

Clinical Data Engagement

Neerja Karnani
Senior Principal Investigator
Datahub Division



Research Scope

Clinical Data - Chronic diseases



Metabolic Health



Immune Health



Mental Well Being



Early
Life

Woman's
Health

Paternal
Health

Aging

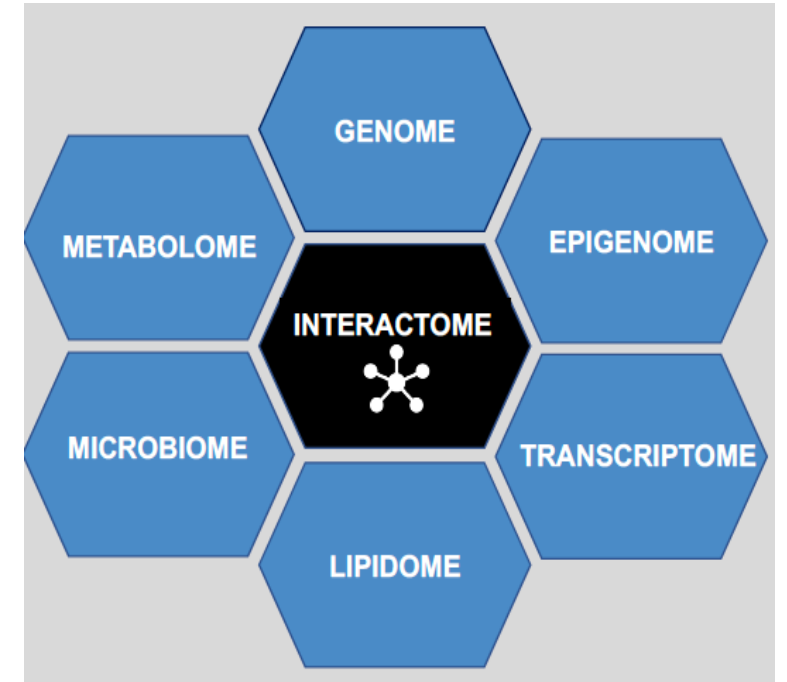
COHORTS

GUSTO, S-PRESTO, iDAD-SG, PREPARE trial, TEAMS Study, NPM cohorts, MEMOSA, ATTRacT, PRISM

EHR

REAL WORLD DATA

Molecular Phenotyping and Precision Health



Risk Predictors

Diagnosis

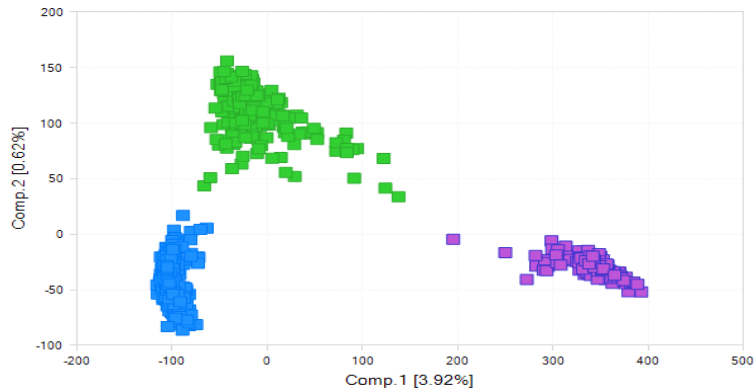
Interventions

Industry, NextGen Apps, Integrated Omics
Databases

1. Early Life: Ethnic variation



Infant genotype (N=1105)

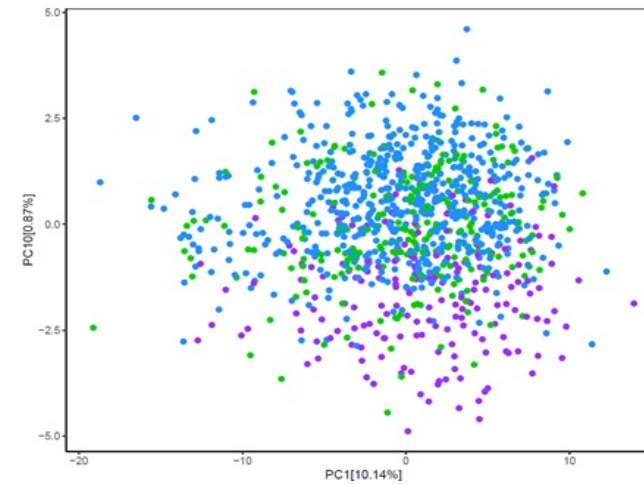


Teh et al Genome Res., 2014

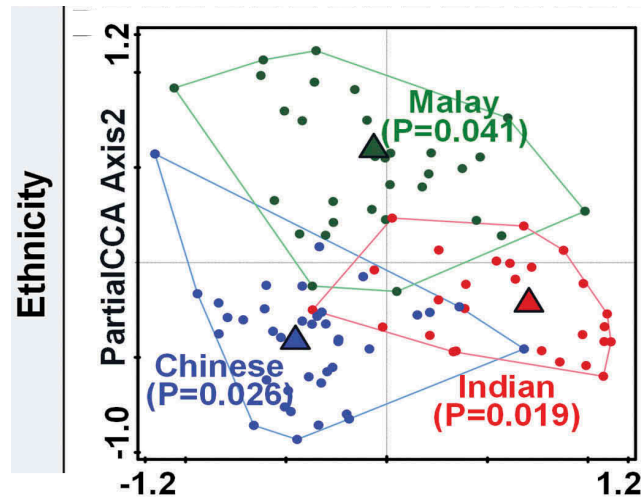


Chinese Malay Indian

Infant epigenome (DNA methylation)
(Cord tissue N=1000)

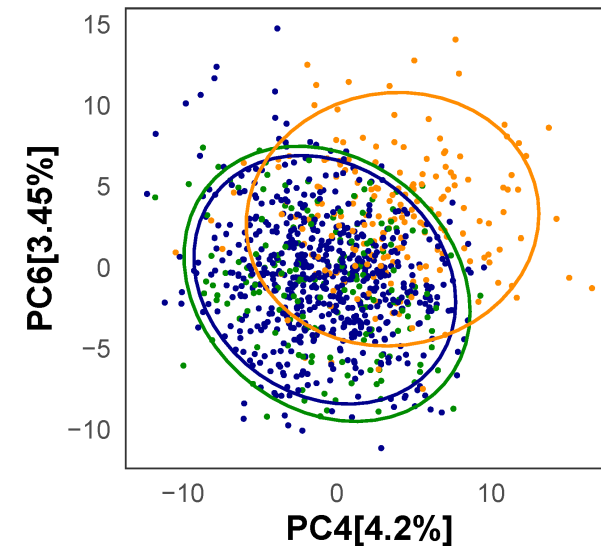


Infant Gut microbiome (N=111, 3months)



Xu, Karnani Gut Microbes 2020

Lipidomics (placenta)



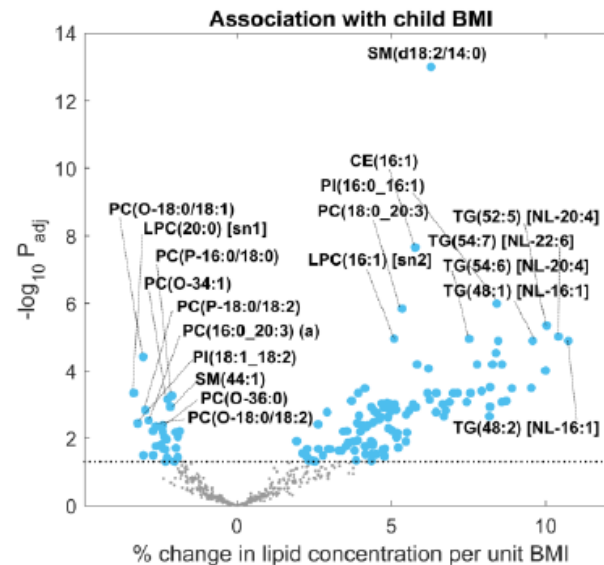
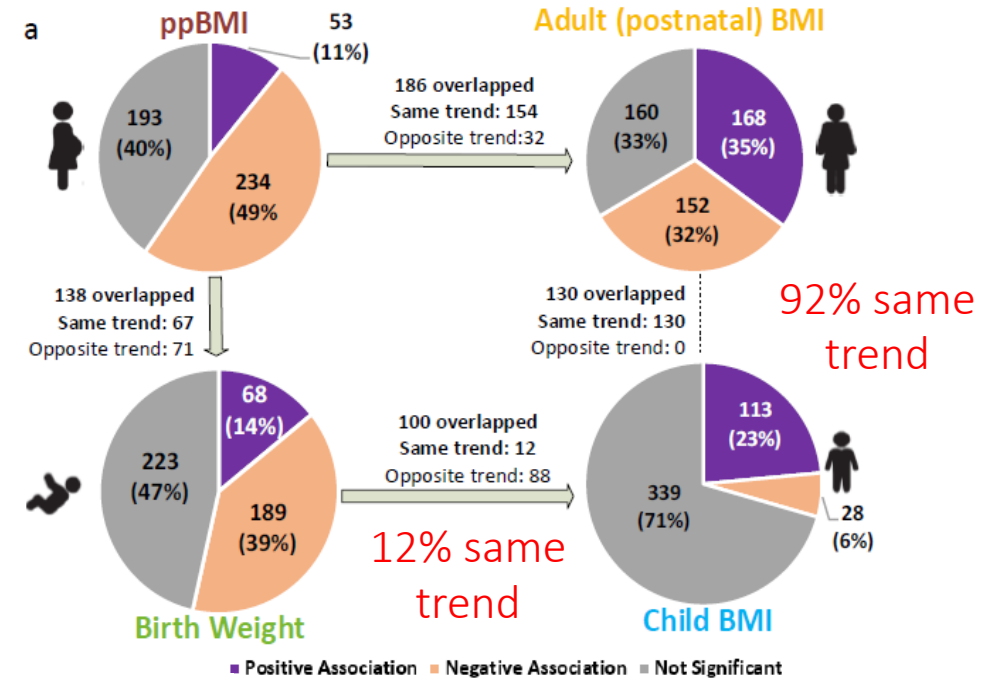
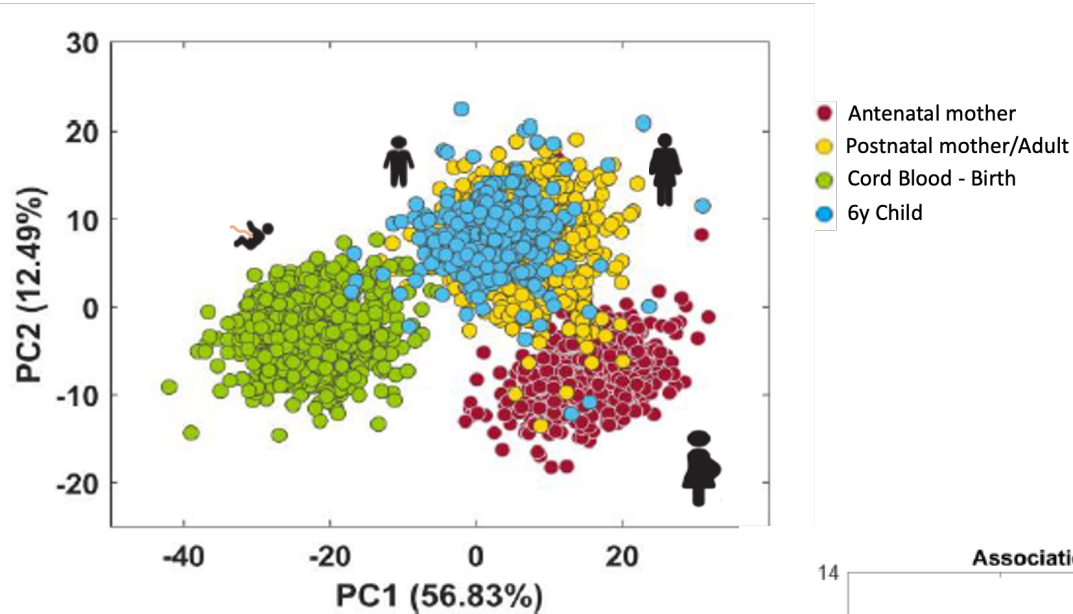
Chinese Malay Indian

Hong, Tan, Lim et al. HMG 2022, under revision

1. Early Life: Lipids and Obesity risk

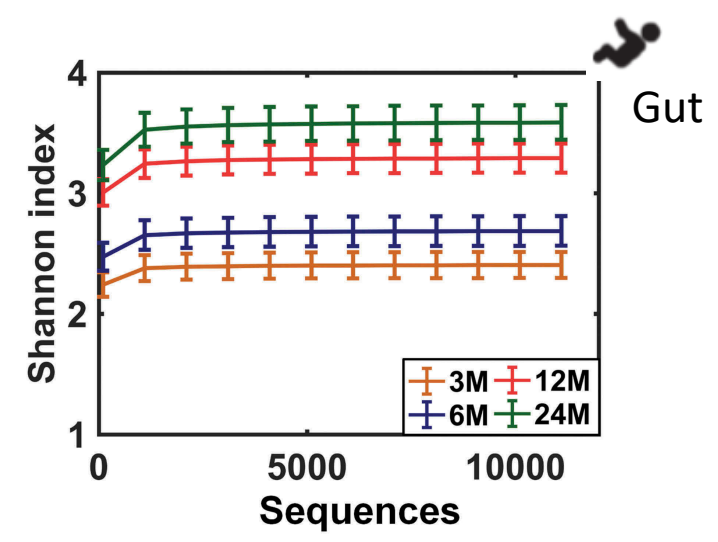
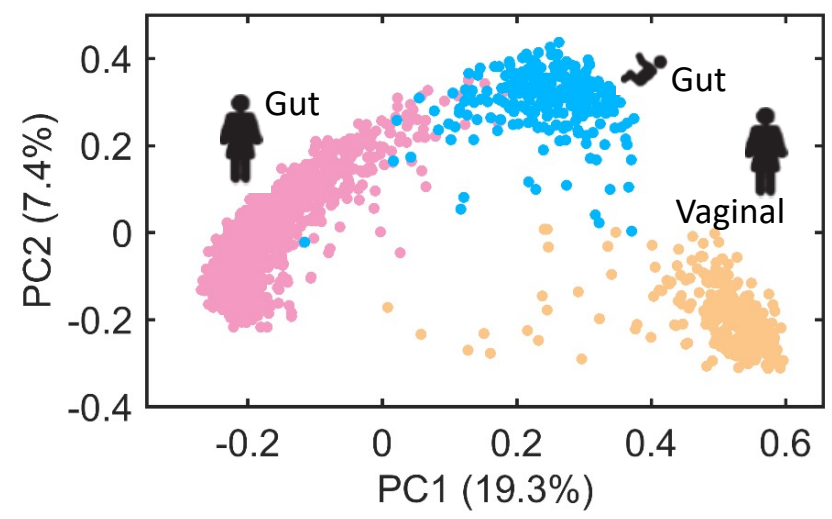


Developmental and Intergenerational Landscape of Human Circulatory Lipidome and its Association with Obesity Risk

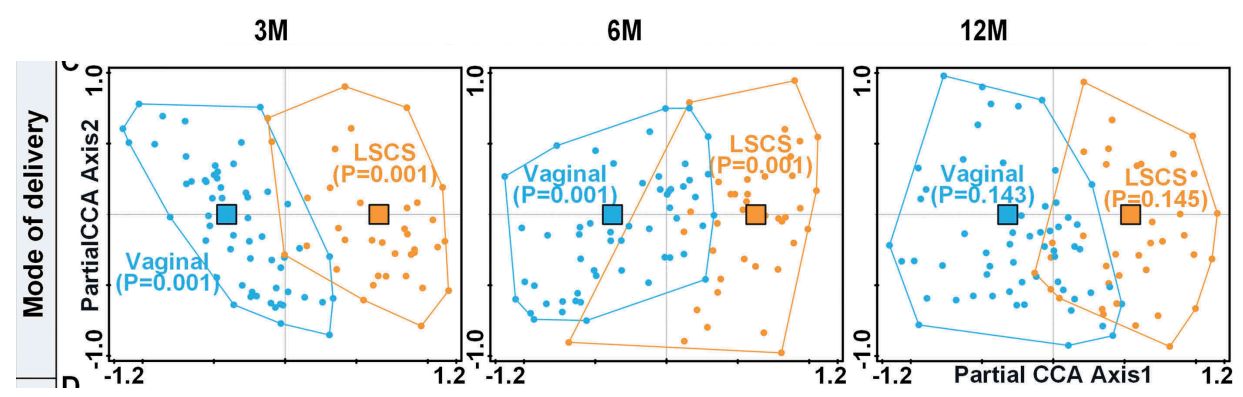


1. Early Life: Factors influencing acquisition of infant gut microbiome

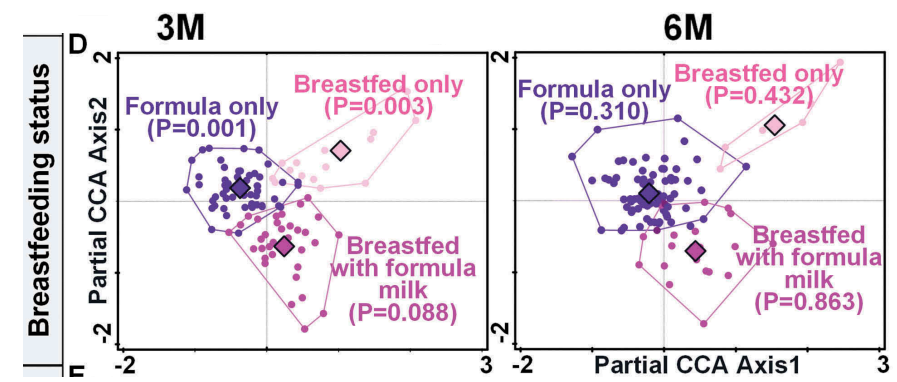
Bray-Curtis
PCoA



Mode of Delivery



Feeding type



Europe PMC Funders Group
Author Manuscript
Int J Obes (Lond). Author manuscript; available in PMC 2021 January 01.

Published in final edited form as:
Int J Obes (Lond). 2020 July 01; 44(7): 1508–1520. doi:10.1038/s41366-020-0572-0.

Implication of gut microbiota in the association between infant antibiotic exposure and childhood obesity and adiposity accumulation



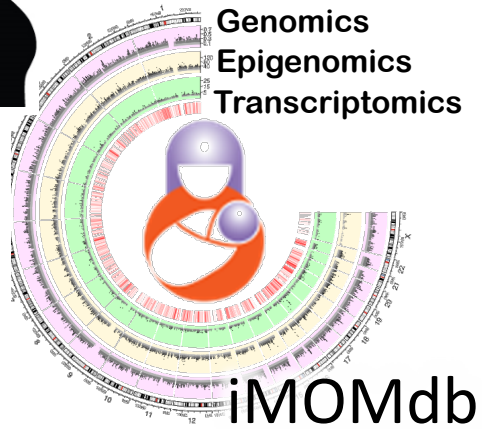
Endangered infant gut microbes and immune health – SIGMA study



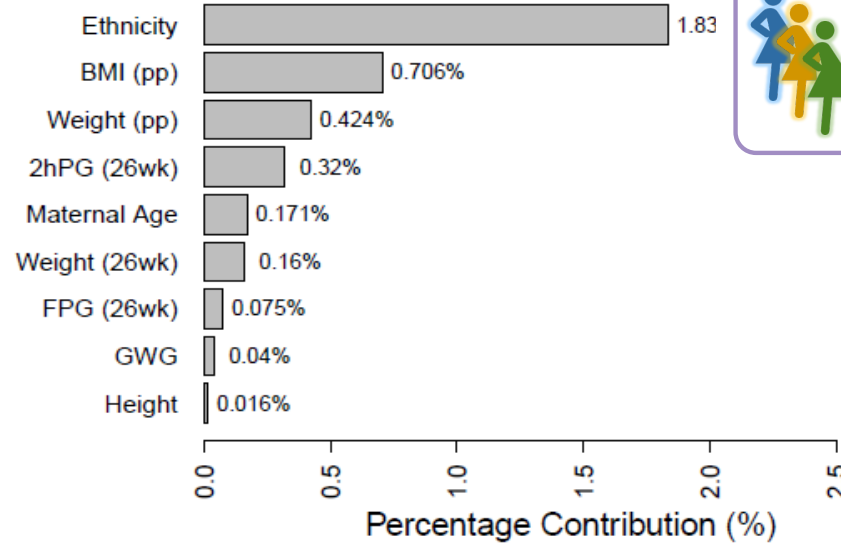
Gut microbes and food allergy IAF-ICP and Nestlé funds

2. Women's Health

Integrative Multi-Omics database (iMOMdb)



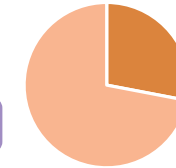
Clinical Phenotypes



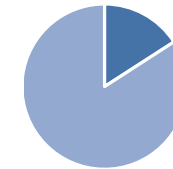
2,561 genes with at least 1 SNP + CpG + RNA sig. assoc with ethnicity



Ethnicity-specific hotspot genes



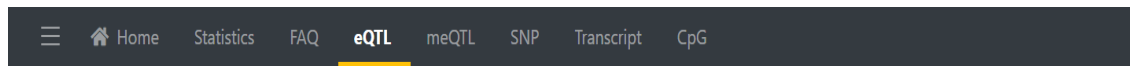
28.0% of all SNPs $F_{ST} > 0.05$
30,350 genes



15.9% of all CpGs $FDR < 0.05$
14,149 genes



27.8% of all RNAs $FDR < 0.05$
4,433 genes



Expression Quantitative Trait Locus

Gene Symbol:

SNP ID:

Transcript ID:

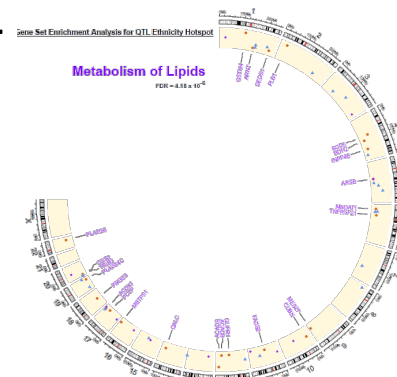
Chromosome:

Start position:

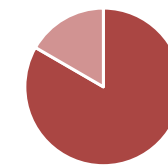
End position:

Ethnicity QTL

395 genes



Plasma lipidome



83.3% of lipids detected sig. assoc. with ethnicity

2. Women's Health – Gestational and T2 Diabetes



> [Diabetes Res Clin Pract.](#) 2022 Feb 4;185:109237. doi: 10.1016/j.diabres.2022.109237. Online ahead of print.

Population-centric risk prediction modeling for gestational diabetes mellitus: A machine learning approach

Mukesh Kumar¹, Li Chen², Karen Tan², Li Ting Ang³, Cindy Ho³, Gerard Wong², Shu E Soh⁴, Kok Hian Tan⁵, Jerry Kok Yen Chan⁶, Keith M Godfrey⁷, Shiao-Yng Chan⁸, Mary Foong Fong Chong⁹, John E Connolly¹⁰, Yap Seng Chong⁸, Johan G Eriksson¹¹, Mendilina Fena¹², Neeria Karnani¹³

UK NICE guidelines showed poor predictability in Singaporean women [AUC:0.60 (95% CI 0.51, 0.70)]. The non-invasive predictive model comprising of 4 non-invasive factors: mean arterial blood pressure in first trimester, age, ethnicity and previous history of GDM, greatly outperformed [AUC:0.82 (95% CI 0.71, 0.93)] the UK NICE guidelines.

Machine Learning Derived Prenatal Predictive Risk Model to Guide Intervention and Prevent the Progression of Gestational Diabetes Mellitus to Type 2 Diabetes. [Accepted for publication in JMIR Diabetes on 22 March 2022]

Kumar M, Ang LT, Ho C, Soh SE, Tan KH, Chan JK, Godfrey KM, Chan SY, Chong YS, Eriksson JG, Feng M, Karnani N

Mukesh and Ives

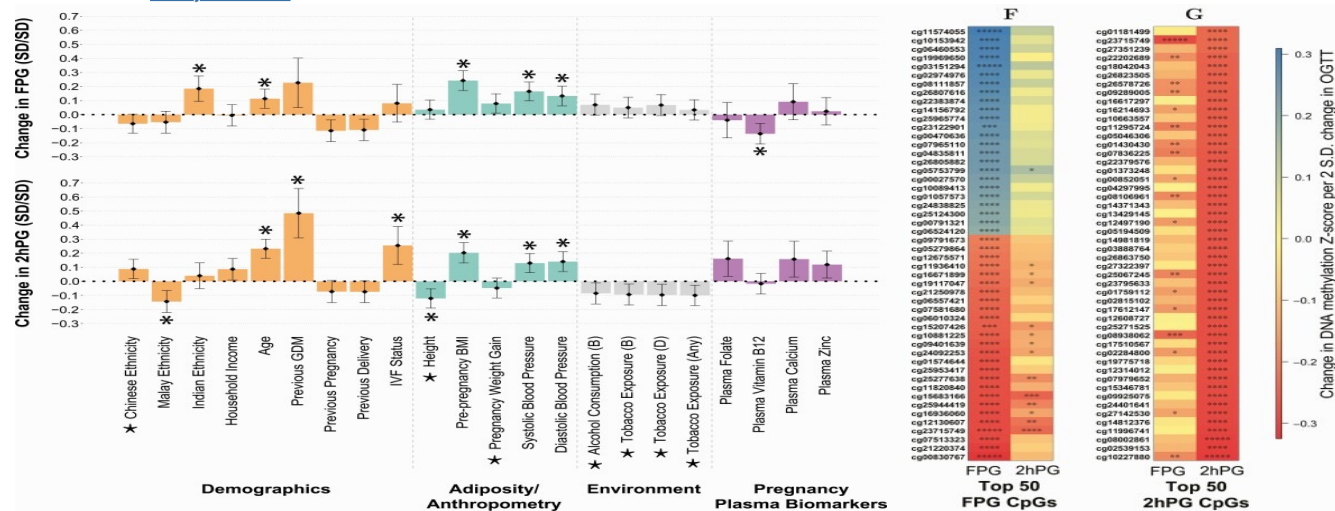


[J Clin Endocrinol Metab.](#) 2022 Mar; 107(3): e1277–e1292. Published online 2021 Oct 11. doi: [10.1210/clinem/dgab710](#)

PMCID: PMC8852163
EMSID: EMS137875
PMID: [34633450](#)

Dichotomy in the Impact of Elevated Maternal Glucose Levels on Neonatal Epigenome

Ives Yubin Lim^{1,2,3}, Xinyi Lin^{1,4,5}, Ai Ling Teh¹, Yonghui Wu¹, Li Chen¹, Menglan He⁶, Shiao-Yng Chan^{1,2}, Julia L Maclsaac⁷, Jerry K Y Chan^{8,9}, Kok Hian Tan⁸, Mary Foong Fong Chong^{1,9}, Michael S Kobor⁷, Keith M Godfrey¹⁰, Michael J Meaney^{1,11}, Yung Seng Lee^{1,12,13}, Johan G Eriksson^{1,2,14,15}, Peter D Gluckman^{1,16}, Yap Seng Chong^{1,2} and Neerja Karnani^{1,3,17}



Meta-Analysis > [Diabetes Care.](#) 2022 Mar 1;45(3):614–623. doi: 10.2337/dc21-1701.

Maternal Glycemic Dysregulation During Pregnancy and Neonatal Blood DNA Methylation: Meta-analyses of Epigenome-Wide Association Studies

Elmar W Tobin¹, Diana L Juvinao-Quintero², Justiina Ronkainen³, Raffael Ott^{4 5 6}, Rossella Alfano⁷, Mickaël Canouil^{8 9}, Madelon L Geurtsen^{10 11}, Amna Khamis^{8 9 12}, Leanne K Küpers^{10 11}, Ives Y Lim^{13 14}, Patrice Perron^{15 16}, Giancarlo Pzesco^{17 18}, Johanna Tuhkanen¹⁹, Anne P Starling^{20 21}, Toby Andrew¹², Elisabeth Binder^{22 23}, Robert Caiazza²⁴, Jerry K Y Chan^{25 26}, Romy Gaillard^{10 11}, Peter D Gluckman^{14 27}, Elina Keikkala^{28 29}, Neerja Karnani^{13 14 30}, Sanna Mustaniemi^{28 29}, Tim S Nawrot⁷, François Pattou²⁴, Michelle Plusquin⁷, Violeta Raverdy²⁴, Kok Hian Tan^{26 31}, Evangelia Tzala³², Katri Raikonen¹⁹, Christiane Winkler^{4 5 6}, Anette-G Ziegler^{4 5 6}, Isabella Annesi-Maesano³³, Luigi Bouchard^{34 35}, Yap Seng Chong^{14 36}, Dana Dabelea^{20 21 37}, Janine F Felix^{10 11}, Barbara Heude³⁸, Vincent W V Jaddoe^{10 11}, Jari Lahti¹⁹, Brigitte Reimann⁷, Marja Väärasmäki²⁹, Amélie Bonnefond^{8 9 12}, Philippe Froguel^{8 9 12}, Sandra Hummel^{4 5 6}, Eero Kajantie^{28 29 39 40}, Marjo-Riita Jarvelin^{3 32 41 42}, Regine P M Steegers-Theunissen¹, Caitlin G Howe⁴³, Marie-France Hivert^{2 44}, Sylvain Sebert³

3. Paternal Origins of Health and Disease



New Results

Short-term diet intervention alters the small non-coding RNA (sncRNA) landscape of human sperm

Epigenetic alterations in male germline by bariatric surgery **Key pathways altered -** glucose metabolism, energy balance, eating behaviour and imprinting genes

- Project 1 (P1)**
Diet intervention
Omega fatty acids
and Vitamin D
- Project 2 (P2)**
TEAM Study
Bariatric surgery
intervention
- Project 3 (P3)**
iDAD_SG
Smoking and lifestyle



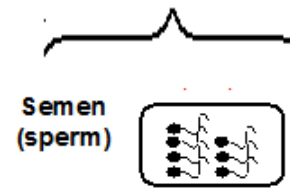
(P1, P2, P3)



Blood Markers

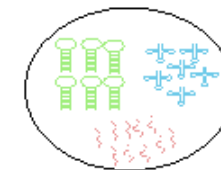


DNA methylation

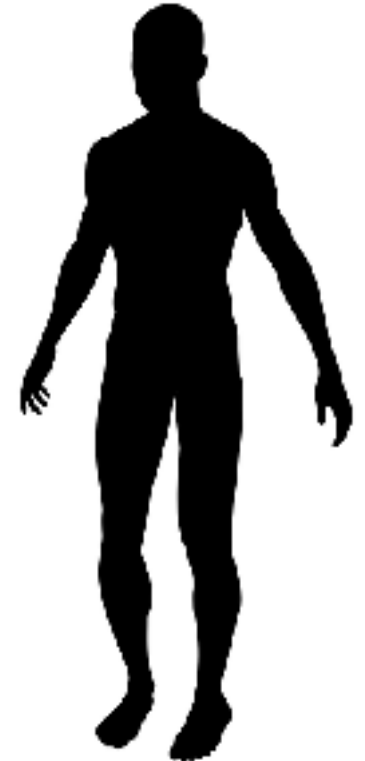


Semen
(sperm)

Small non-coding RNA

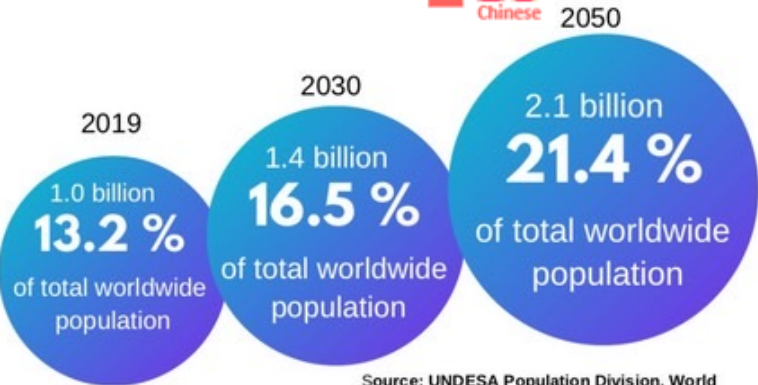


(P1, P3)



4. Aging in Asians

Growing Global Ageing Population >60ys

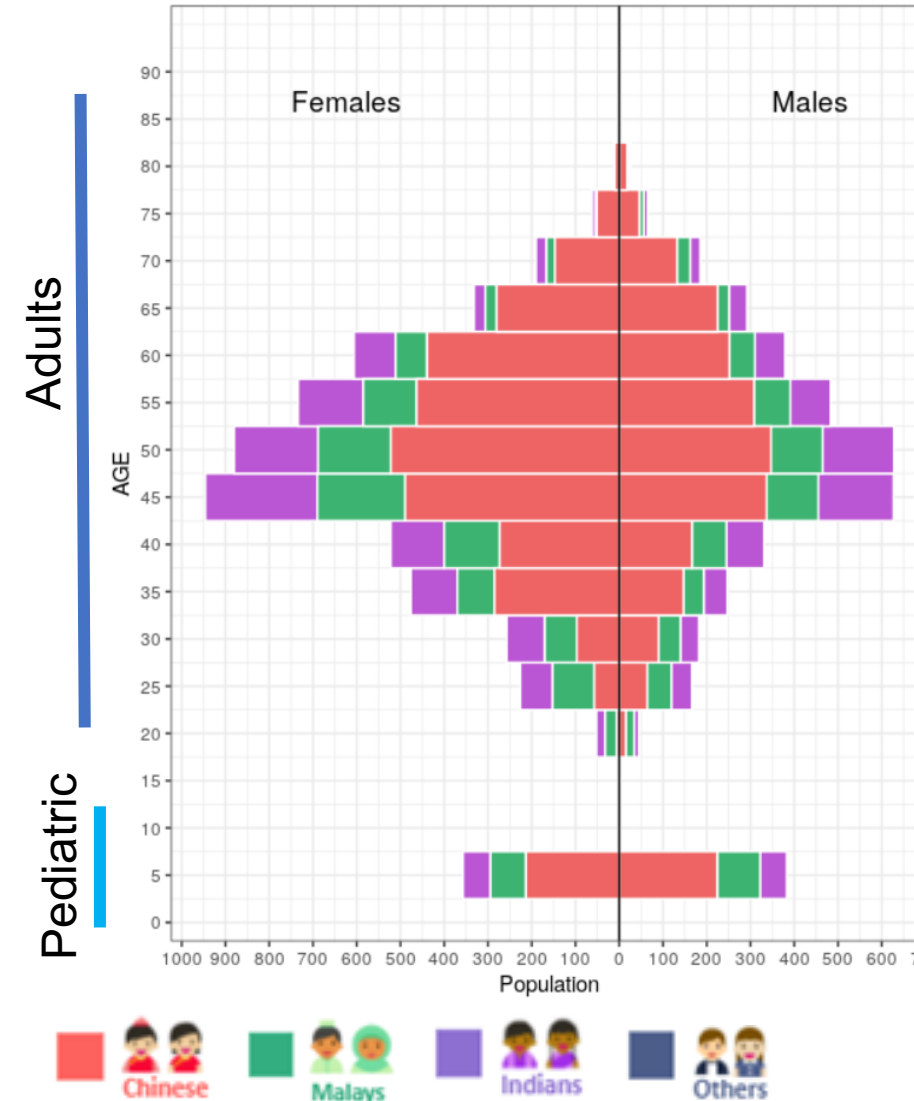


By 2030, 1 in 4 Singaporeans will be aged >65y

Chronological age is not a predictor of biological aging, healthspan and longevity



SG10K-Health: Age distribution



4. Aging in Asians

Biological aging markers

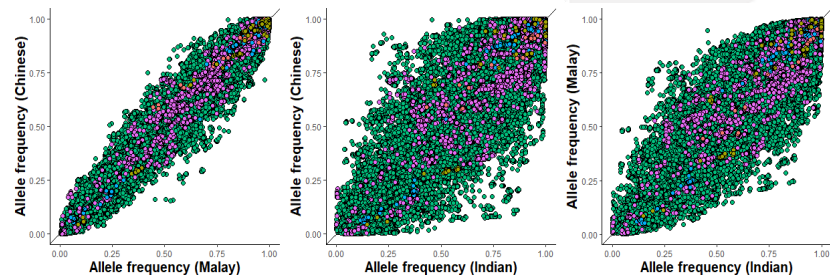
and clocks



SNPs

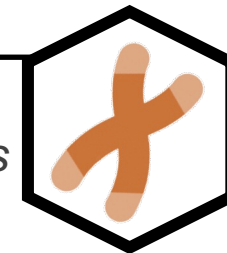
Trans-ethnic and ethnicity specific variants associated with *ageing and healthspan*

63K SNPs



EpiAge

Asian EpiAge estimates for pediatric and adult sub-populations



Telomere length

Ethnic variation and SNP variants

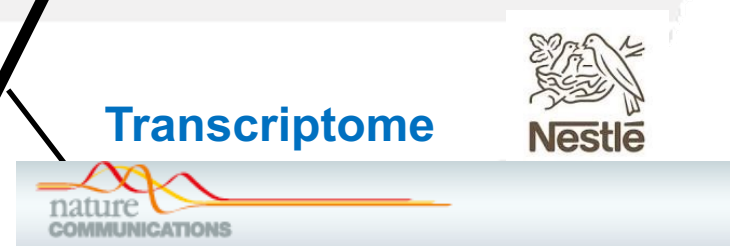
Chen et al. *BMC Medicine* (2022) 20:20
<https://doi.org/10.1186/s12916-021-02217-9>

BMC Medicine

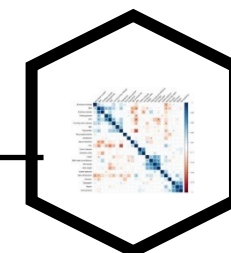
RESEARCH ARTICLE

Open Access

Variability in newborn telomere length is explained by inheritance and intrauterine environment



Transcriptome



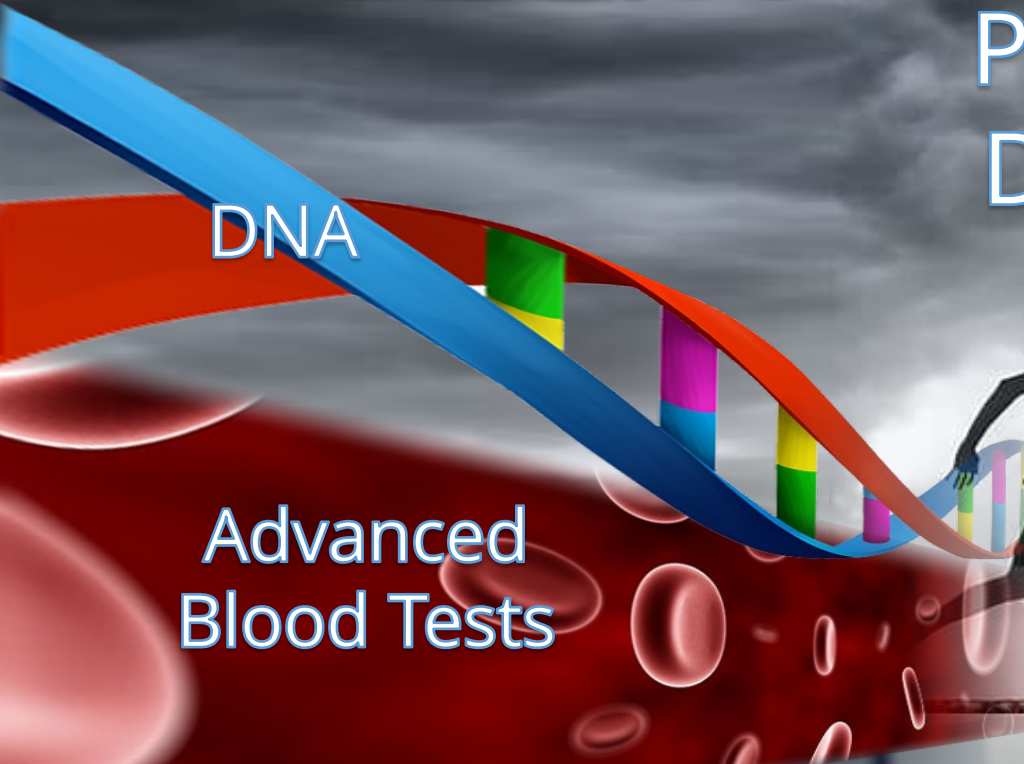
ARTICLE

<https://doi.org/10.1038/s41467-019-13494-1> OPEN

Mitochondrial oxidative capacity and NAD⁺ biosynthesis are reduced in human sarcopenia across ethnicities

5. Next Gen Apps

Patient Journey Apps Disease Surveillance



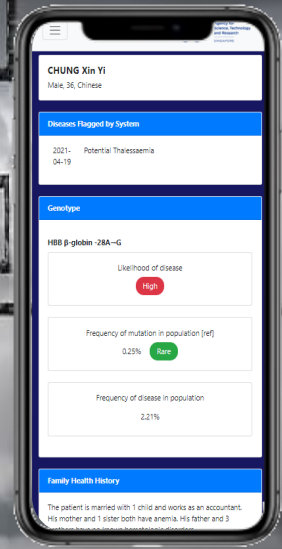
DNA

Advanced
Blood Tests



Electronic
Health Records

Real World Data

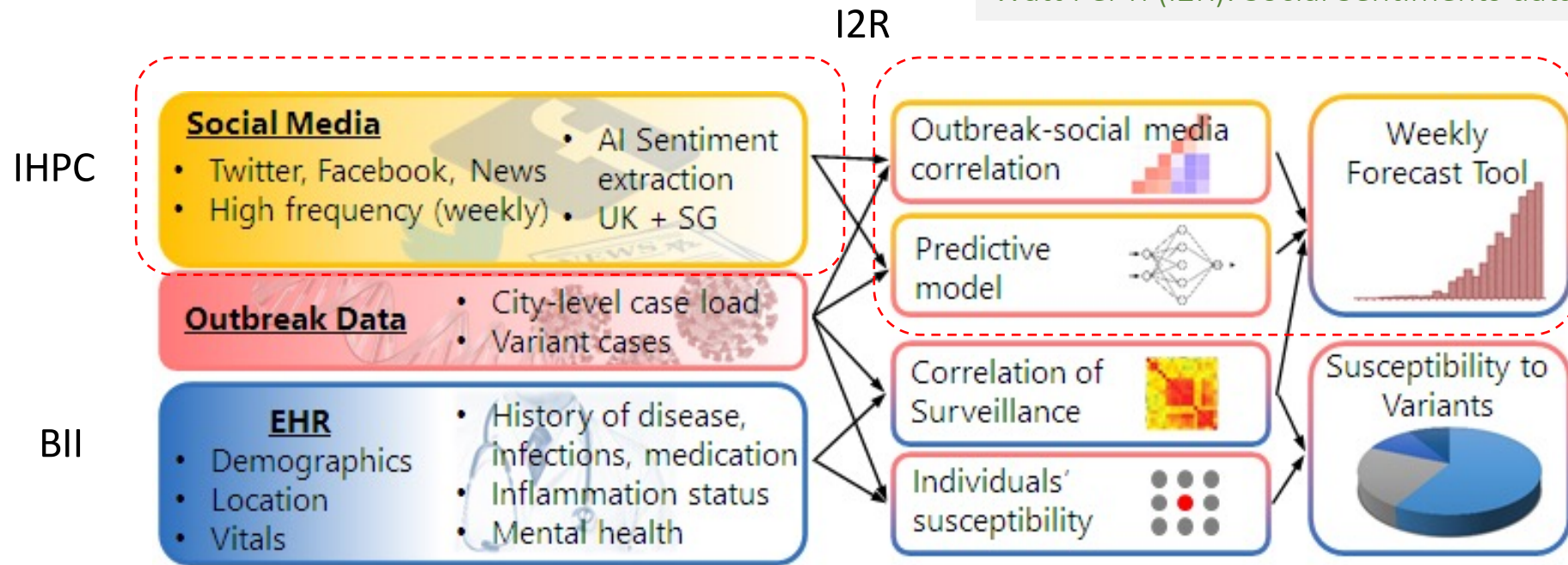


Healthy
Living

Scientific
literacy

5. Improving infectious disease forecasting through social media and electronic health record surveillance

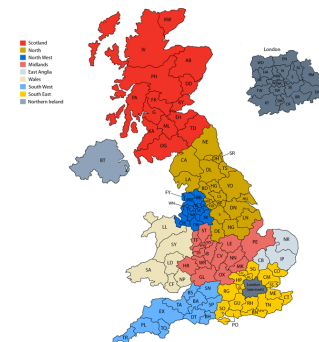
Rajaraman Kanagasabai (I2R): Co-Investigator
 Watt Pei Yi (I2R): Social Sentiments data analyst



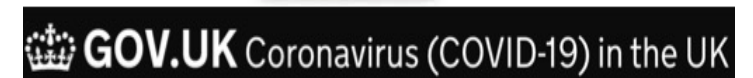
242,376,717 English tweets worldwide related to COVID-19 made from 28 January 2020 to 01 Mar 2022

Neerja Karnani (BII): Lead PI
 Matthew Choo (BII): Population dynamics and predictive modeling
 Jason Huan (BII): Full Stack developer starting in April (EHR data acquisition)

Sebastian Maurer-Stroh (BII) : Co-Investigator
 Joses Ho (BII): Virus variant data analyst



UK 310 postal codes data analyzed



Acknowledgements

Data Analysts @ BII



Ives LIM

Matthew CHOO

Jason HUAN

Penny CHAN

Data Analysts Supervised @ SICS



Priti MISHRA

Candida VAZ

Jia XU

Mukkesh KUMAR

Hospitals/Universities/A*STAR RIs



Cohorts



PRISM



S-RESTO



Public Sector/National Platforms



Industry



Funding



ASTAR-NMRC Joint Call
IAF-PP
ID-HTPO
LCG

International collaborations



Covid data resources





THANK YOU

www.a-star.edu.sg