

METABOLIC HEALTH

The Diabetes Tsunami: a rising tide for Asia

Prof. Sally Poppitt, on behalf of the PANA MAH team

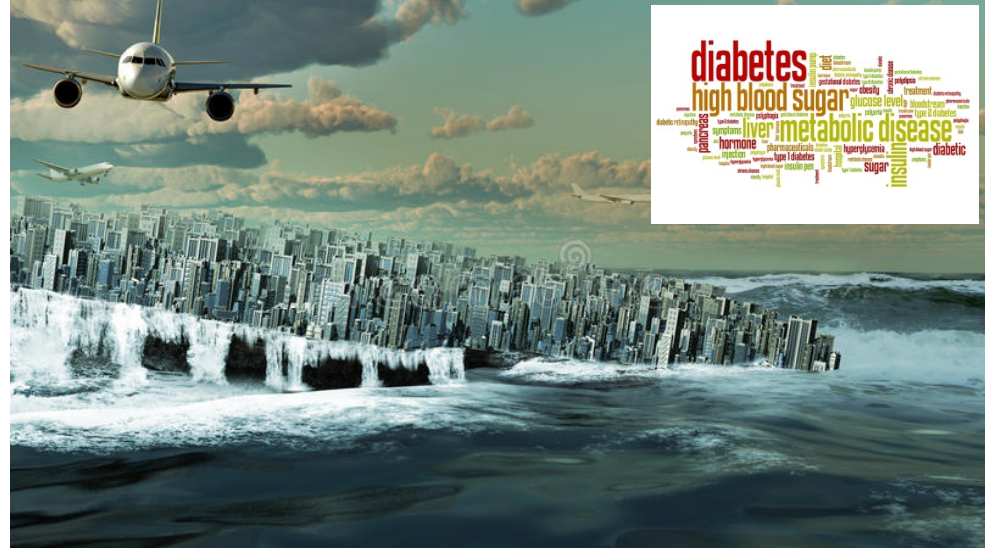
HVN Symposium, 25 September 2017

Host Institution



A rising tide of diabetes for Asia...

One of the most concerning health statistics globally is the **rising tide of diabetes** in Asia



A rising tide of diabetes for Asia...

One of the most concerning health statistics globally is the **rising tide of diabetes** in Asia



Focus on China



National
Science
Challenges

HIGH-VALUE
NUTRITION

Ko Ngā Kai
Whai Painga



THE LANCET

Lancet 2016; 387: 1513-30



Prof. Majid Ezzati

leading the NCD risk factor collaboration

Articles

Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4·4 million participants



*NCD Risk Factor Collaboration (NCD-RisC)**

Summary

Background One of the global targets for non-communicable diseases is to halt, by 2025, the rise in the age-standardised adult prevalence of diabetes at its 2010 levels. We aimed to estimate worldwide trends in diabetes, how likely it is for countries to achieve the global target, and how changes in prevalence, together with population growth and ageing, are affecting the number of adults with diabetes.



Lancet 2016; 387: 1513-30

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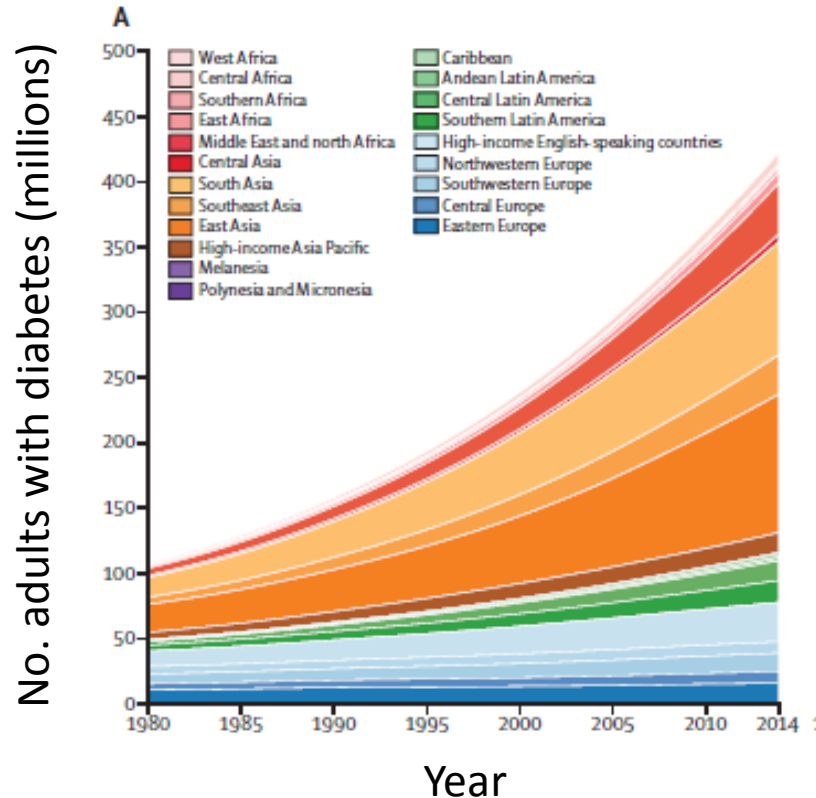
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The Diabetes Tsunami



Prof. Majid Ezzati

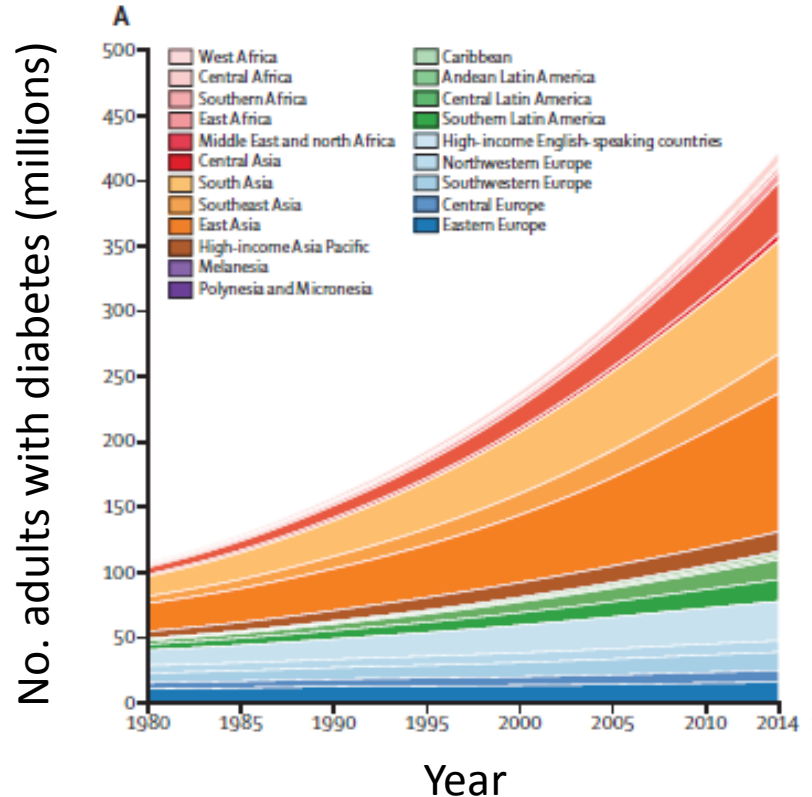
leading the NCD risk factor collaboration



Worsening crisis in Asia,
particularly China



“China - the world’s largest diabetes epidemic”



Worsening crisis in Asia,
particularly China

**Where >100 Million adults
now have diabetes**

And >400 million have pre-diabetes
and so are at high risk

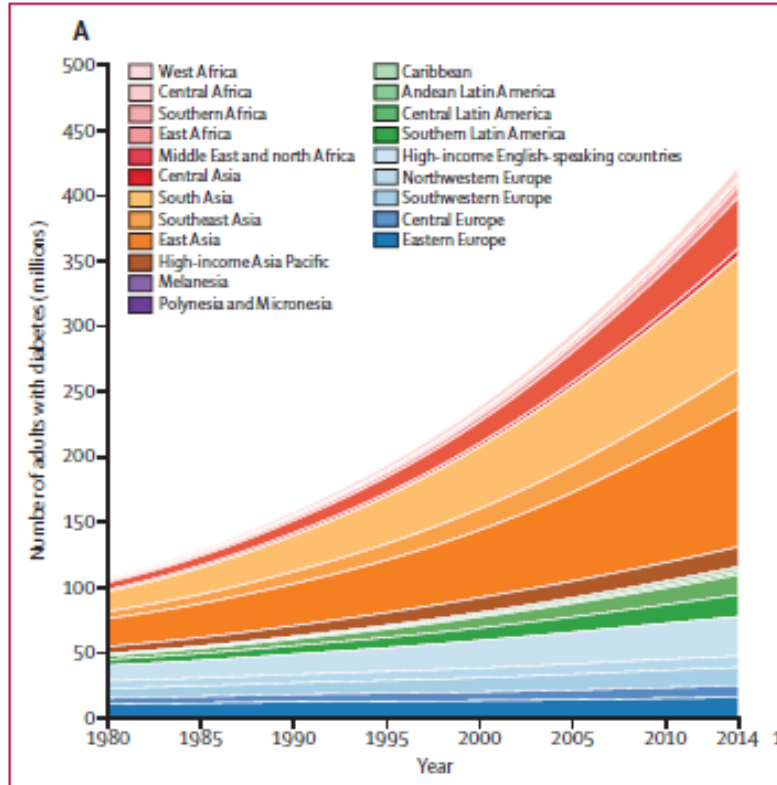
Wang et al., JAMA 2017

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“China - the world’s largest diabetes epidemic”



- Asian Chinese are at **particularly high risk of poor metabolic health** as they gain weight and
- the problem may start when they are still young and (fairly) slim

PANAMAH - PEAK NUTRITION FOR METABOLIC HEALTH

PHASE I: PHENOTYPING THE ASIAN CONSUMER

WHY ARE SOME PEOPLE MORE SUSCEPTIBLE [EG. ASIAN CHINESE] YET OTHERS MORE RESILIENT [EG. CAUCASIAN EUROPEAN]?



FAT DEPOSITION MAY BE AT THE ROOT OF THE PROBLEM
the TOFI profile = lipid 'overspill' into key organs,
eg. pancreas



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PANAMA - PEAK NUTRITION FOR METABOLIC HEALTH

PHASE I: PHENOTYPING THE ASIAN CONSUMER

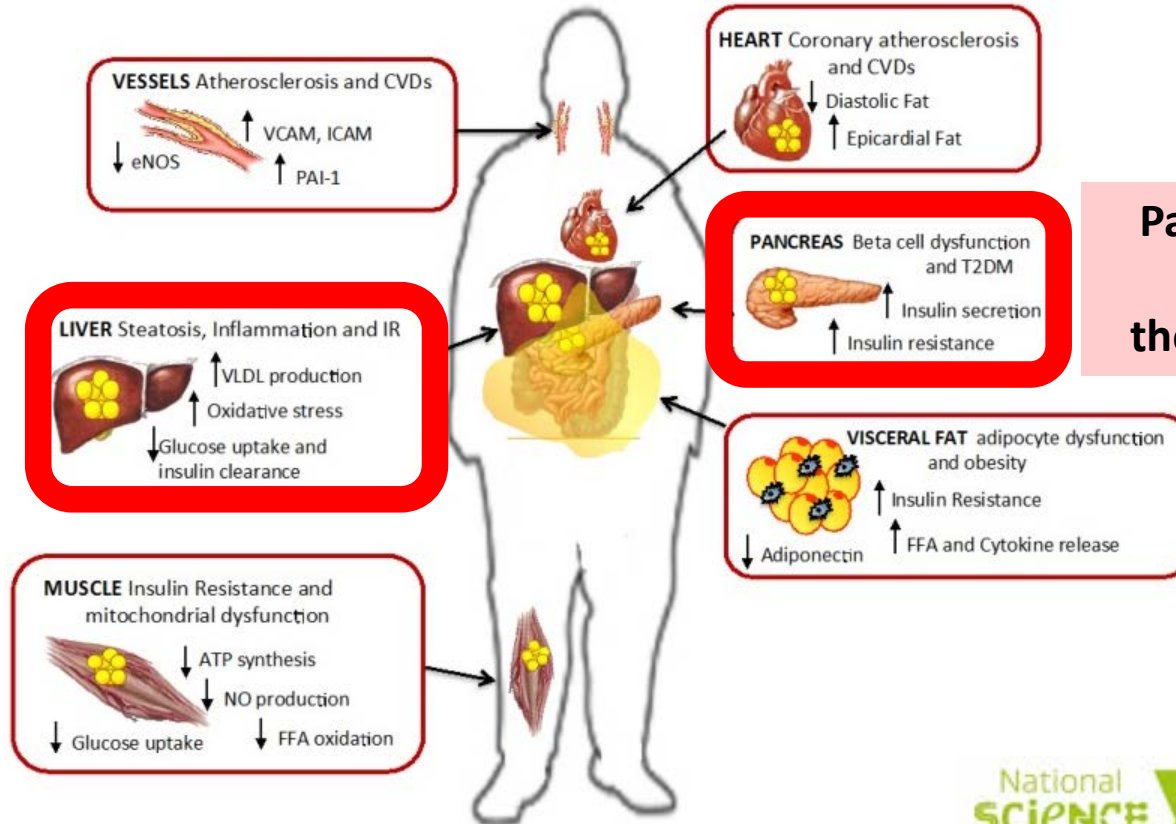


TOFI

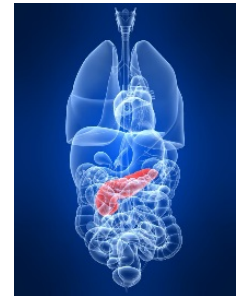
Thin on the Outside
Fat on the Inside

- Whilst obesity is strongly associated with poor glucose control & diabetes
 - it may not just be the fat (*that you can see*) on the outside that's important
 - but also the fat on the inside

FAT ON THE INSIDE.....



Particularly
fat in
the PANCREAS

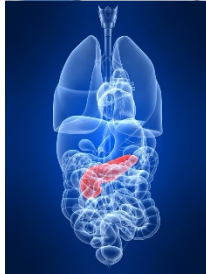


from Sapanaro *et al.*, Nutrients, 2015

The TOFI_Asia Study

1. BODY COMPOSITION

MRI assessment of organ fat



Pancreatic fat deposition



2. RISK BIOMARKERS

Metabolomics platform – plasma biomarkers



agresearch

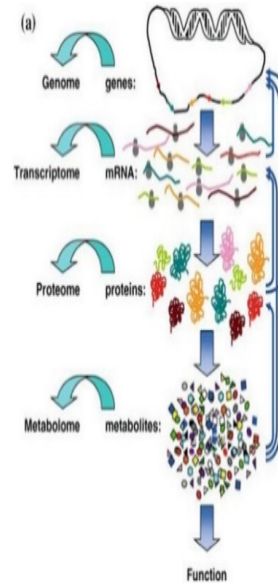
HVN Metabolomics Hub



Dr Karl Fraser & Emily Wu, Ag Research, NZ

Prof Garth Cooper, University of Manchester, UK

Dr Jean-Charles Martin, INSERM, France



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The TOFI_Asia Study

Caucasian European



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Characterising the Pre-diabetic Asian and Caucasian Phenotype: The 'TOFI' Profile

PARTICIPANT INFORMATION SHEET

We invite you to participate in a clinical study where we aim to assess your current risk of diabetes and then investigate whether this is related to your body composition and/or other newly discovered markers that circulate in your blood. Your participation in this research is entirely voluntary (your choice). If you do agree to take part, you are free to withdraw from the research at any time, without having to give a reason.

Asian Chinese



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亚裔和高加索裔前期糖尿病辨证分型:

'TOFI' 性征 (The TOFI Profile)

参与者信息

我们邀请您参加一项临床研究。我们的目标是评估前期糖尿病的风险，然后调查这是否与您的身体结构和/或其他新发现的血液循环内生物指标。参与这个研究宜是出完全自愿（您的选择）。如果您同意参加，您也可以随时从研究撤出，而无需说明理由。



Dr Ivana
Sequeira



Dr Louise
Weiwei Lu



Mr Wilson
Yip (PhD)

Are there circulating plasma biomarkers that may characterise susceptible Asian individuals (? and 'lipid overspill' pancreatic fat)

➤ beyond established markers such as glucose & insulin....

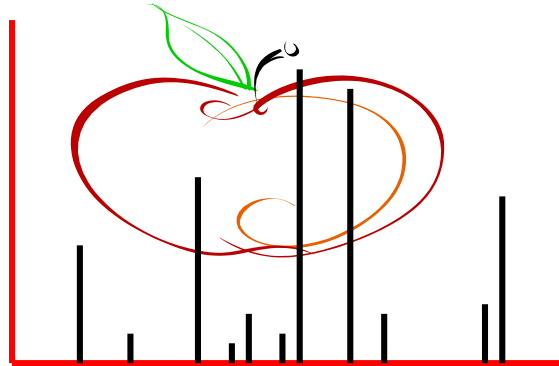
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PHASE II: RESPONSE OF THE PHENOTYPE TO F&B INTERVENTIONS

nutrition studies to determine food components that
(i) modulate risk biomarkers



Dr Ivana Sequeira
Dr Louise WeiWei Lu
Dr Marta Silvestre
Wilson Yip, PhD

2017 to 2019

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PHASE II: RESPONSE OF THE PHENOTYPE TO F&B INTERVENTIONS

nutrition studies to determine food components that
(ii) promote healthy organ structure/function



Pancreas



Liver



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2017 to 2019

PHASE II: RESPONSE OF THE PHENOTYPE TO F&B INTERVENTIONS

PRESENT 2 UPCOMING HIGHLIGHTS:

- **COLLABORATION 1** - WITH INDUSTRY PARTNER **Nuku ki te Puku**
- **COLLABORATION 2** – WITH HVN SCIENCE OF FOOD/BIOACTIVES DELIVERY TEAM



Asian Chinese cohorts

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PHASE II: RESPONSE OF THE PHENOTYPE TO F&B INTERVENTIONS

➤ **COLLABORATION 1** - WITH INDUSTRY PARTNER = NUKU MĀORI BUSINESS CLUSTER

RESPONSE TO HIGHER PROTEIN/LOWER GI FOODS, EG. NUTS & DRIED FRUIT [MED DIET]

Dr Meika Foster

Nuku ki te Puku



Asian cohort

Characterise phenotype, incl MRI

Identify novel biomarkers- metabolomics

F&B Intervention –
higher protein/lower GI

product development



Luo *et al.*, Am J Clin Nutr 2014
Asghari *et al.*, Diab Metab 2017

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PHASE II: RESPONSE OF THE PHENOTYPE TO F&B INTERVENTIONS

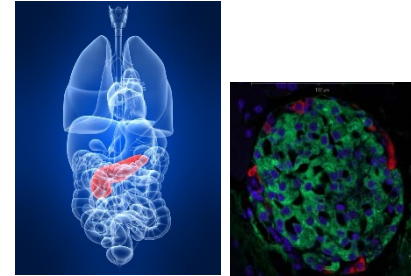
➤ COLLABORATION 2 - WITH HVN SCIENCE OF FOOD/BIOACTIVES DELIVERY PLATFORM

**CAN WE TARGET THE UNDERLYING CAUSE OF THE PROBLEM (=failure of the pancreas)
AND NOT JUST THE CONSEQUENCES (=high blood glucose)**



Leveraging work from an aligned MBIE program

Suppressing Diabetes, PI Prof GJS Cooper; AI Prof SD Poppitt



Pancreatic β -cell



**CLINICIAN & GLOBAL LEADER: METABOLOMICS &
MET HEALTH – TYPE 2 DIABETES**

Visiting Professor

- U of Hong Kong
- Chinese Acad Sci

National
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Challenges

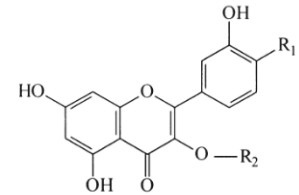
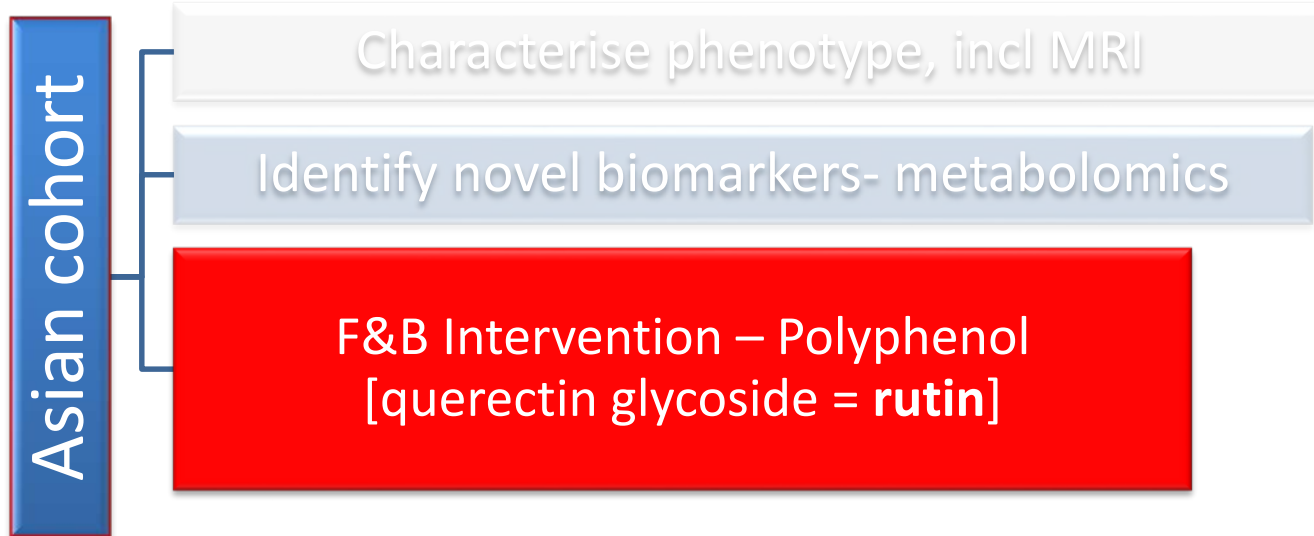
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**CAN WE TARGET THE UNDERLYING CAUSE OF THE PROBLEM (=failure of the pancreas)
AND NOT JUST THE CONSEQUENCES (=high blood glucose)**



Flavonol	R ₁	R ₂
Rutin	OH	Rutinoside
Quercitrin	OH	Rhamnoside
Quercetin	OH	H
Kaempferol	H	H
Isorhamnetin	OCH ₃	H

Rutin:
quercetin glycoside

PHASE II: RESPONSE OF THE PHENOTYPE TO F&B INTERVENTIONS

➤ COLLABORATION 2 - WITH HVN SCIENCE OF FOOD/BIOACTIVES DELIVERY PLATFORM

Background - in vitro & rodent studies

- MBIE **Suppressing Diabetes** program showed: some quercetin-related flavonols can delay and/or prevent gradual failure of the pancreatic β -cells
- and so maintain adequate insulin secretion [and hence normal glucose levels]



PHASE II: RESPONSE OF THE PHENOTYPE TO F&B INTERVENTIONS



Rutin suppresses human-amylin/hIAPP misfolding and oligomer formation *in-vitro*, and ameliorates diabetes and its impacts in human-amylin/hIAPP transgenic mice

Jacqueline F. Aitken^{a, b}, Kerry M. Loomes^{a, b}, Isabel Riba-Garcia^d, Richard D. Unwin^d, Gordana Prijic^a, Ashley S. Phillips^e, Anthony R.J. Phillips^{a, b, c}, Donghai Wu^{f, g}, Sally D. Poppitt^a, Ke Ding^h, Perdita E. Barran^e, Andrew W. Dowsey^{d, i, 1}, Garth J.S. Cooper^{a, b, d, *, 1}



Polyphenol rutin prevents hyperglycaemia (= high blood glucose) and onset of diabetes



MECHANISM: Rutin prevents misfolding of a key circulating peptide = amylin, and so prevents amyloid aggregation in the pancreas; which kills β -cells

PHASE II: RESPONSE OF THE PHENOTYPE TO F&B INTERVENTIONS



HVN SCIENCE OF FOOD/
BIOACTIVES DELIVERY TEAM



Asian Chinese
population
in Auckland



Jan 2018 onwards



PANaMAH team: NZ & worldwide

PREVIEW
European
Union



A/Prof Kieren
Hollingsworth



Prof Garth Cooper



& Hong Kong;
China

Prof Jean-Charles Martin
Inserm

Institut national
de la santé et de la recherche médicale



Prof Sally Poppitt

Dr Ivana Sequiera

Dr Louise WeiWei Lu
Wilson Yip, PhD student

Dr Rinki Murphy

A/Prof Lindsay Plank

Dr Justin O'Sullivan

Tayaza Fadason, PhD student

Plant & Food
RESEARCH
RANGAHAU AHUMARA KAI



Dr John Ingram

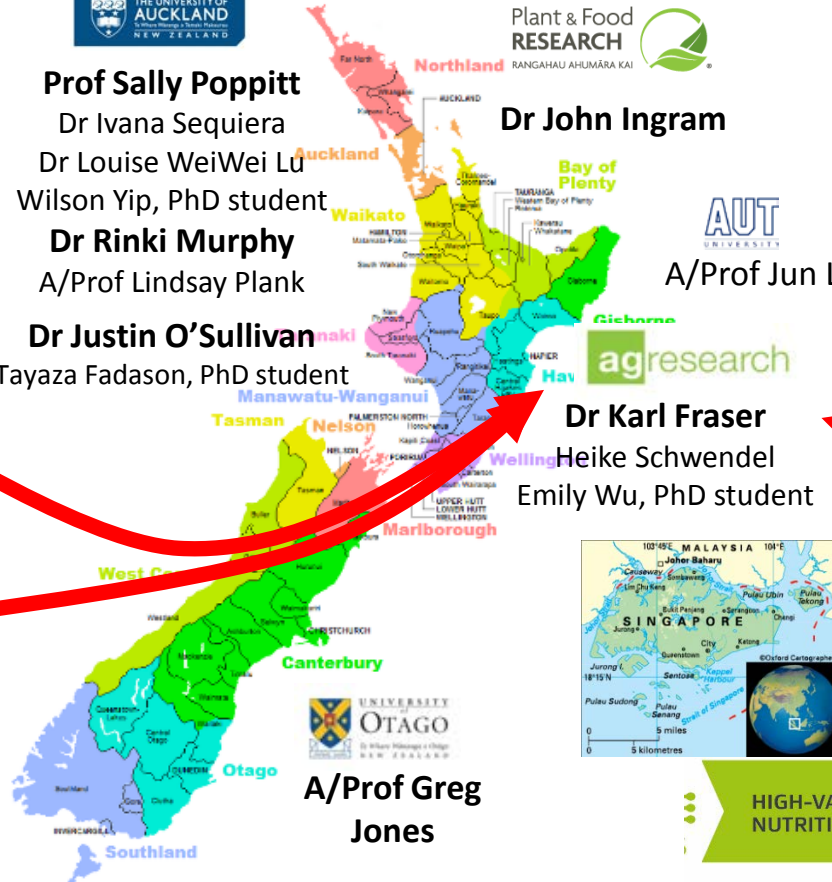


A/Prof Jun Lu



Dr Karl Fraser

Heike Schwendel
Emily Wu, PhD student



**A/Prof Greg
Jones**



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TOFI_Asia Study: our early findings from phenotyping

Caucasian European



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Your participation in this research is entirely voluntary (your choice). If you do agree to take part, you are free to withdraw from the research at any time, without having to give a reason.

Who can take part?

You can take part if you are of Asian (mainland Chinese; Hong Kong, Singapore or Malaysian Chinese; or Korean) or Caucasian European ethnicity, aged 18-70 years old, overweight with a body mass index (BMI=weight/height²) of between 25-50kg/m², but are otherwise healthy.

To take part in the study you need to be available for 1 clinic visit of about 4 hours, which will take place at the University of Auckland Human Nutrition Unit (HNU) in Mt Eden and the Body Composition Unit of Auckland City Hospital in Grafton. Occasionally, if it is more convenient for you, we can split this long visit into 2 shorter visits.

Background to the study

Perhaps surprisingly, people of Asian descent are at much greater risk of poor metabolic health and diabetes at a younger age and a lower body weight than Europeans, Maori or Pacific people. The reason why some individuals are more susceptible than others and what controls their diabetes risk may lie in the storage of body fat. Gaining even small amounts of body weight can lead to the fat being stored in dangerous places and this has been

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参与这个研究完全是完全自愿 (您的选择)。如果您同意参加，您也可以随时从研究撤出，而无需说明理由。

谁可以参加?

如果您是亚裔 (包括中国大陆、中国香港、新加坡或马来西亚的中国裔; 或韩国家裔) 或高加索裔 (欧洲裔)，年龄 18-70 岁，体重指数 (BMI=体重/身高²) 在之间 25-50kg/m²，且其他方面均健康，您就可以参加。

此项临床研究需要您参加一次大约 4 小时左右的临床访问。这将会在位于伊甸山 (Mt Eden, 邻近的奥克兰大学人类营养研究所 (Human Nutrition Unit (HNU)) 和位于 Grafton 奥克兰市医院 (Auckland City Hospital) 的身体结构研究部 (Body Composition Unit)。

有时，基于更方便于您的出行和时间安排，我们可以将此访问分为 2 个较短的访问。

研究背景

或许会令人惊讶，相比同年龄段的欧洲裔、毛利裔、或太平洋岛裔人群，虽然年轻亚裔人群有相对较低的体重却有大得多的风险有代谢健康方面的问题和糖尿病。

之所以有些人比其他人更容易患代谢性疾病或更难控制患糖尿病风险的原因可能在于他们体内脂肪的储存。往往即使是少量的体重增加可以导致脂肪从脂肪组织“蔓延”，并进入重要器官，如肌肉，肝脏和肾脏，进而显著增加疾病的风险。这个性征通常被称为“TOFI”性征——“外面瘦，里面胖” (“Thin on the Outside, Fat on the Inside”)。有些外型



Dr Ivana Sequeira
HVN Postdoctoral fellow
University of Auckland



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