Agency for Science, Technology and Research
SINGAPORE

Decoding the Link Between Human Variation and Health Adversities through iOmics and Deep Phenotyping in Pediatric and Adult Populations

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CLINICAL SCIENCES and BIOINFORMATICS

BEST OF BOTH WORLDS

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Ai Ling


Xinyi Lin (Cindy)


Yonghui Wu

POWERING DISCOVERIES

SINGAPORE: HEALTH ADVERSITIES ON A RISE

POWERING DISCOVERIES

Metabolic Health


THE STRAITS TIMES SINGAPORE

Singapore 'has 2nd-highest proportion of diabetics'

At 10.53% of people with disease, Republic is behind US among developed nations: Study

12% obesity among school-going children

Mental Health


THE STRAITS TIMES SINGAPORE

More in Singapore seek help for mental health issues amid Covid-19 pandemic

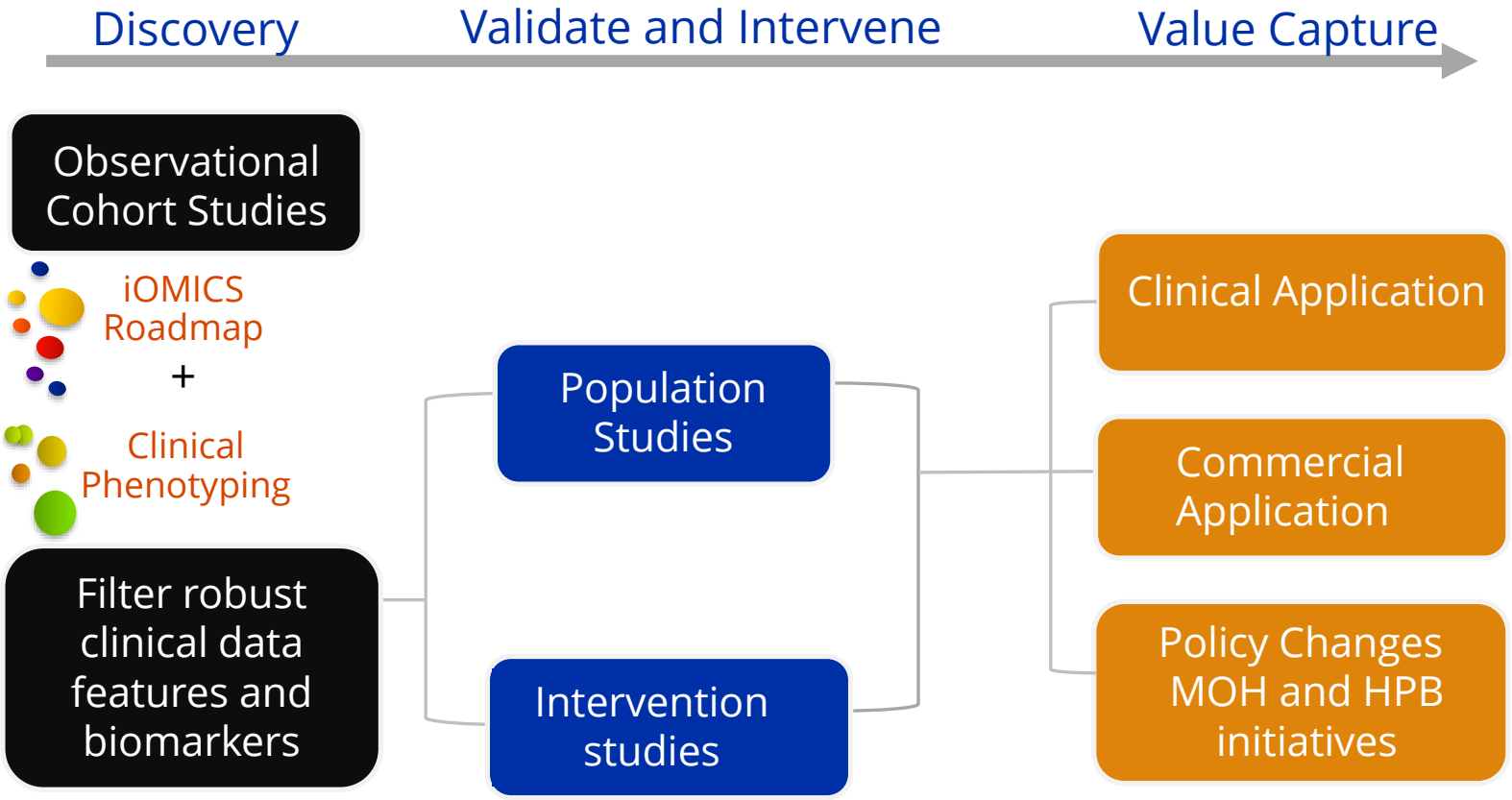
Significant increase seen across different age groups; spike in calls to suicide helpline

al Health issues

Aging and Health Span

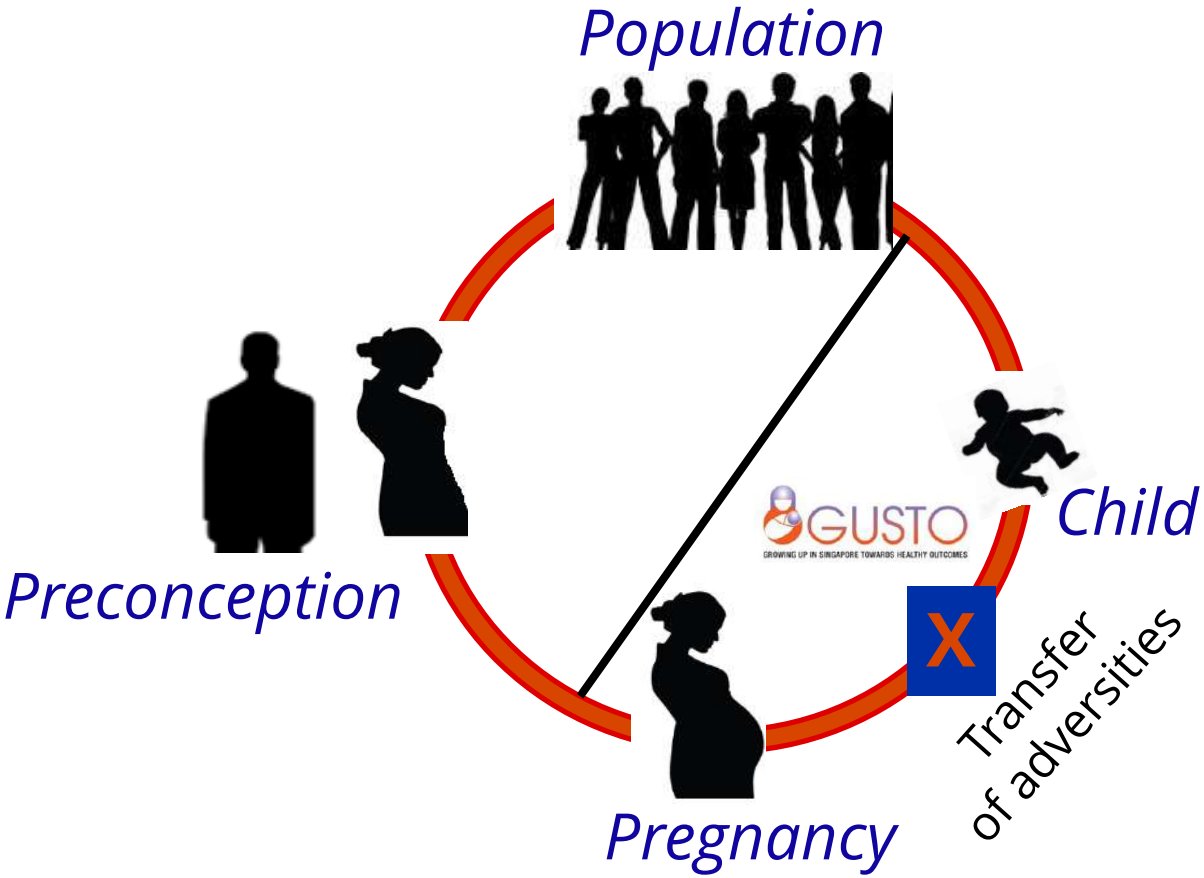
Singaporeans aged 65 and older form 13.1 per cent of citizen population

Our approach



POWERING DISCOVERIES

BREAKING THE CYCLE EARLY IN LIFE



POWERING DISCOVERIES

Growing Up in Singapore Towards healthy Outcomes

GUSTO
GROWING UP IN SINGAPORE TOWARDS HEALTHY OUTCOMES

POWERING DISCOVERIES

National University Hospital

KK Women's and Children's Hospital
SingHealth

Singapore Institute for Clinical Sciences
SICS

LIVING WITH GUSTO

Launched in 2009

Closest longitudinal follow-up ever in Singapore

1,247 mother-child pairs with basic participation and support from fathers

81% retention rate with oldest child 8 years old in late 2017

Over 29 home & clinic visits for each participant since pregnancy until today

Covers the three major Asian ethnic groups (representing 40% of global population) – Chinese, Malay and Indian, which few other studies represent

Revealed important findings that

<14th wk | 26th-28th wk | Birth | 3 wk | 3mth | 6mth | 9mth | 12mth | 15mth | 18mth

2 yr | 3 yr | 4 yr | 4.5 yr | 5 yr | 6 yr | 7 yr | 8 yr | 9 yr | 10 yr

http://gusto.sg/

POWERING DISCOVERIES

> 15,000 phenotypes collected across 10 health domains

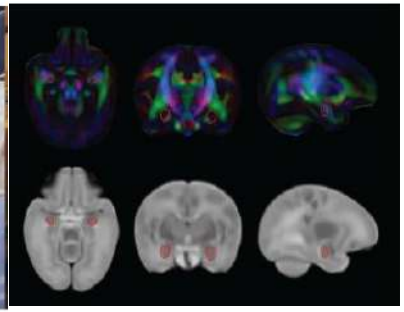
- Pregnancy conditions
- Metabolism
- Mental Well Being
- Neurodevelopment
- Diet and eating behaviour
- Myopia
- Allergy
- Oral Health
- Physical Activity and sleep (wearables)
- Women Reproductive Health

>260 PUBLICATIONS

Extensive Biosampling

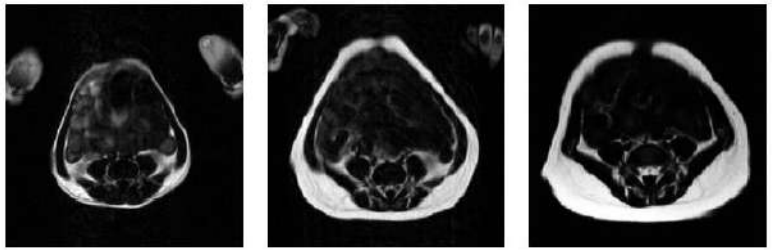
maging

EEG on day 1

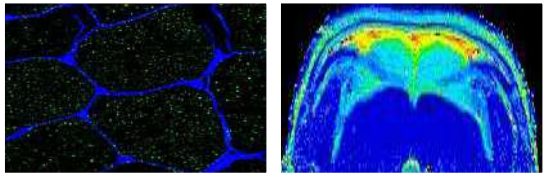


Brain imaging day 7

Abdominal adipose tissue



Liver & Muscle fat (MRS)



Brown fat

GUSTO phenotypes in sync with Singaporean health adversities

1 in 5 mothers developed GDM

- Incidence of GDM is greatest in Chinese and Indian
- Women with GDM have 10X greater risk of Type 2 Diabetes
- ↑ Fasting glucose linked with ↑ Offspring abdominal fat at birth

13% GUSTO-Kids are obese/overweight by age 6

↑ Prehypertension risk
↑ Insulin resistance↑
↑ Abdominal fat ↑
↑ Obesogenic eating behaviors

40% Singapore Women Show Signs of Perinatal Depression

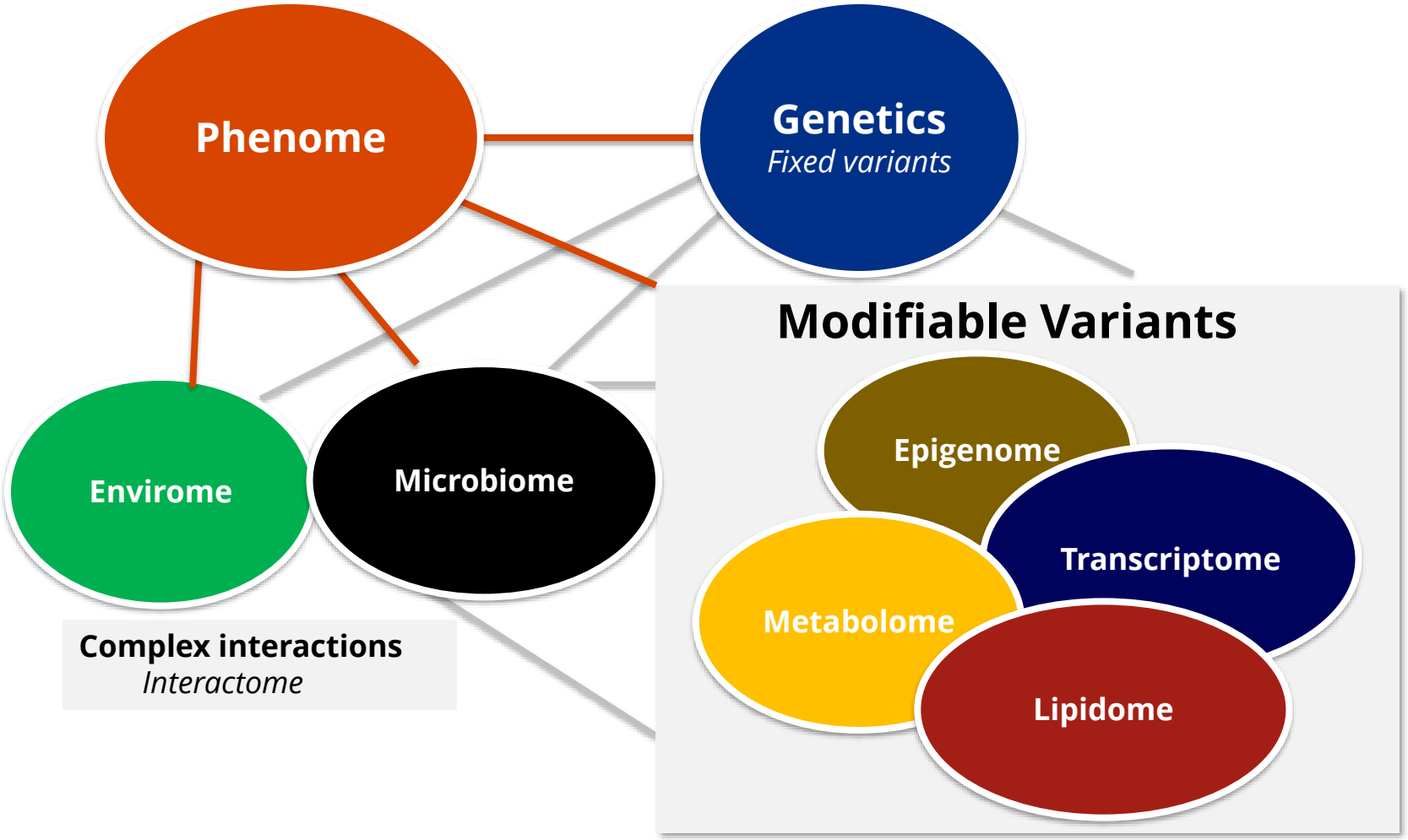
Maternal mental health is associated with child's brain development and socio-emotional outcomes

POWERING DISCOVERIES

POWERING DISCOVERIES

GUSTO OMICS ROADMAP

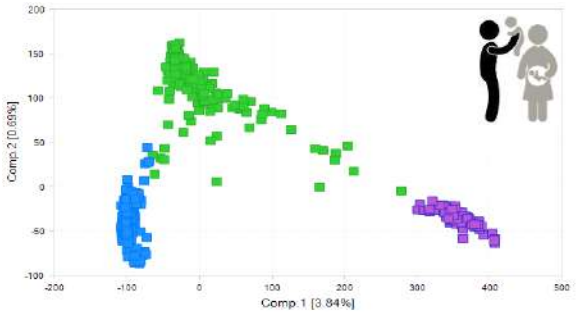
THE COMPLEX WORLD OF OMICS



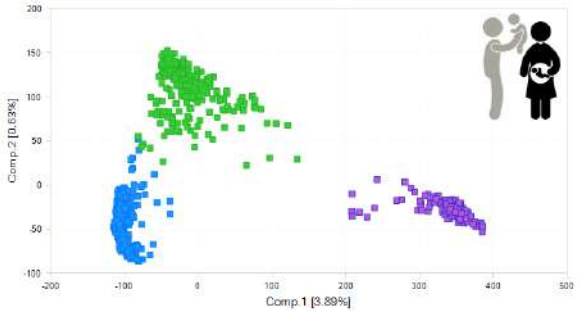
POWERING DISCOVERIES

Genetics
Fixed variants

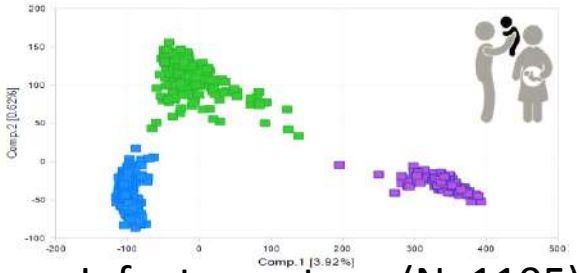
ETHNIC DIFFERENCES IN GENOTYPES OF OFFSPRING-PARENT TRIOS



Paternal genotype (N=719)



Maternal genotype (N=1077)



Infant genotype (N=1105)

Chinese Malay Indian

Illumina Omniexpress + exome array + imputation ~ 7 million SNPs

Teh et al, Genome Research 2015

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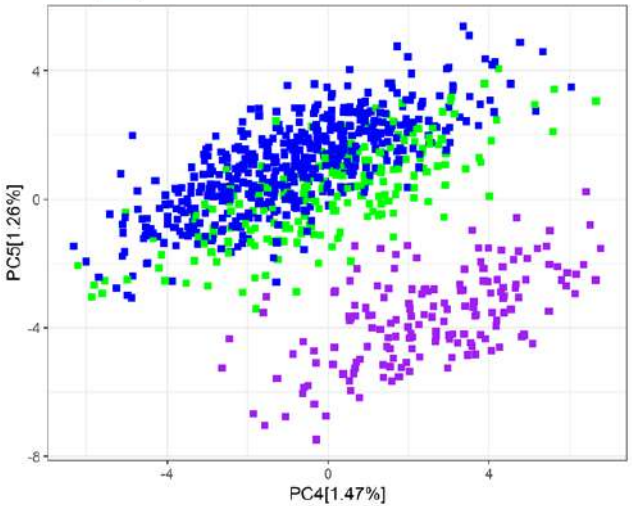
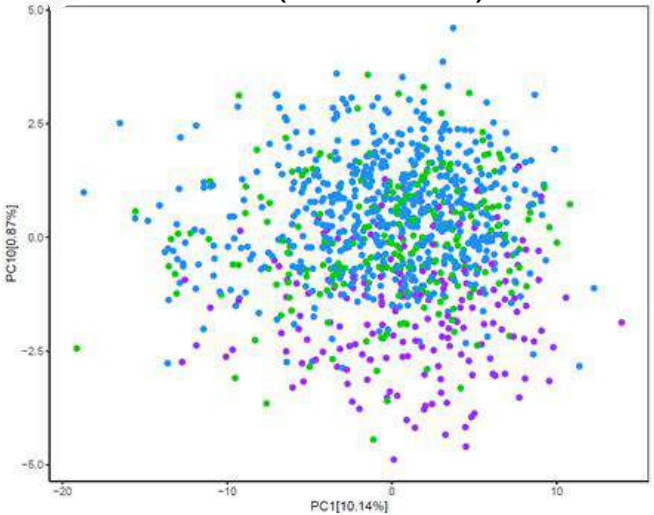
Epigenome

MODIFIABLE VARIANTS – DNA methylation

Maternal epigenome during mid-gestation



Offspring epigenome at birth (Cord tissue)



Infinium 450K arrays

Chinese Malay Indian

Hong, and Lim et al 2021

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Epigenome

Birthweight

Lin at al. BMC Medicine 2017 (Journal highlight)

Preterm babies

Wu et al. Clin Epigenetics. 2019

Epigenetic Variants

Maternal hyperglycemia & neonatal epigenome

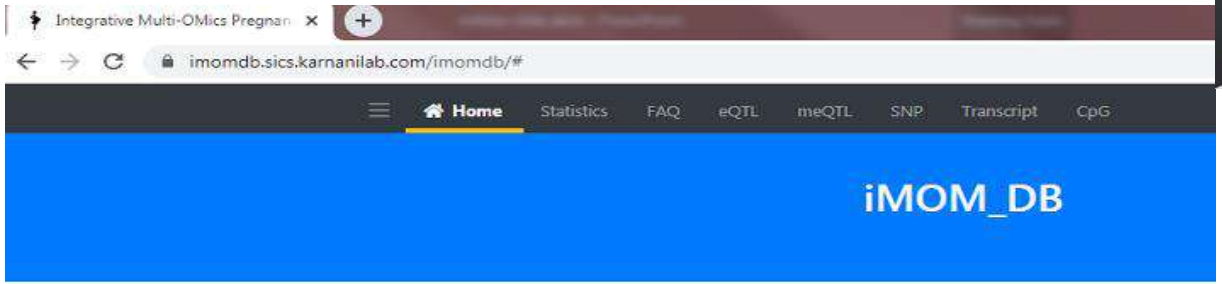
Lim et al. J Clin Endoc & Metab. (In Revision)

Early-onset of myopia

Lian et al. BMC Ophthalmol. 2019

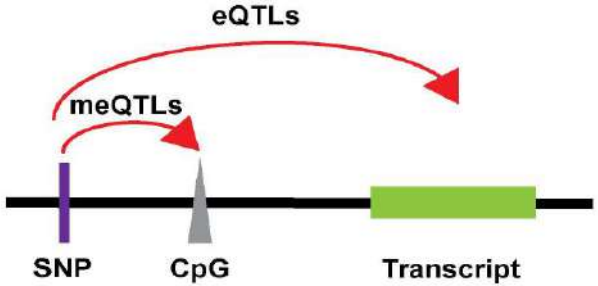
POWERING DISCOVERIES

Hong, Lim, Huang et al. 2021 (unpublished)



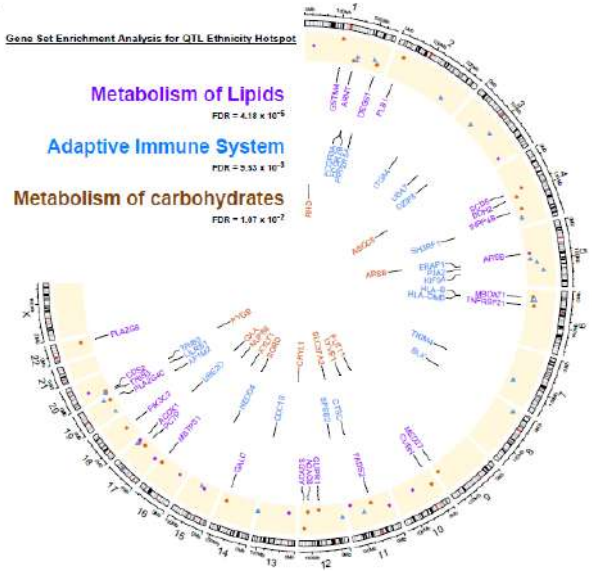
What is included in iMOMdb?

iMOMdb consists of ethnicity based genome-wide association (GWAS), epigenome-wide association (EWAS) and transcriptome-wide association (TWAS) results. To identify potential molecular interactions between genetic and epigenetic mechanisms, Quantitative Trait Loci (QTL) information and their association with ethnicity were also made available. Most importantly, iMOMdb is open accessed with result tables and visualization charts made freely available for downloading.



Ethnicity hotspot genes

395 Ethnicity meQTL and eQTL



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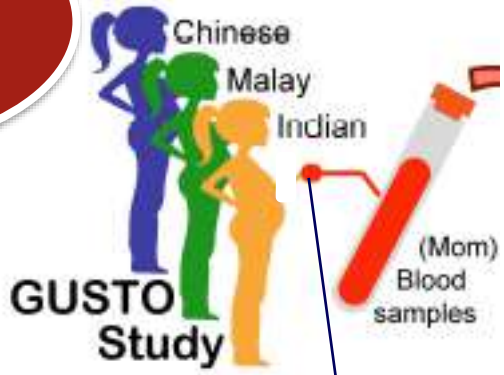
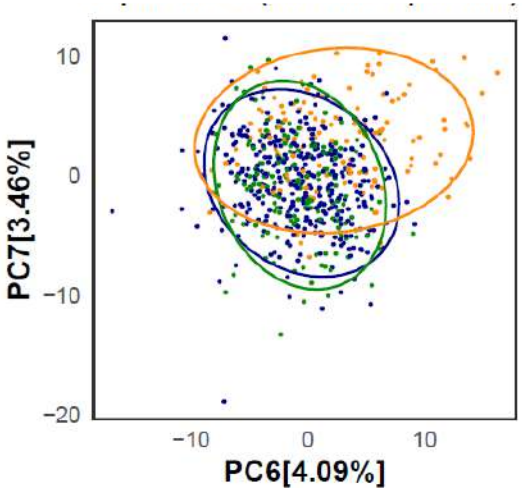
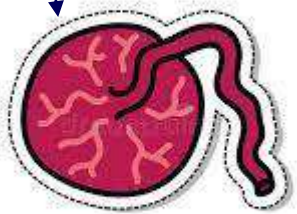
Lipidome

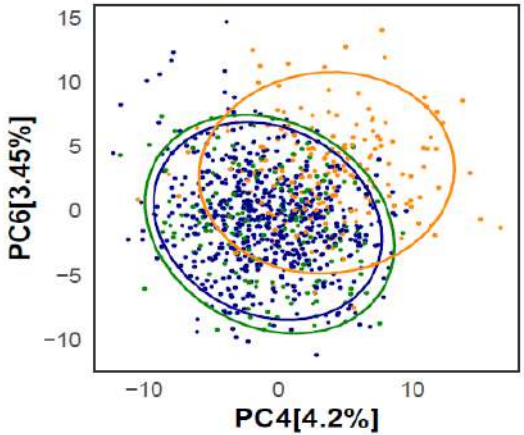




~480 lipid species
25 Lipids classes



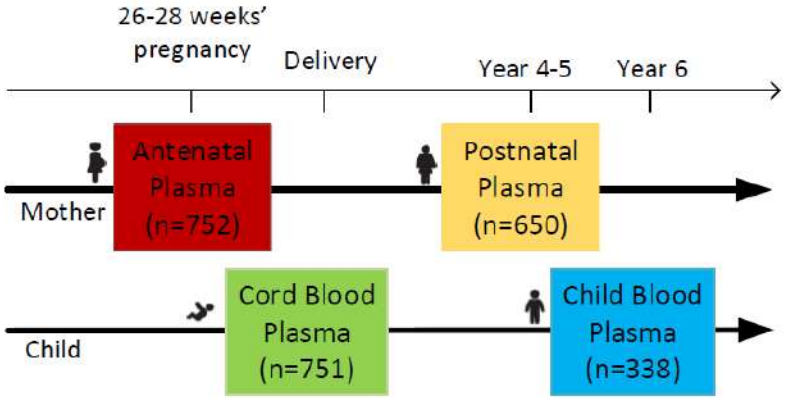
Placenta

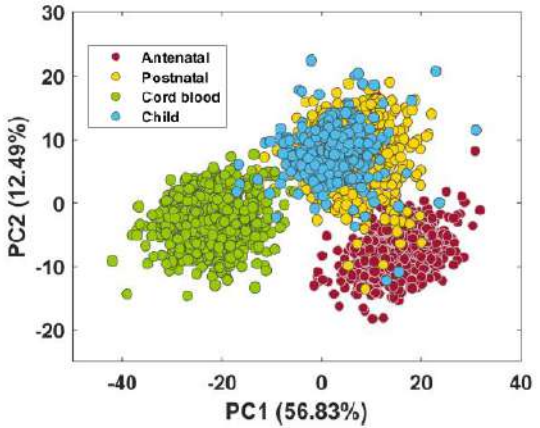


POWERING DISCOVERIES

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

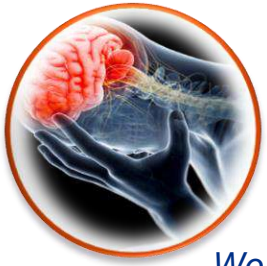
Sartaj Ahmad Mir[1,2#], Li Chen[2,3#], Satvika Burugupalli[4], Bo Burla[2], Shanshan Ji[2], Adam Alexander T. Smith[4], Kothandaraman Narasimhan[3], Gerard Wong[3], Adaikalavan Ramasamy[3], Ding Mei[2], Karen Mei-Ling Tan[3], Fabian Yap[5], Kok Hian Tan[5], Fiona Collier[6,7,8], Richard Saffery[8,9], Peter Vuillermin[6,7,8], Anne K. Bendt[2], David Burgner[8,9], Anne-Louise Ponsonby[8,9], Yung Seng Lee[3,10], Yap Seng Chong[3,11], Peter D Gluckman[3,12], Johan G. Eriksson[3,11,13,14], Peter J. Meikle[4*], Markus R. Wenk[1,2*] and Neerja Karnani[1,3*]





Mir, Chen, et al. 2021 BioRxiv

EFFECTS OF SUBOPTIMAL OMEGA FATTY ACIDS IN WOMEN & CHILD HEALTH



Low omega fatty acids → High Depression

Wong et al. Transl. Psychiatry 2021

High Omega 6 → High Birthweight
Lin at al. BMC Medicine 2017 (Journal highlight)

High Omega 6 → High metabolic risk

Low n3 PUFA → High risk for preterm birth
Wong et al. under review

POWERING DISCOVERIES

Microbiome

What affects your baby's first gut microbes

2 Dec 2020

Apart from the mode of delivery and breastfeeding, genetics and cultural practices could also have a profound impact on the type of bacteria in an infant's gut.

The dark side of antibiotics and what we can do about it

8 Mar 2021

Understanding the impact of antibiotics on both infants and adults could help restore the delicate balance of the gut microbiome.

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Breaking the cycle – *Beyond GUSTO*

Wu et al, Cell 2019 (SG10K)

Migliavacca et al.
Nature Comm. 2020

iDAD_SG (smoking)
TEAM's Study (Bariatric surgery)
PREPARE TRIAL
Vaz et al. 2021

Population

Aging

MEMOSA

Nestlé

3 patents and industry liceses

Child

DANONE

Preconception

Pregnancy

SG10K-Health HPB EHR

S-PRESTO NiPPeR

GUSTO

X

X

X

X

DSM

Nestlé

Evolve BioSystems

Loo et. Al. Eur J Epidemiol. 2021
Godfrey et al. Trials. 2017
Godfrey et al. Diabetes Care 2021

Teh et al, Genome Research 2015
Lin et al. BMC Medicine 2017
Xu et al. Gut Microbes 2020
Wong at al. Transl. Psych 2021

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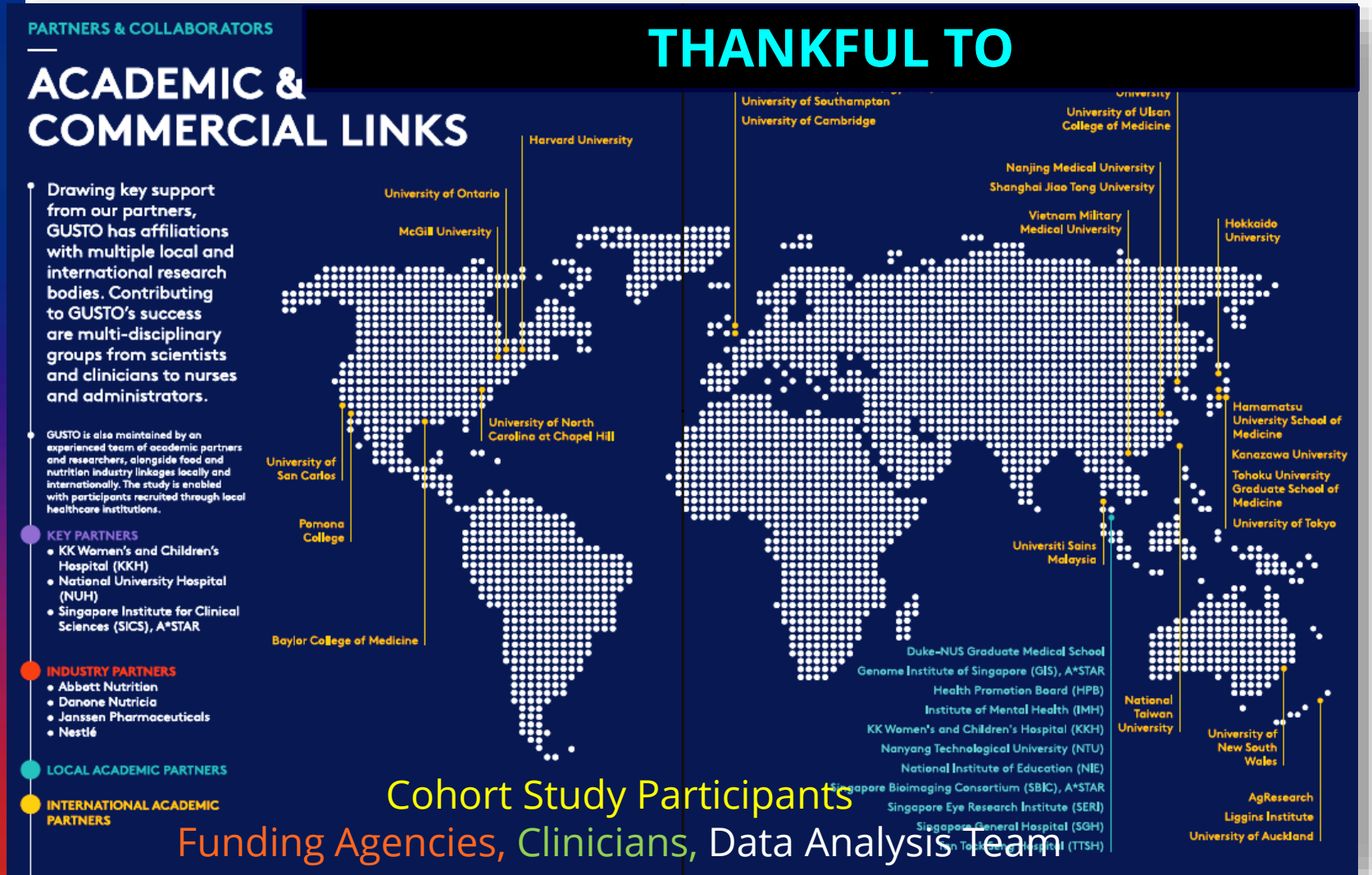
THANKFUL TO



Cohort Study Participants

Funding Agencies, Clinicians, Data Analysis Team