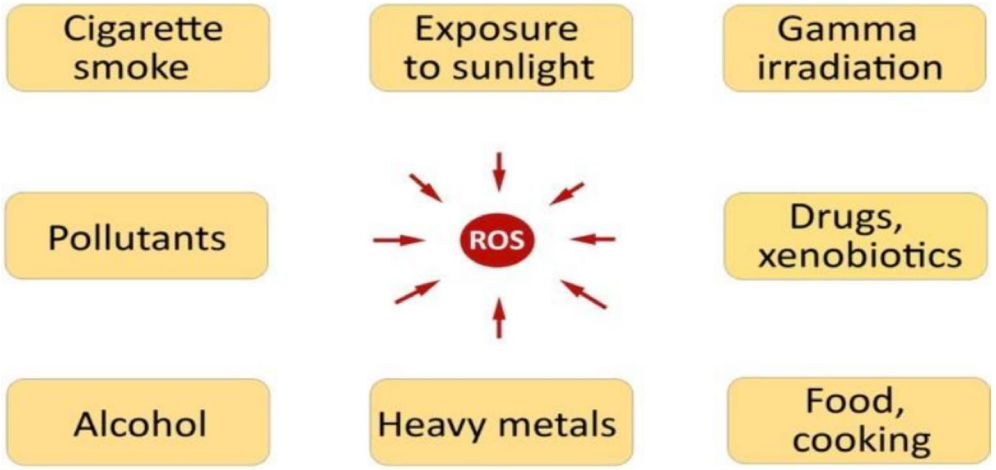


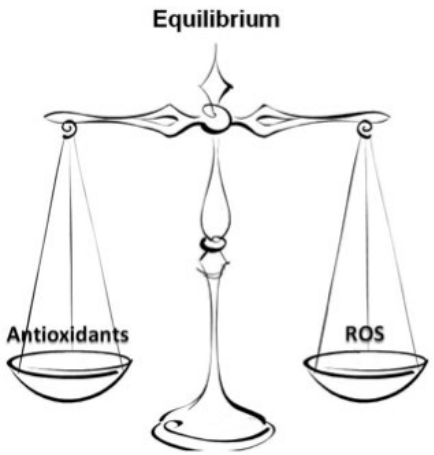


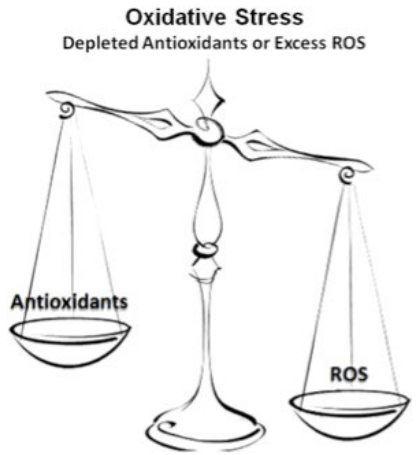
Health outcomes

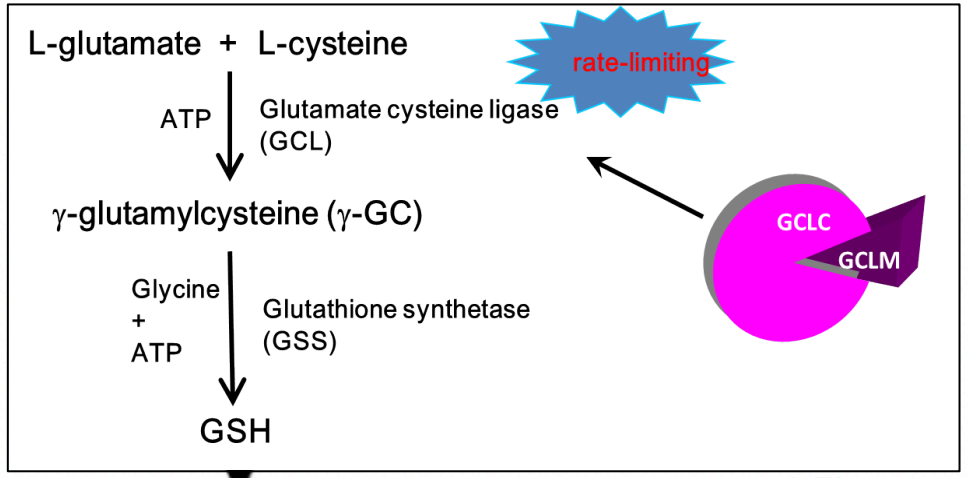
Cancer	Cardiorespiratory	Mental health	Metabolic diseases

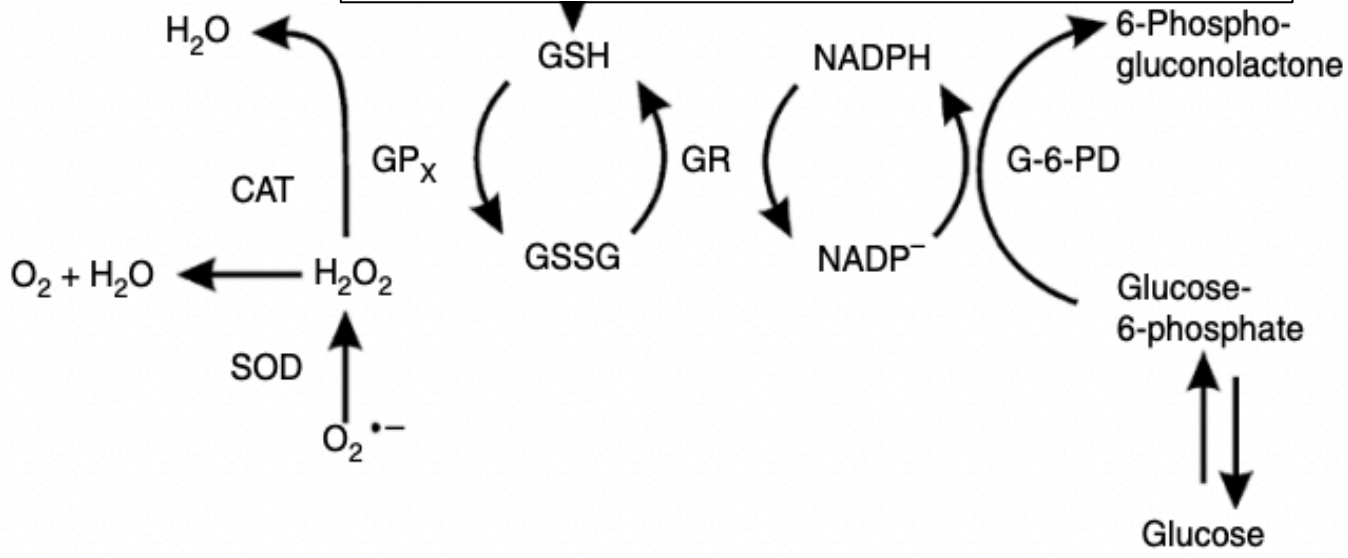
Oxidative Stress and the Antioxidant System



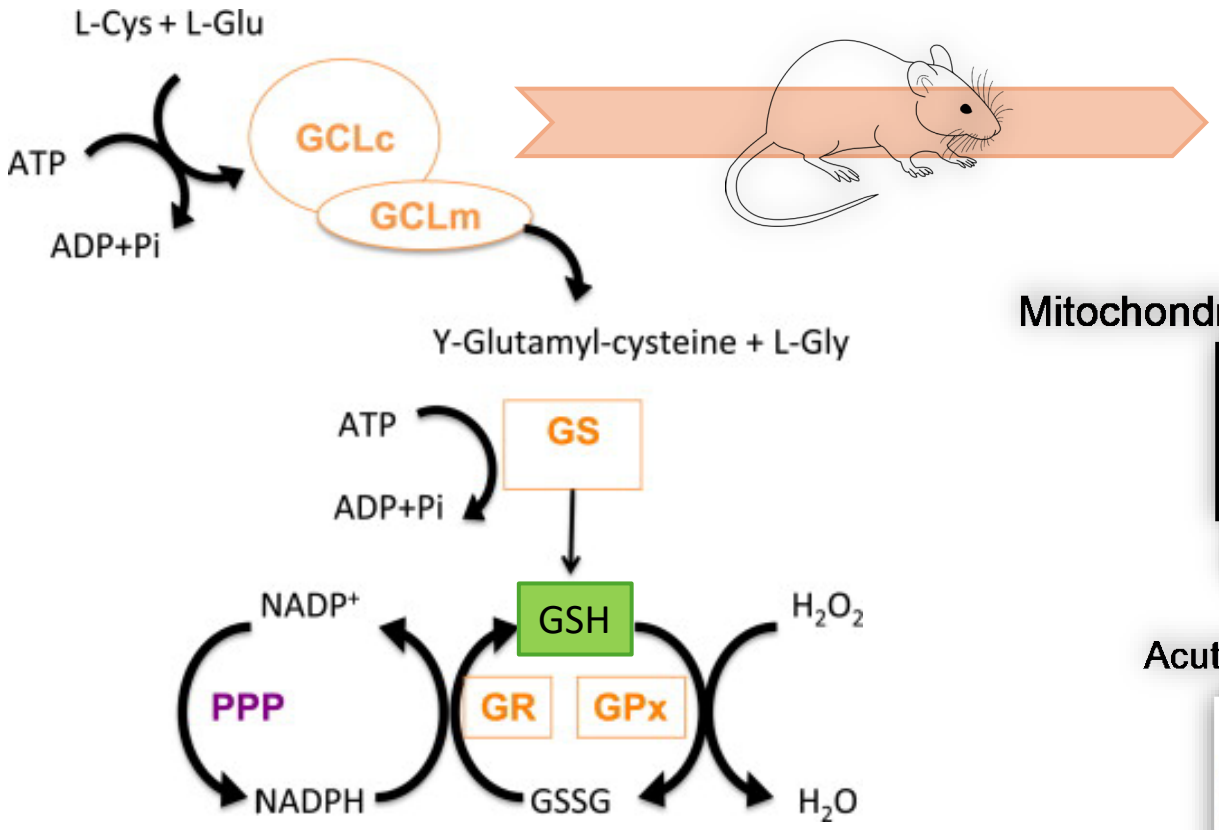




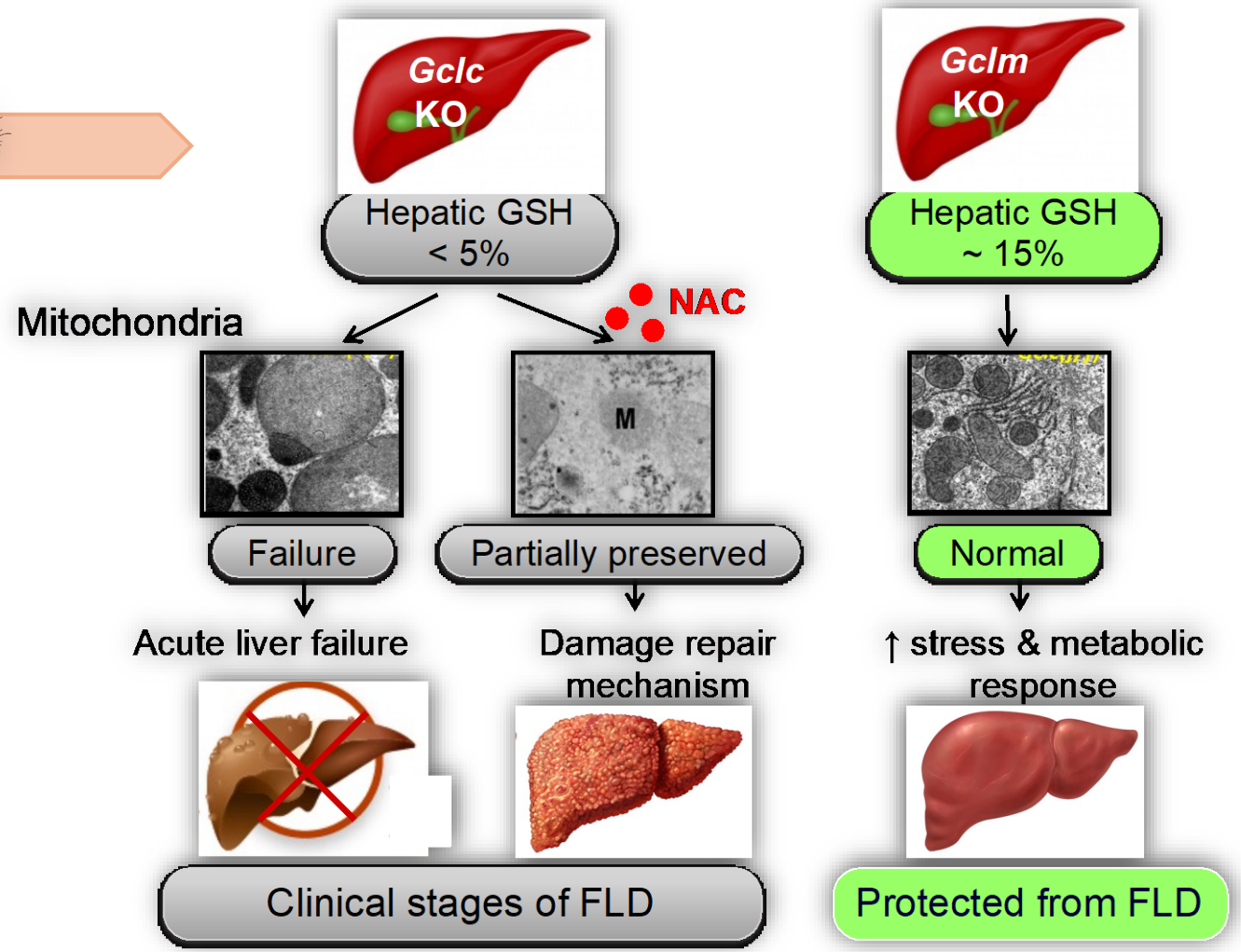




Glutathione in the Pathogenesis of Fatty Liver Disease (FLD)

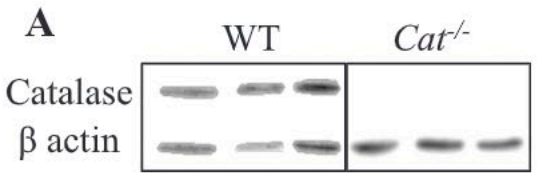


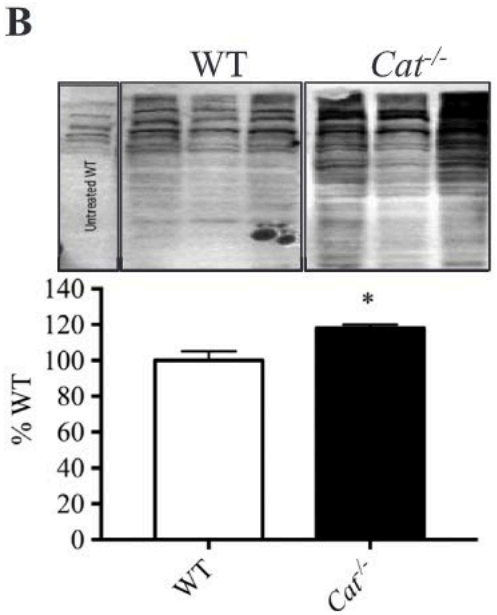
Glutathione (GSH) biosynthesis

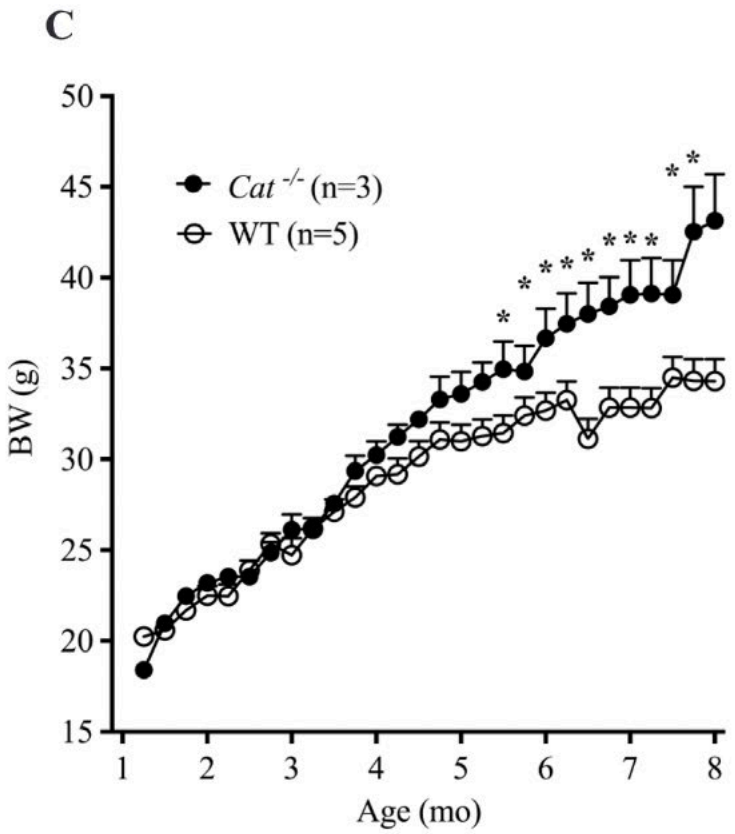


Chen et al. Food Chem Toxicol. 2013

Catalase Gene Deletion Promotes Prediabetic and Obesity Phenotype







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journal homepage: www.elsevier.com/locate/freeradbiomed

Catalase deletion promotes prediabetic phenotype in mice

Claire Heit[a], Stephanie Marshall[b], Surrendra Singh[b], Xiaoqing Yu[c], Georgia Charkoftaki[b], Hongyu Zhao[c], David J. Orlicky[d], Kristofer S. Fritz[a], David C. Thompson[e], Vasilis Vasiliou[b,*]

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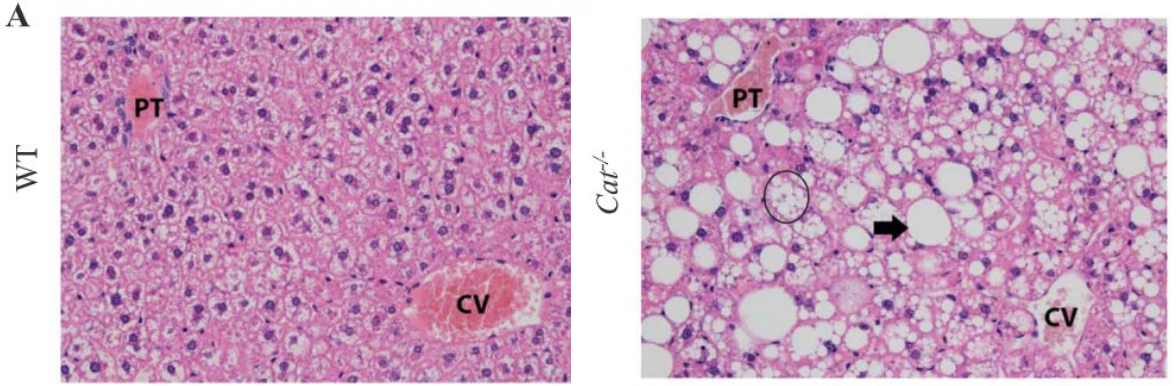
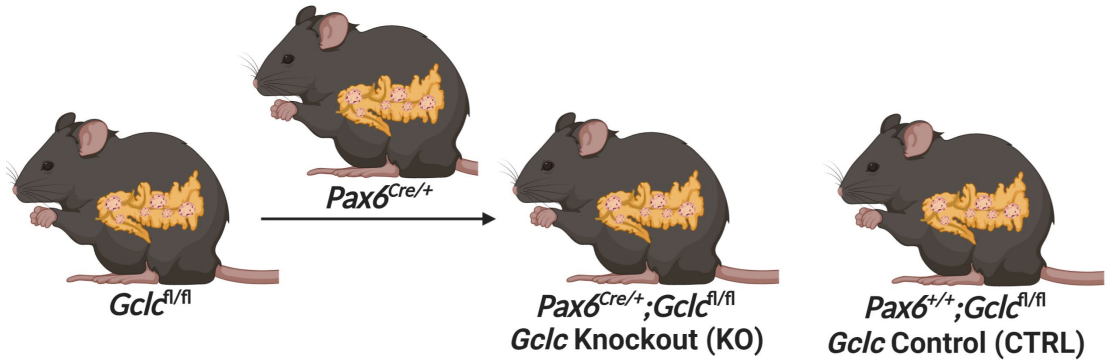
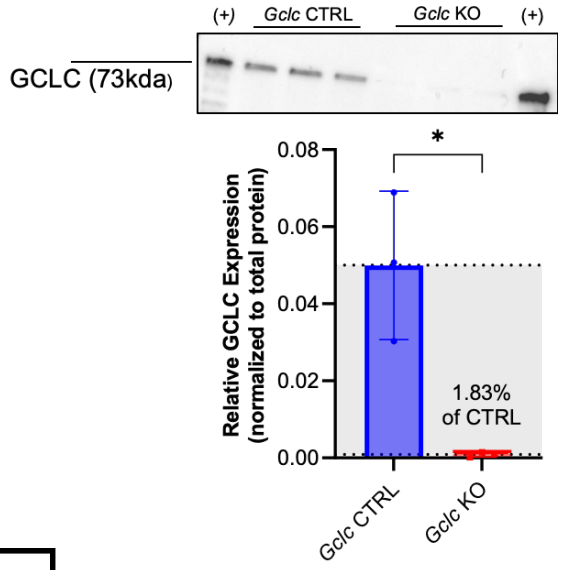
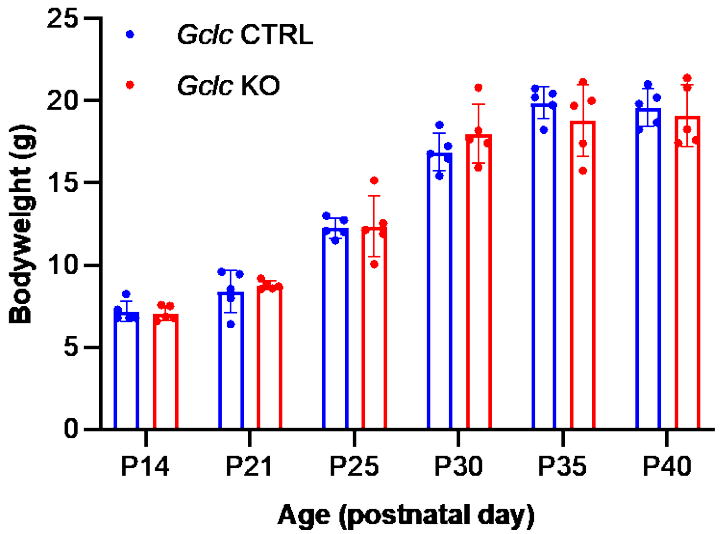
[e] Department of Clinical Pharmacy, School of Pharmacy, University of Colorado Anschutz Medical Campus, 12850 East Montview Boulevard, Aurora, CO 80045, USA

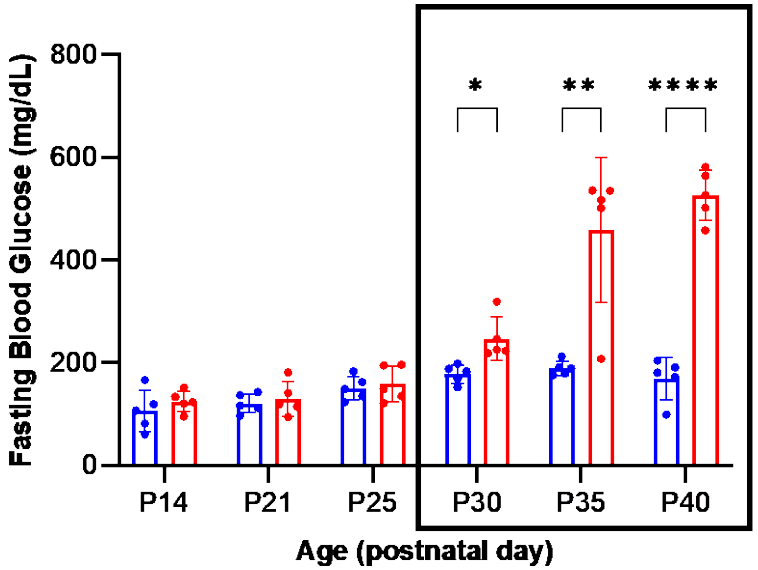


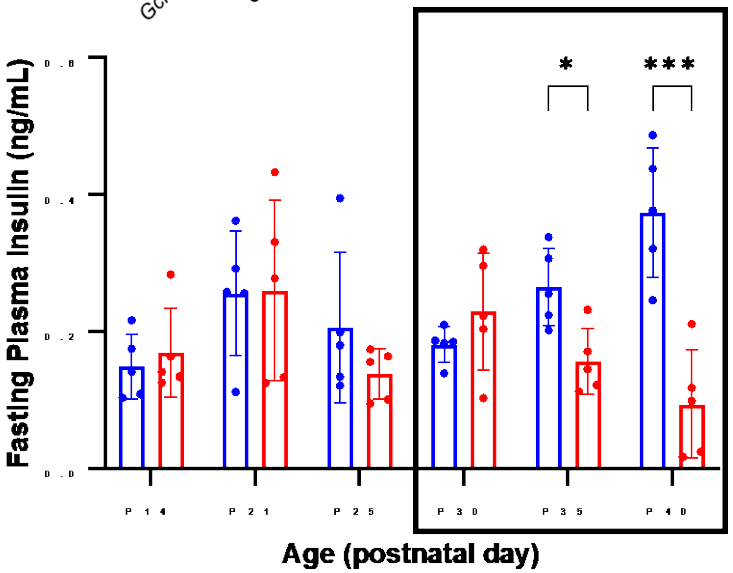
Pancreas *Gclc* Deletion Causes a Severe Diabetes



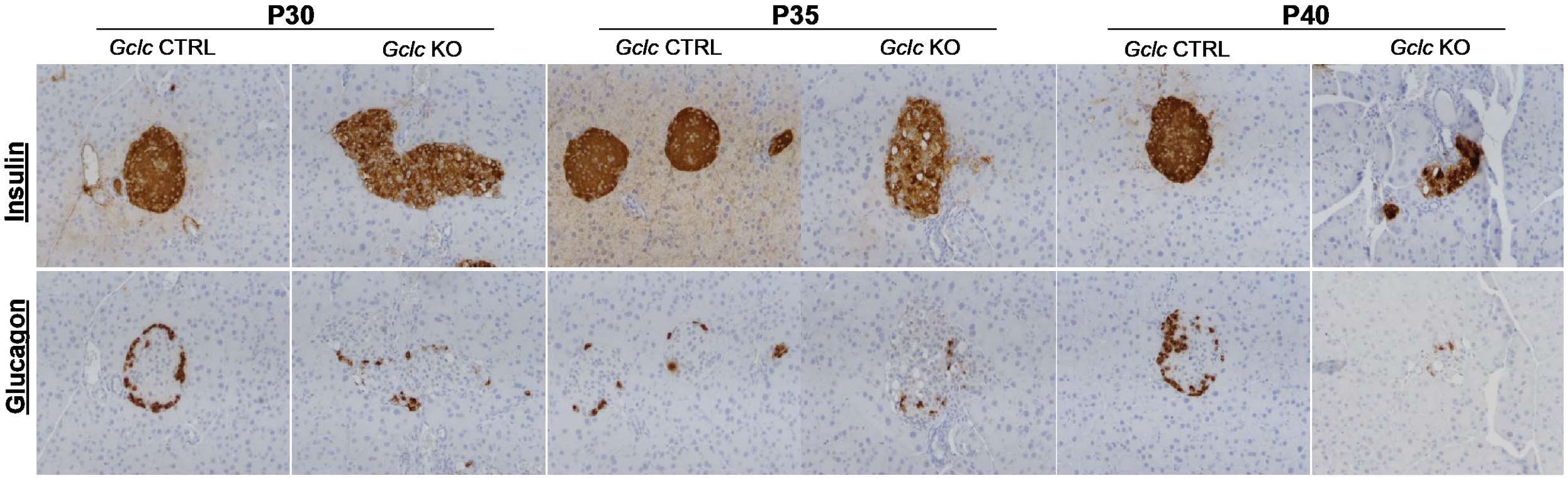






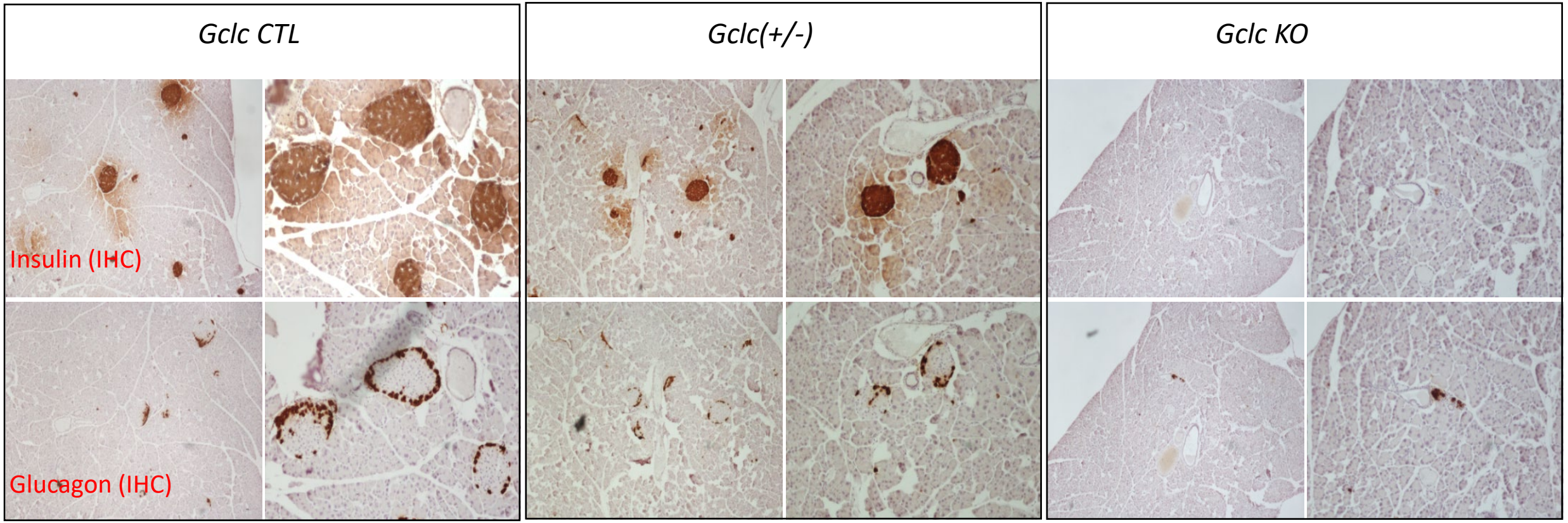


Islet-specific progressive vacuolation

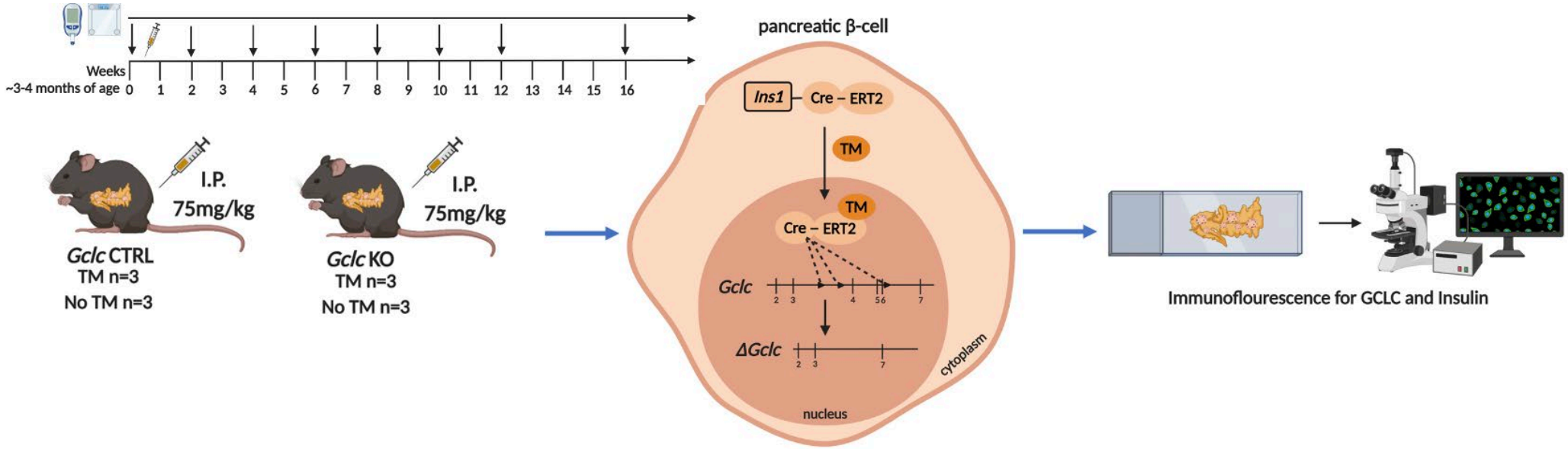


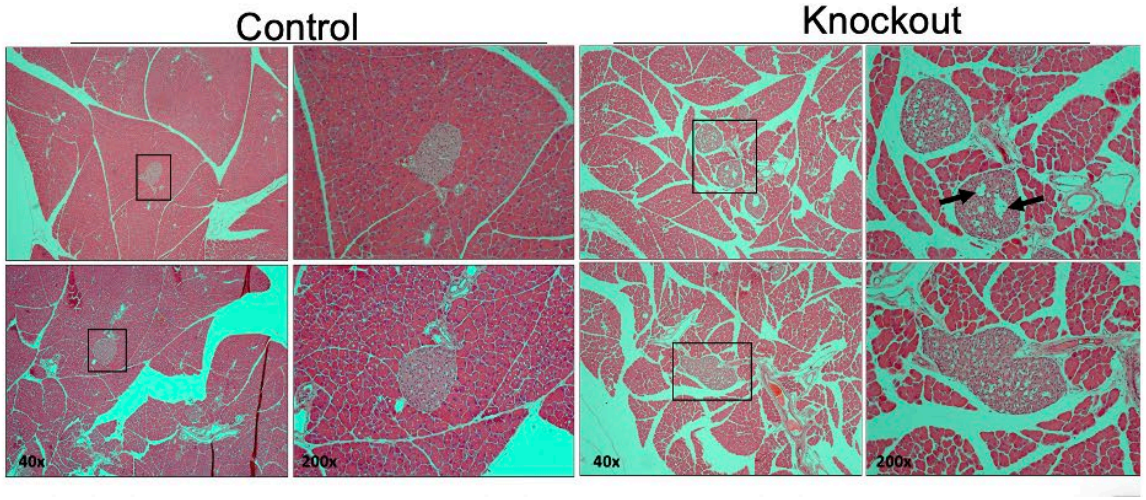
Representative Images, 200x

No Islets after PND 45

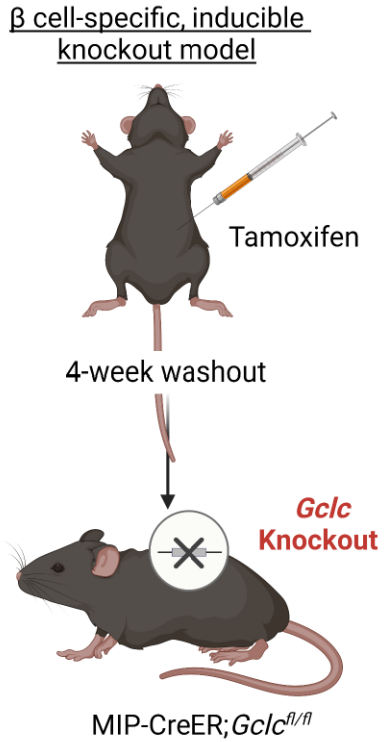


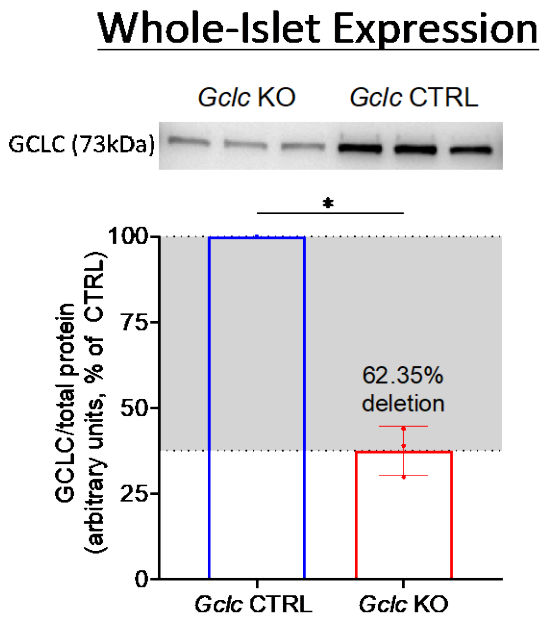
Gclc Gene Deletion in β cells

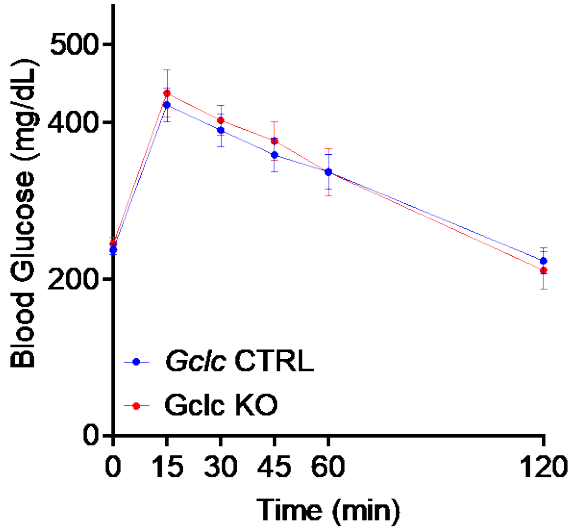


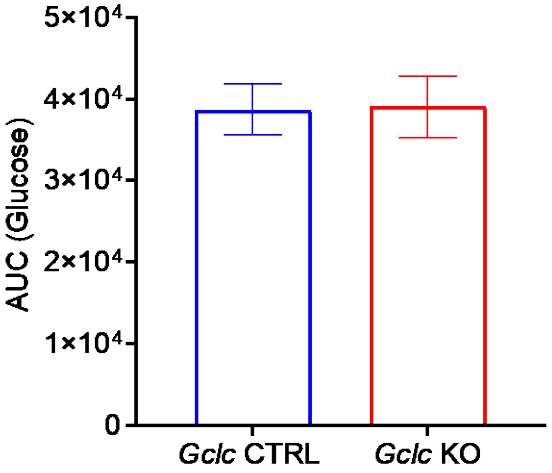


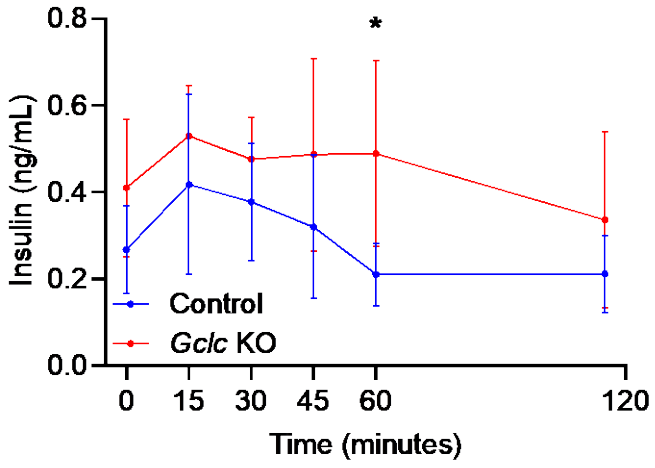
β cell-specific deletion of Gclc in adult mice causes mild hyperinsulinemia

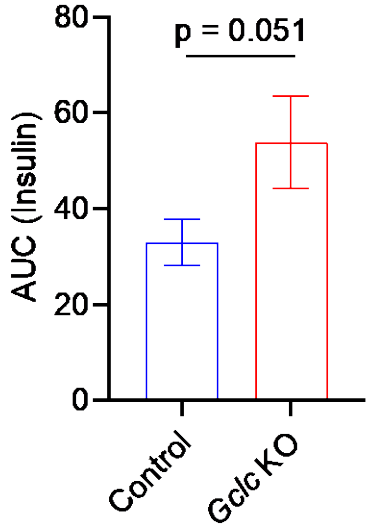












Thank you!

NIH
NIEHS

P42ES033815 (VV)
R24ES036135 (KC)
R01ES032712 (VV)
R25ES029052 (VV)