National SCIENCE Challenges

HIGH-VALUE NUTRITION

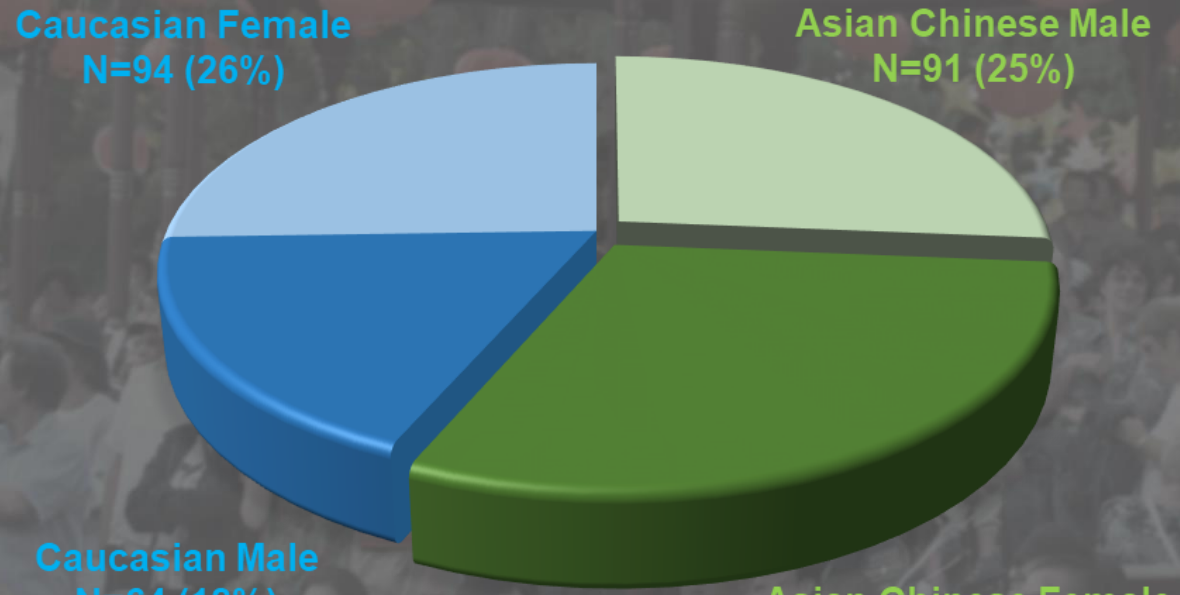
Ko Ngā Kai Whai Painga

Appearances can be deceiving: the TOFI_Asia cohort

Dr Ivana Sequeira on behalf of the PANaMAH program

- Detailed phenotyping to determine new (early, more sensitive) markers of diabetes risk
  - That are amenable to dietary (F&B) intervention

Recruitment of an important cohort

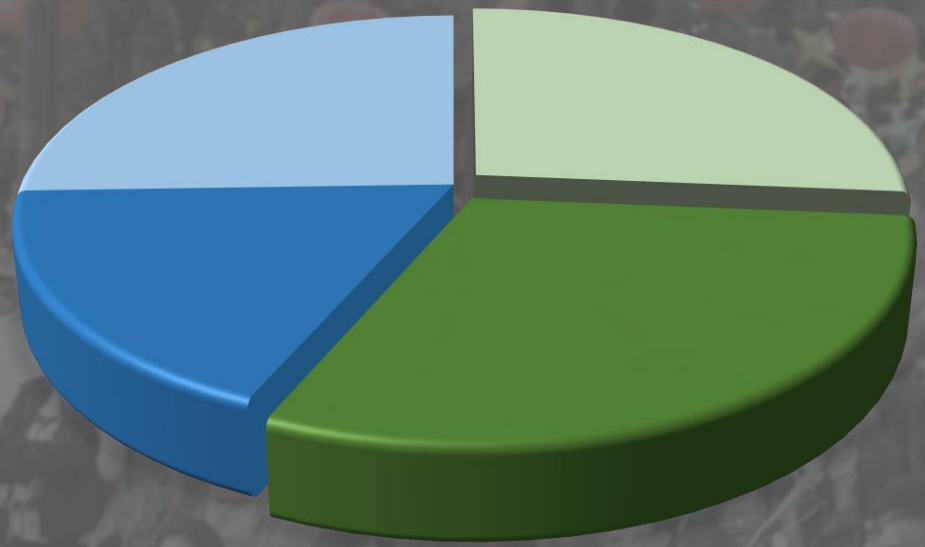


N=357 (158 Caucasian, 199 Asian Chinese)

Dr Louise Lu

Wilson Yip (PhD)

Primarily migrated to New Zealand.....



40%*

99%*

Born outside New Zealand

N=357 (158 Caucasian, 199 Asian Chinese)

* Data collected from a sub cohort of participants N = 177


✓ 158 European Caucasian
✓ 199 Asian Chinese
Both parents
18 – 70 yrs
BMI
20 - 45 kg/m²
healthy
Pre-Diabetic

TOFI_Asia study: Protocol

N = 357 ♀♂

199 Asian Chinese
158 Caucasian

Anthropometry

Height Weight

Waist Hip

TOFI_Asia study: Protocol

N = 357 ♀♂

199 Asian Chinese
158 Caucasian

Anthropometry

Fasting blood samples

- *Established* markers

Fasting plasma glucose
Hb_{A1c}
Insulin
GI Peptides
Amylin, Adiponectin
Full lipid profile
Liver function tests
Cytokines

TOFI_Asia study: Protocol

N = 357 ♀♂

199 Asian Chinese
158 Caucasian

Anthropometry

Fasting blood samples

agresearch


Dr Karl Fraser **Emily Wu (PhD)**

International collaborators


Dr John-Charles Martin **Prof Garth Cooper**

- *Novel (metabolomics)* markers
  Using an untargeted LC-MS

TOFI_Asia study: Protocol

N = 357 ♀♂

199 Asian Chinese
158 Caucasian

Anthropometry

Fasting blood samples

DEXA scan

Auckland City Hospital

A/Prof Lindsay Plank

- *Total body and abdominal fat*

TOFI_Asia study: Protocol

N = 357 ♀♂

199 Asian Chinese
158 Caucasian

Anthropometry

Fasting blood samples

DEXA scan

N = 68 ♀

34 Asian Chinese
34 Caucasian

CENTRE FOR Advanced MRI

A/Prof Jun Lu

Dr Rinki Murphy

- *Lipid overspill into organs*
  Pancreas fat, liver fat

TOFI_Asia study protocol

N = 357 ♀♂

199 Asian Chinese
158 Caucasian

Anthropometry

Fasting blood samples

DEXA scan

N = 68 ♀

34 Asian Chinese
34 Caucasian

Centre for Advanced MRI

Newcastle University

International collaborators renowned for MR imaging

Dr. Keiren Hollingsworth

MR-OPSY METHOD*

*Al-Mrabeh A *et al*. PLoS ONE 2017 12(4): e0174660; Crane JC *et al*. J Biomed Imag 2013:169256

TOFI_Asia Study: Findings

N = 357 ♀♂

199 Asian Chinese
158 Caucasian

Anthropometry

Fasting blood samples

DEXA scan

(i)

N = 68 ♀

34 Asian Chinese
34 Caucasian

MRI/S scan

(ii)

TOFI_Asia Study: Findings

N = 357 ♀♂

199 Asian Chinese
158 Caucasian

	CAUCASIAN	CHINESE ASIAN	*p* value
Height (m)	1.72 ± 0.1	**1.66 ± 0.1**	<0.001
Weight (kg)	80.0 ± 15.7	75.6 ± 14.4	0.007
BMI (kg/m^2)	26.9 ± 4.6	27.2 ± 3.9	ns
Age (yrs)	41.7 ± 16.1	40.5 ± 13.3	ns
Total body fat (%)	33.8 ± 10.2	35.0 ± 7.2	ns
Abdominal fat (%)	36.8 ± 14.1	40.8 ± 9.1	0.003

NOT AS TALL

Mean ± SD

Sequeira IR et al. Predicting susceptibility to type 2 diabetes in an Asian Chinese and Caucasian cohort: the TOFI_Asia Study. For submission to Diab Obes Metab, 2019

TOFI_Asia Study: Findings

N = 357 ♀♂

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158 Caucasian

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WEIGHED LESS

Mean ± SD

Sequeira IR et al. Predicting susceptibility to type 2 diabetes in an Asian Chinese and Caucasian cohort: the TOFI_Asia Study. For submission to Diab Obes Metab, 2019

TOFI_Asia Study: Findings

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but SIMILAR BMI

Mean ± SD

Sequeira IR et al. Predicting susceptibility to type 2 diabetes in an Asian Chinese and Caucasian cohort: the TOFI_Asia Study. For submission to Diab Obes Metab, 2019

TOFI_Asia Study: Findings

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SIMILAR AGE

Mean ± SD

Sequeira IR et al. Predicting susceptibility to type 2 diabetes in an Asian Chinese and Caucasian cohort: the TOFI_Asia Study. For submission to Diab Obes Metab, 2019

At same Age and BMI – higher central adiposity

N = 357 ♀♂

199 Asian Chinese
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Height (m)	1.72 ± 0.1	1.66 ± 0.1	<0.001
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DEXA

Mean ± SD

Sequeira IR et al. Predicting susceptibility to type 2 diabetes in an Asian Chinese and Caucasian cohort: the TOFI_Asia Study. For submission to Diab Obes Metab, 2019

GREATER ABDOMINAL FAT

At same Age and BMI – higher central adiposity

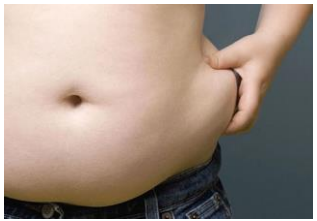
N = 357 ♀♂

199 Asian Chinese
158 Caucasian

	CAUCASIAN	CHINESE ASIAN	*p* value
Height (m)	1.72 ± 0.1	1.66 ± 0.1	<0.001
Weight (kg)	80.0 ± 15.7	75.6 ± 14.4	0.007
BMI (kg/m^2)	26.9 ± 4.6	27.2 ± 3.9	ns
Age (yrs)	41.7 ± 16.1	40.5 ± 13.3	ns
Visceral fat (%)	32.2 ± 19.9	**39.7 ± 16.4**	**<0.001**
Subcutaneous fat (%)	67.8 ± 19.9	**60.3 ± 16.4**	**<0.001**

DEXA Abdominal fat

Mean ± SD



GREATER VISCERAL FAT

Sequeira IR et al. Predicting susceptibility to type 2 diabetes in an Asian Chinese and Caucasian cohort: the TOFI_Asia Study. For submission to Diab Obes Metab, 2019

TOFI_Asia Study: Findings

N = 357 ♀♂

199 Asian Chinese
158 Caucasian

Established BLOOD markers for diabetes risk

	CAUCASIAN	CHINESE ASIAN	*p* value
Fasting plasma glucose (mmol/L)	5.0 ± 0.6	**5.3 ± 0.5**	<0.001
Hb_{A1c} (mmol/mol)	33.3 ± 3.6	**35.8 ± 3.9**	<0.001
Triglycerides (mmol/L)	1.1 ± 0.6	**1.4 ± 0.9**	<0.001
HDL-C (mmol/L)	1.6 ± 0.4	1.4 ± 0.4	<0.001
ALT (U/L)	15.8 ± 10.3	19.3 ± 14.0	0.02
GGT (U/L)	23.6 ± 18.2	30.2 ± 23.8	<0.001

ALL HIGHER in Asian Chinese

Mean ± SD

Sequeira IR et al. Predicting susceptibility to type 2 diabetes in an Asian Chinese and Caucasian cohort: the TOFI_Asia Study. For submission to Diab Obes Metab, 2019

TOFI_Asia Study: Findings

N = 357 ♀♂

199 Asian Chinese
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Triglycerides (mmol/L)	1.1 ± 0.6	1.4 ± 0.9	<0.001
HDL-C (mmol/L)	1.6 ± 0.4	**1.4 ± 0.4**	<0.001
ALT (U/L)	15.8 ± 10.3	19.3 ± 14.0	0.008
GGT (U/L)	23.6 ± 18.2	30.2 ± 23.8	0.003

LOWER in Asian Chinese

Mean ± SD

Sequeira IR et al. Predicting susceptibility to type 2 diabetes in an Asian Chinese and Caucasian cohort: the TOFI_Asia Study. For submission to Diab Obes Metab, 2019

At same Age and BMI – worse metabolic profile

N = 357 ♀♂

199 Asian Chinese
158 Caucasian

	CAUCASIAN	CHINESE ASIAN	*p* value
Fasting plasma glucose (mmol/L)	5.0 ± 0.6	5.3 ± 0.5	<0.001
Hb_{A1c} (mmol/mol)	33.3 ± 3.6	35.8 ± 3.9	<0.001
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ALT (U/L)	15.8 ± 10.3	**19.3 ± 14.0**	**0.008**
GGT (U/L)	23.6 ± 18.2	**30.2 ± 23.8**	**0.003**

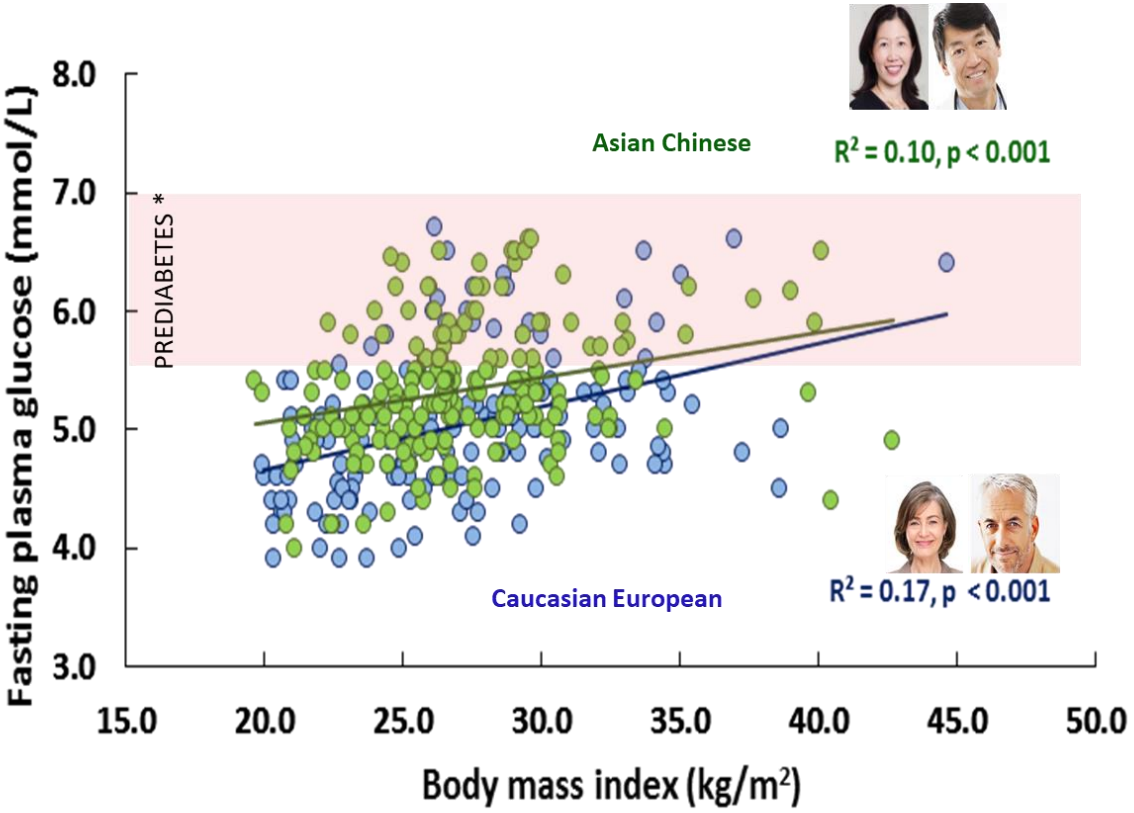
Liver function enzymes

BOTH HIGHER in Asian Chinese

Mean ± SD

Sequeira IR et al. Predicting susceptibility to type 2 diabetes in an Asian Chinese and Caucasian cohort: the TOFI_Asia Study. For submission to Diab Obes Metab, 2019

Established markers in the TOFI cohort



As expected,
fasting glucose levels are significantly correlated with BMI in both Ethnicities

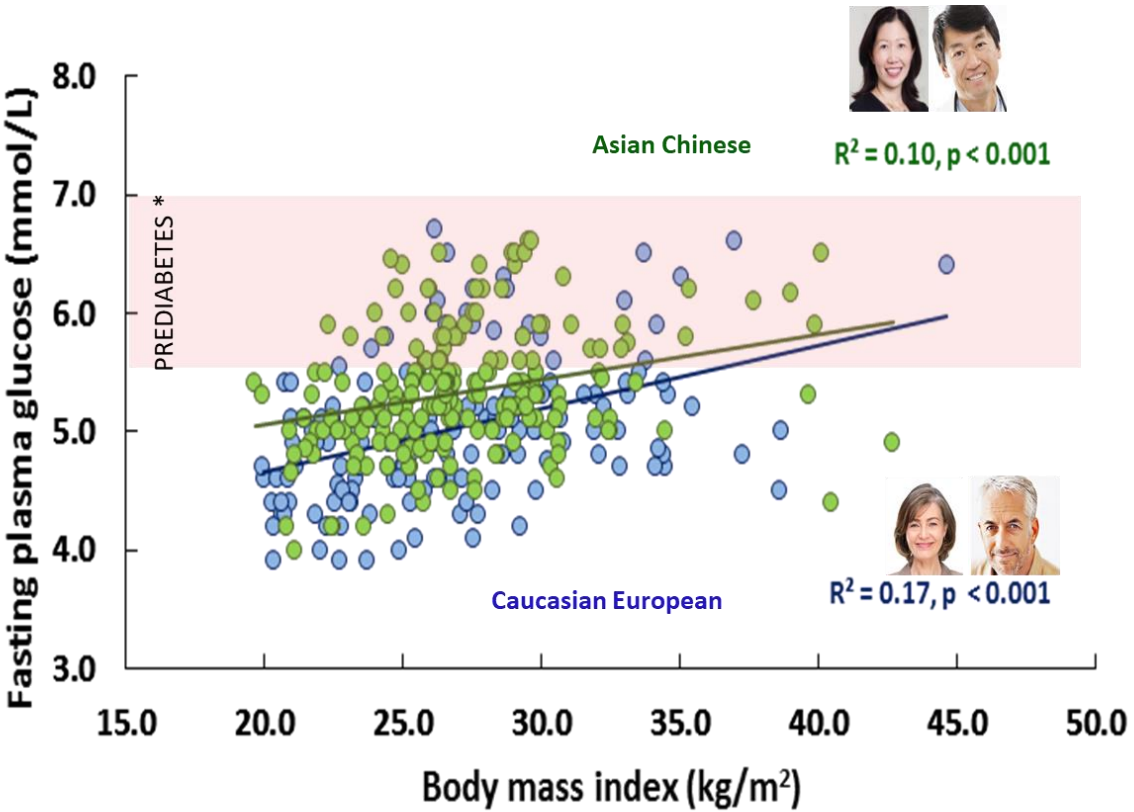
If anything higher in Asian Chinese at LOWER BMI

(Intercept: t = 1.97, d.f = 353, p <0.05)

* American Diabetes Association, 2016

Sequeira IR et al. For submission to Diab Obes Metab, 2019

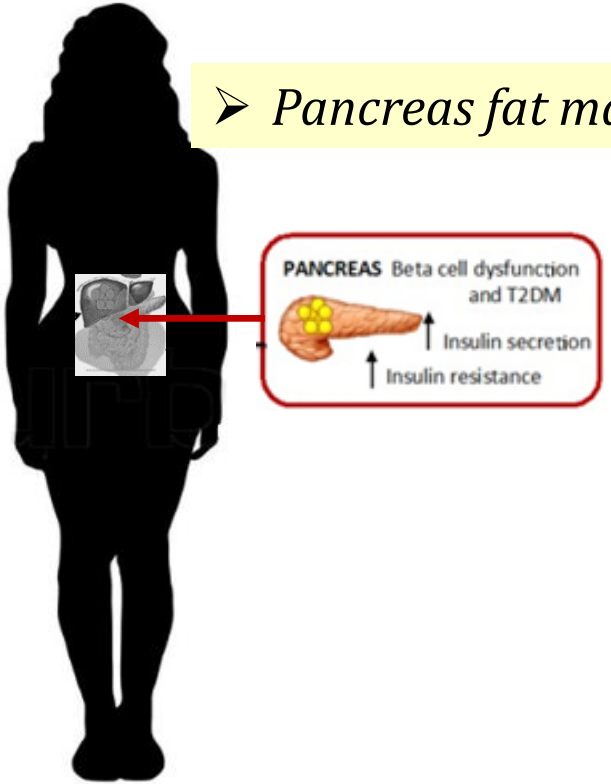
Established markers in the TOFI cohort



At LOWER BMI, Asian Chinese had HIGHER FPG (0.3-0.5 mmol/L) than Caucasians.

* American Diabetes Association, 2016 **Age and gender included in multiple linear regression analyses; Sequeira IR et al.* For submission to Diab Obes Metab, 2019

Is fasting glucose associated with increased pancreas fat?



➢ *Pancreas fat may be an **EARLY** marker of T2D risk*

PANCREAS FAT (even in normoglycaemic individuals)

TOFI profile

INCREASED RISK

Saponaro C *et al*. Nutrients 2015;7(11):9453-74; Hocking S *et al*. Endocrine Rev. 2013;34(4):463-500

Is fasting glucose associated with increased pancreas fat?

N = 357 ♀♂

199 Asian Chinese
158 Caucasian

Anthropometry

Fasting blood samples

DEXA scan

(i) ✓

N = 68 ♀

34 Asian Chinese
34 Caucasian

MRI/S scan

(ii)

Newcastle University

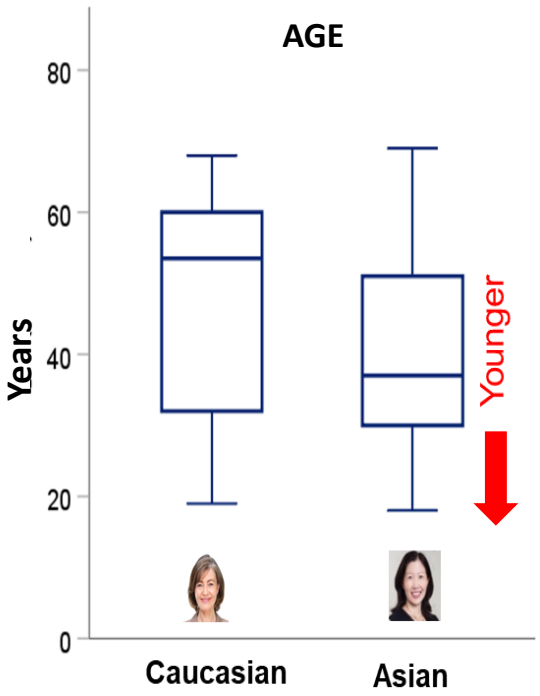
Only scanned **women**

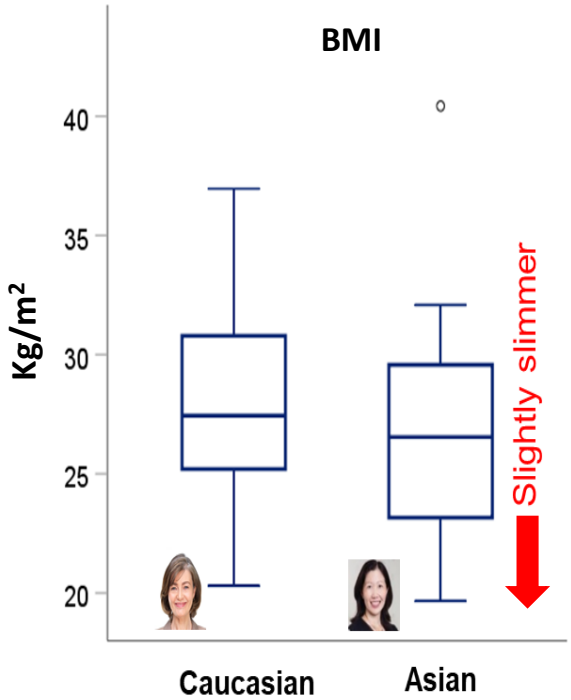
- Due to gender differences in body composition

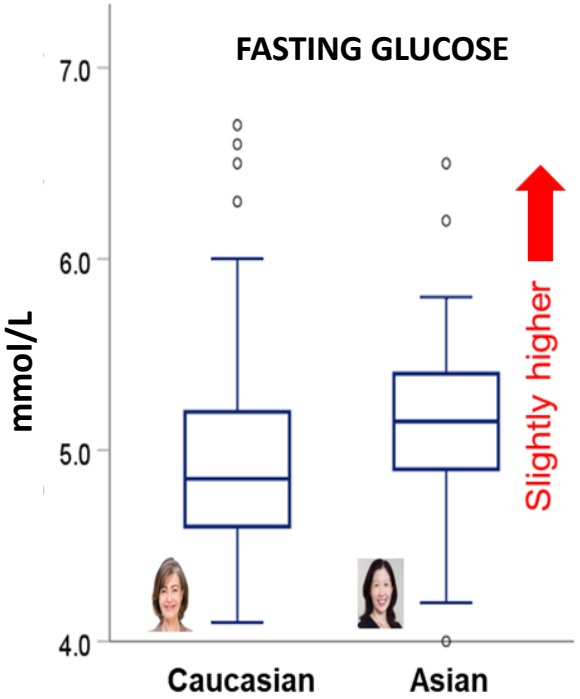
TOFI_Asia MR Study: Findings

N = 68 ♀

34 Asian Chinese
34 Caucasian







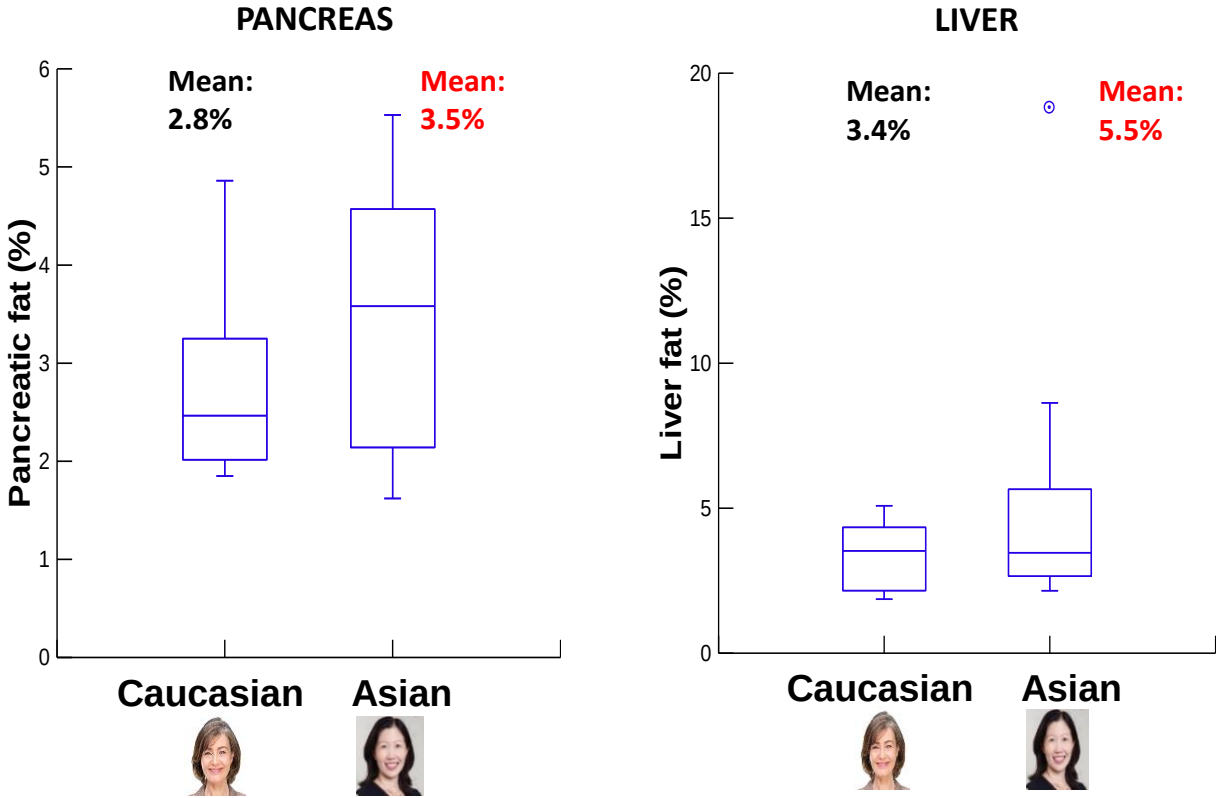
Box plots showing median and interquartile range

Sequeira IR et al. Does the 'thin on the outside fat on the inside' (TOFI) phenotype hide an increased metabolic risk due to ectopic lipid storage in the pancreas and liver: an MRI/MRS study. For submission to Diab Obes Metab, 2019

Organ fat in women with lower BMI……

N = 68 ♀

34 Asian Chinese
34 Caucasian



Box plots showing median and interquartile range

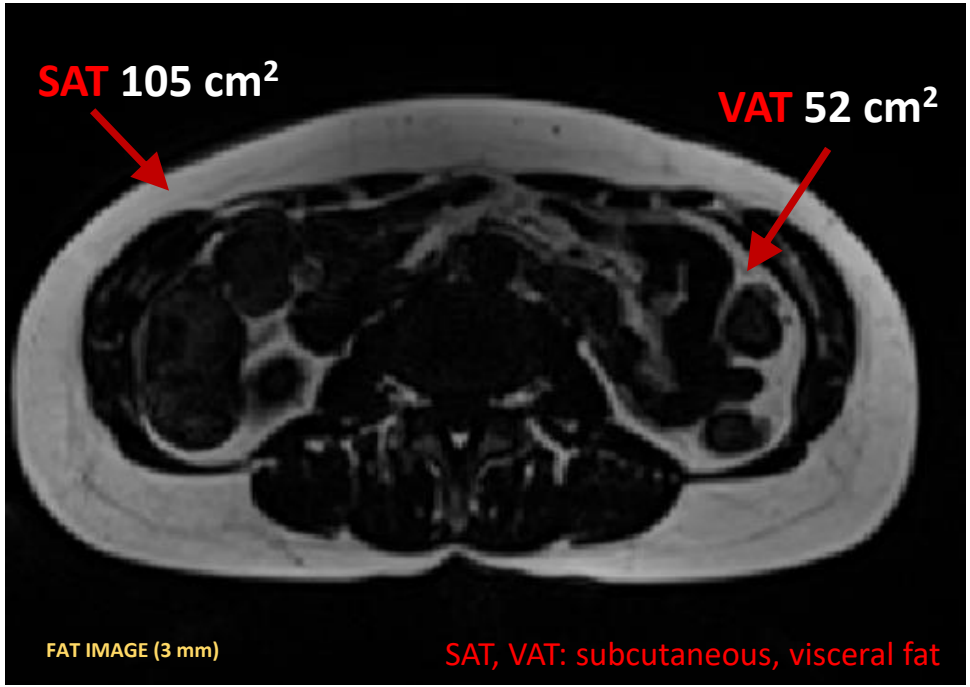
Higher in Asian Chinese

TOFI profile

MRI Scan

Caucasian female, 51 y

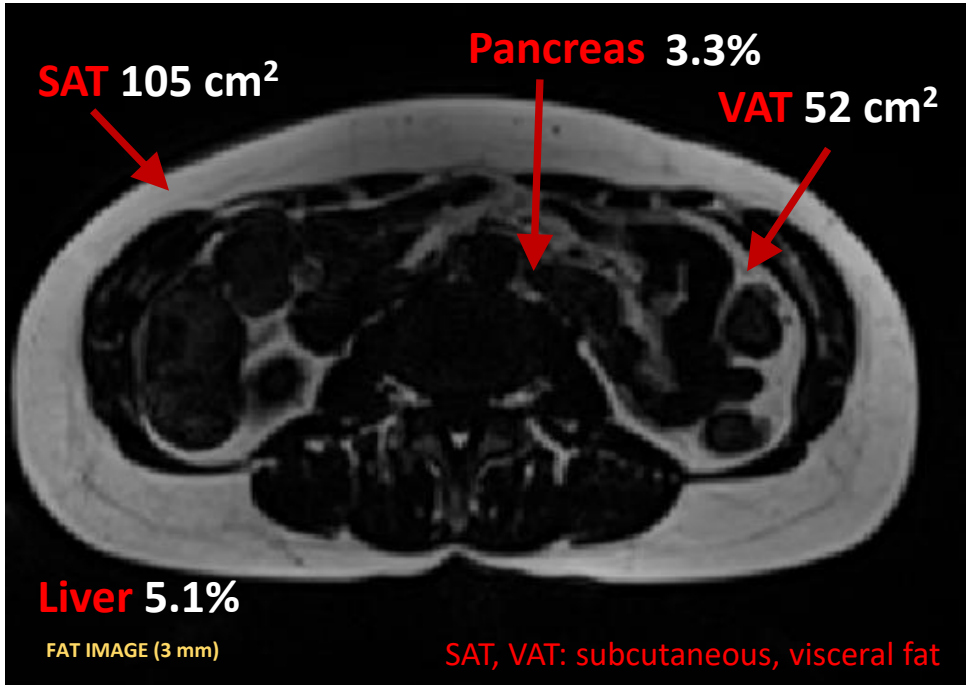
BMI 23 kg/m²



MRI Scan

Caucasian female, 51 y

BMI 23 kg/m²



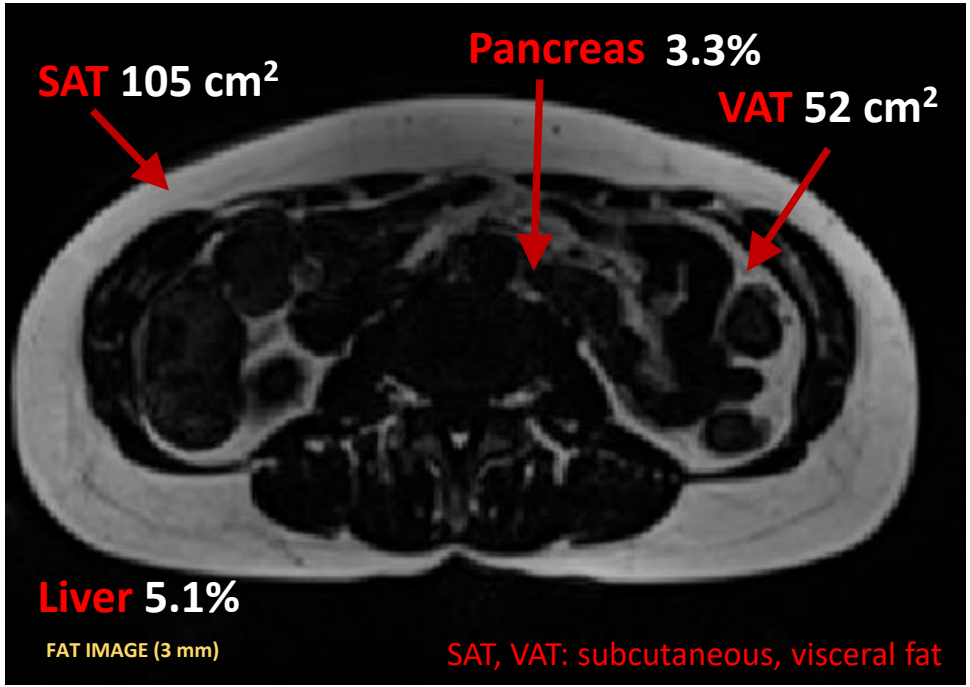
Low Risk

Fasting glucose
4.7 mmol/L

MRI Scan

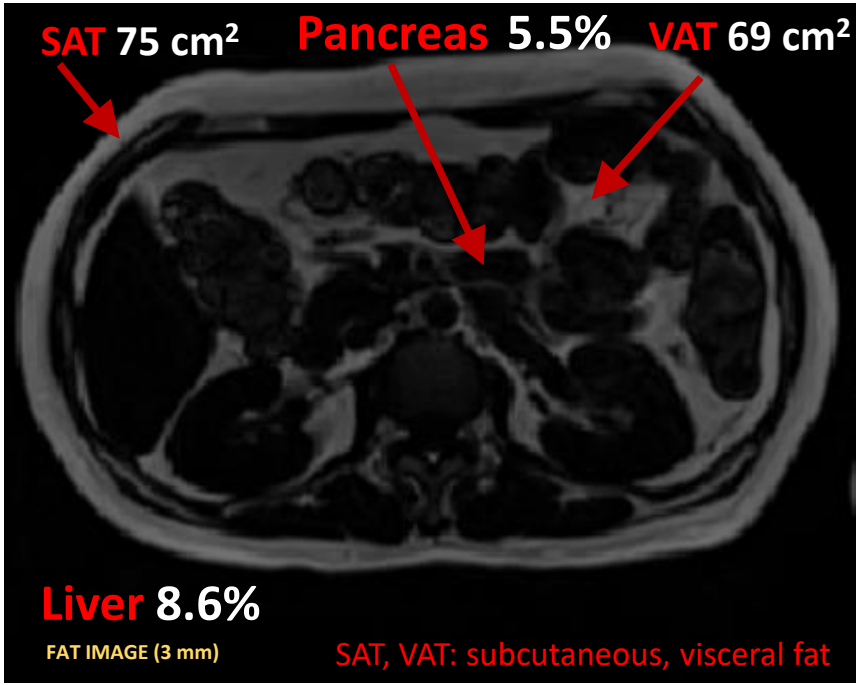
Caucasian female, 51 y

BMI 23 kg/m²



Asian Chinese female, 45 y

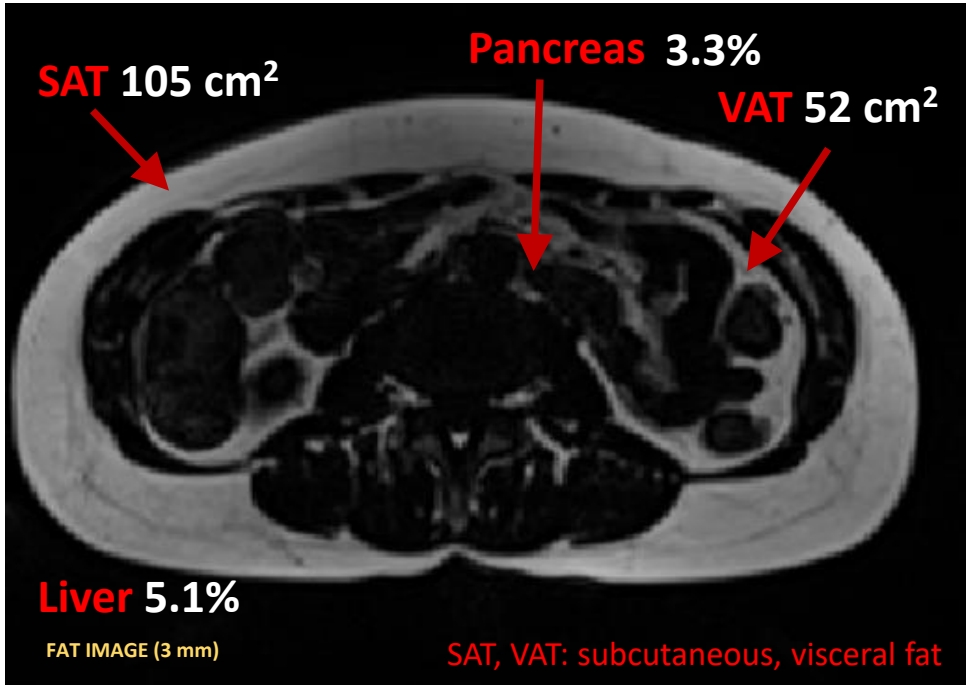
BMI 23 kg/m²



MRI Scan

Caucasian female, 51 y

BMI 23 kg/m²



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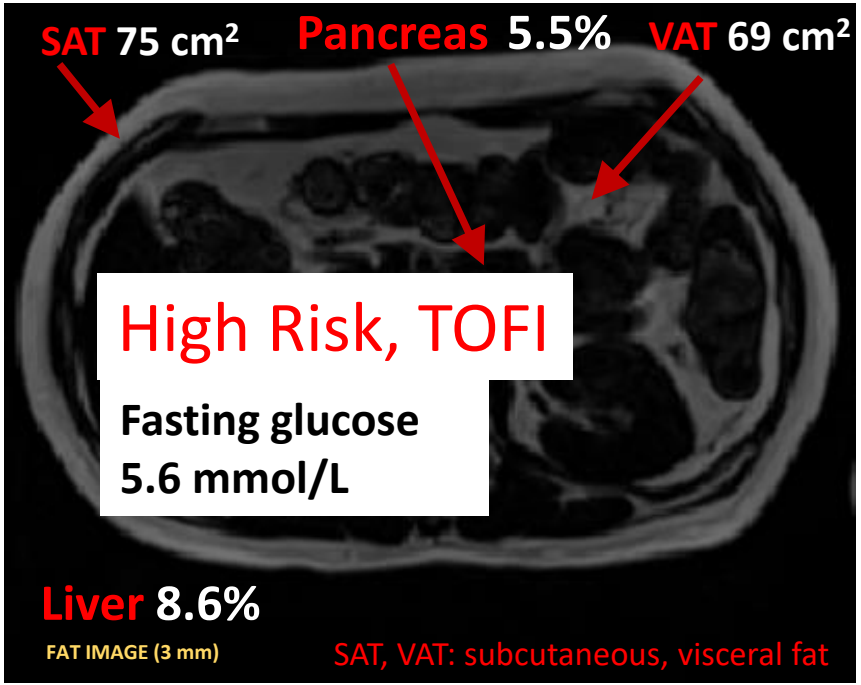
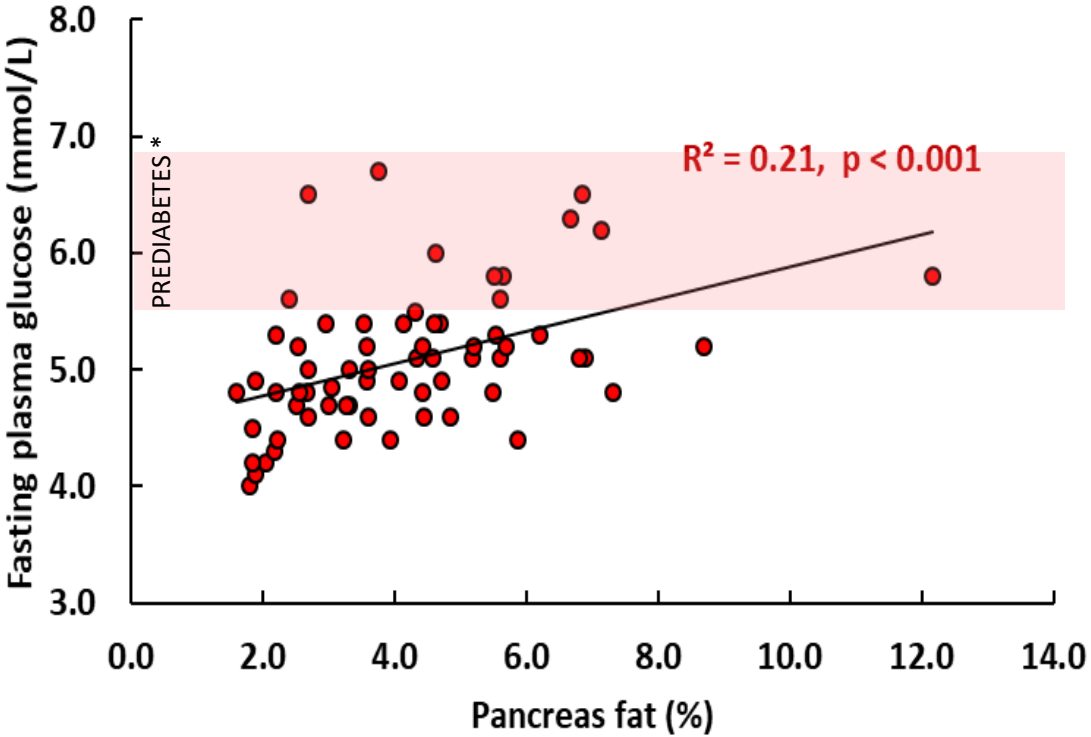


Relationships with fasting glucose

N = 68 ♀

34 Asian Chinese
34 Caucasian



- ***PANCREAS FAT maybe a possible EARLY MARKER***

* American Diabetes Association, 2016 *Sequeira IR et al* For submission to Diab Obes Metab, 2019

Relationships with fasting glucose

N = 68 ♀

34 Asian Chinese
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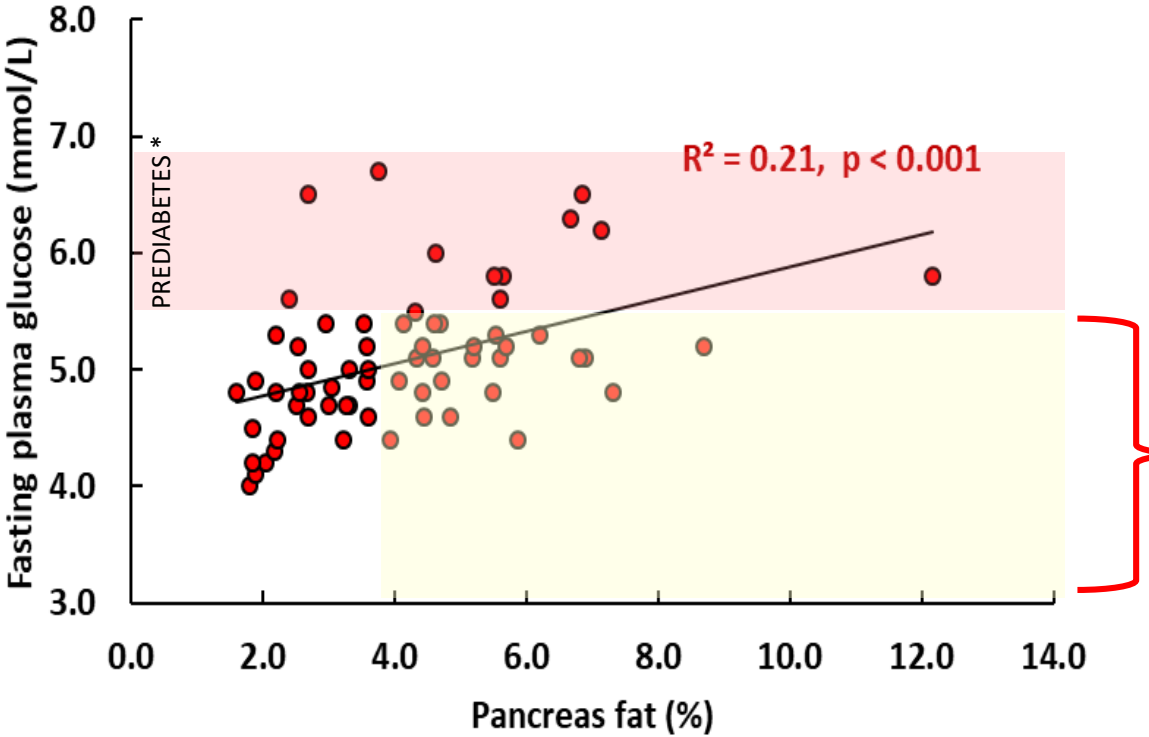


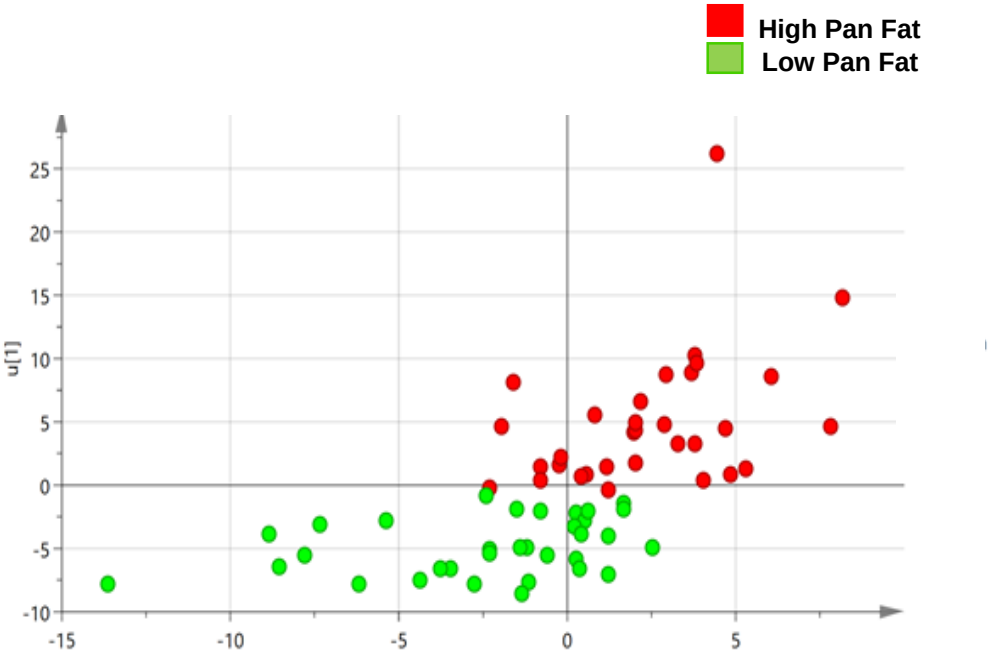
- ***PANCREAS FAT maybe a possible EARLY MARKER***

May occur even before blood glucose levels rise and diabetes develops

National SCIENCE Challenges | HIGH-VALUE NUTRITION | Ko Ngā Kai Whai Painga

* American Diabetes Association, 2016 *Sequeira IR et al* For submission to Diab Obes Metab, 2019

Identified novel (metabolomic) risk markers of pancreas fat



Orthogonal partial least squares regression analyses, HILIC data

$R^2Y = 0.64$, $Q^2 = 0.13$, p = 0.08

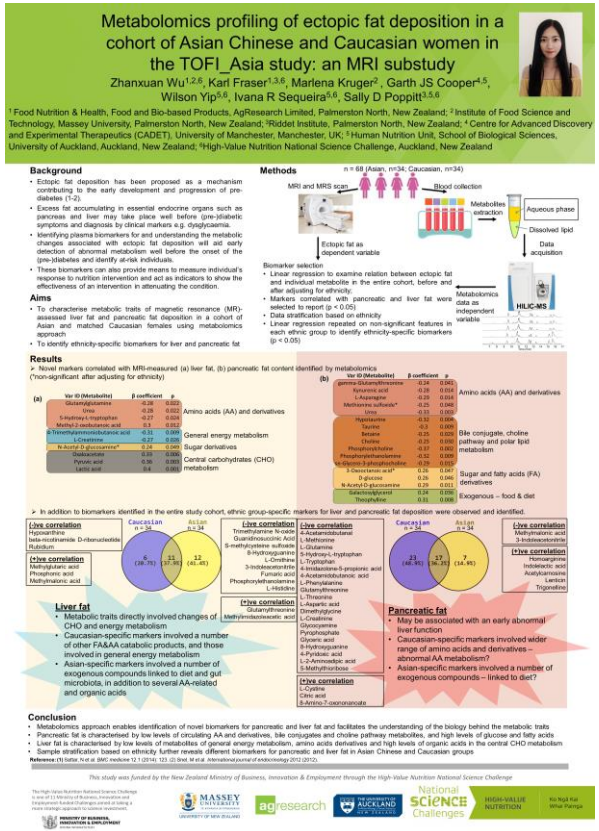
Dr Karl Fraser **Emily Wu (PhD)**

Blood metabolites correlated with high (red) and low (green) pancreas fat

NOVEL DATA - NOT YET PUBLISHED BY ANY OTHER INTERNATIONAL GROUP

Wu Z et al. A metabolomic signature that reflects ectopic pancreatic fat in a cohort of healthy and pre-diabetic adults: data from the TOFI_Asia study. For submission to Diabetes, 2019

For more details about the Novel markers for pancreas fat



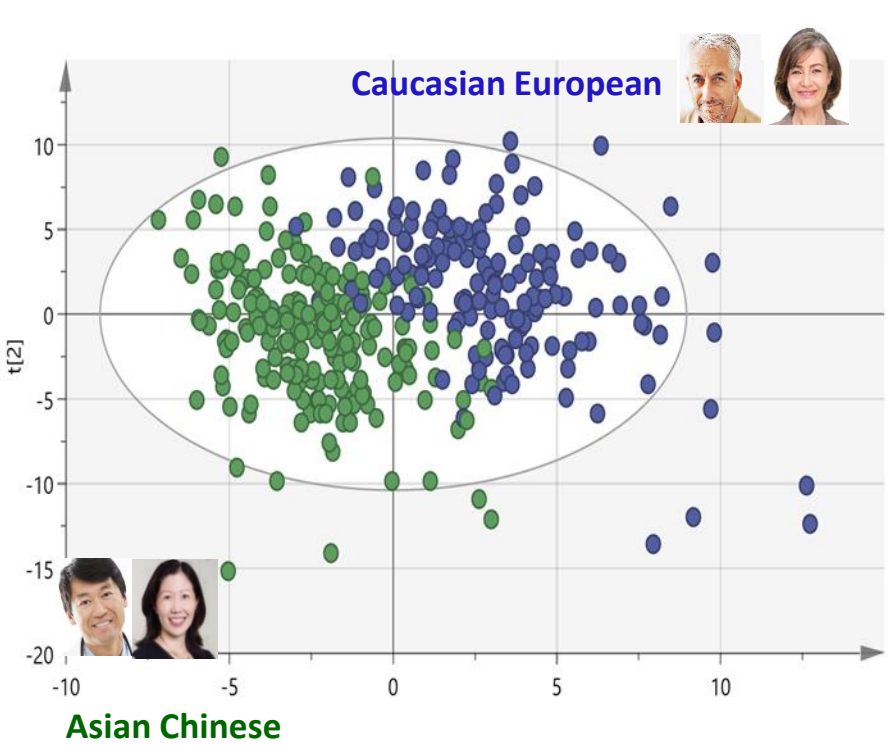
Emily Wu (PhD)

HVN Poster presentation I

Between the two ethnic groups

Wu Z et al. A metabolomic signature that reflects ectopic pancreatic fat in a cohort of healthy and pre-diabetic adults: data from the TOFI_Asia study. For submission to Diabetes, 2019

Identified novel markers in the full TOFI_Asia cohort (N=357)



Caucasian
Chinese

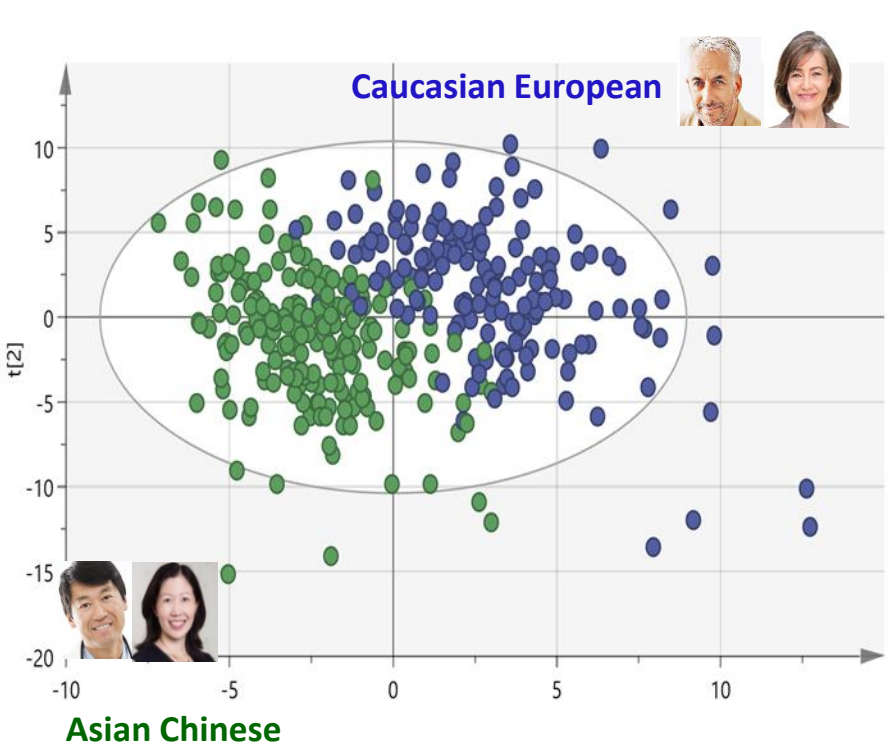

Dr Karl Fraser **Emily Wu (PhD)**

Robust separation *of blood metabolites:* Caucasians (blue) and Asian Chinese (green)

Partial least squares discriminatory analyses, HILIC data
Q^2 = 0.678, cross validation p value = 0

Wu Z et al. For submission to Diabetes, 2019

Identified novel markers in the full TOFI_Asia cohort (N=357)



Caucasian
Chinese

Partial least squares discriminatory analyses, HILIC data
Q^2 = 0.678, cross validation p value = 0

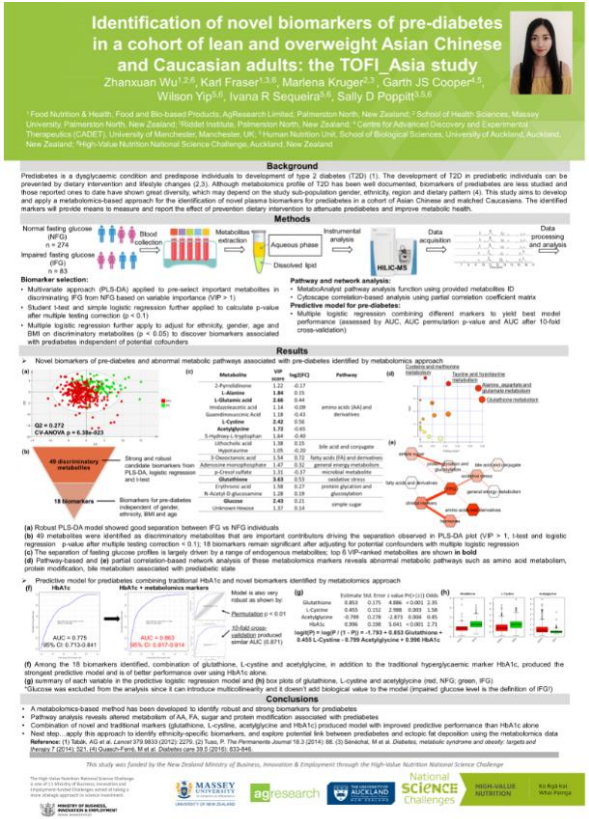
Robust separation *of blood metabolites MAY BE DUE TO:*

(i) ETHNICITY

(ii) PHYSIOLOGY/PATHOLOGY (i.e. higher glucose)

(iii) DIETARY DIFFERENCES

For more details on novel metabolomics markers (N=357)



Emily Wu (PhD)

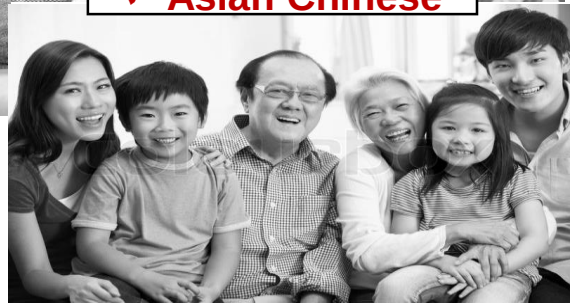
HVN Poster presentation II

Based on fasting glucose levels

Building on our TOFI_Asia findings……

European Caucasian

✓ Asian Chinese



PANaMAH Phase I:
TOFI_Asia study

Novel markers are sensitive to F&B intervention

Tū Ora *Study*
Collaboration with

12 week intervention
In collaboration with Dr Jeremy Krebs, Wellington Hospital