Insights into diabetes susceptibility and resilience: outcomes of the TOFI_Asia Study

Dr Ivana Sequeira on behalf of the PANaMAH program
TOFI_Asia study: Conducted in Auckland

Multi-ethnic city hosting a wider Asian population

Cross sectional phenotyping to determine markers of diabetes risk
TOFI_Asia study: Conducted in Auckland

Pre-screened: N = 383 individuals

Eligible: N = 365

And enrolled into the study
TOFI_Asia cohort: Eligibility criteria

Both parents

- Asian Chinese
- European Caucasian

18 – 70 yrs

20 – 40 kg/m²

Healthy

Pre-Diabetic
TOFI_Asia cohort: Successful recruitment!

159 Caucasian, 206 Asian Chinese

N = 365

- CAUCASIAN MALE N = 65 (18%)
- ASIAN CHINESE MALE N = 94 (26%)
- CAUCASIAN FEMALE N = 94 (26%)
- ASIAN CHINESE FEMALE N = 112 (30%)

Mandarin speaking
Dr Louise Lu

Cantonese speaking
Wilson Yip (PhD)
TOFI_Asia study protocol: Phenotyping the cohort

N = 365
206 Asian Chinese
159 Caucasian

Anthropometry

Height  Weight  Waist  Hip

Study timeline: June 2016 – April 2017
TOFI_AAsia study protocol: Phenotyping the cohort

- Established markers
  - Fasting plasma glucose
  - Hb$_{A1c}$
  - Insulin
  - GI Peptides
  - Amylin, Adiponectin
  - Full lipid profile
  - Liver function tests
  - Cytokines

N = 365
206 Asian Chinese
159 Caucasian

Fasting blood samples

Study timeline: June 2016 – April 2017
TOFI_Asia study protocol: Phenotyping the cohort

N = 365
206 Asian Chinese
159 Caucasian

Fasting blood samples

Novel (metabolomic) markers
Untargeted LC-MS

Dr Karl Fraser
Emily Wu (PhD)

Dr John-Charles Martin
Prof Garth Cooper

Study timeline: June 2016 – April 2017
TOFI_Asia study protocol: Phenotyping the cohort

- Total body fat and abdominal fat

N = 365
206 Asian Chinese
159 Caucasian

DeXA Scan

A/Prof Lindsay Plank

Auckland City Hospital

Study timeline: June 2016 – April 2017
TOFI_Asia study protocol: Phenotyping the cohort

- **Lipid ‘Overspill’ into the organs**
  - Pancreas fat, Liver fat

- **N = 365**
  - 206 Asian Chinese
  - 159 Caucasian

- **N = 70**
  - 36 Asian Chinese
  - 34 Caucasian

**Magnetic Resonance Imaging and Spectroscopy (MRI/S)**

**Study timeline:** June 2016 – April 2017
TOFI_Asia study protocol: Phenotyping the cohort

- **Lipid ‘Overspill’ into the organs**
  - Pancreas fat, Liver fat

**Study timeline:** June 2016 – April 2017

- **N = 365**  
  - 206 Asian Chinese
  - 159 Caucasian

- **N = 70**  
  - 36 Asian Chinese
  - 34 Caucasian

**A/Prof Jun Lu**

**Dr Rinki Murphy**
TOFI_Asia study protocol: Phenotyping the cohort

N = 365
206 Asian Chinese
159 Caucasian

N = 70
36 Asian Chinese
34 Caucasian

MRI/S

➢ Lipid ‘Overspill’ into the organs
Pancreas fat, Liver fat

International collaborators renowned for MR imaging

Dr. Keiren Hollingsworth

Study timeline: June 2016 – April 2017
TOFI_Asia study protocol: Phenotyping the cohort

Cardiorespiratory fitness
YMCA submaximal bike test

Study timeline: June 2016 – April 2017
TOFI_Asia study protocol: Phenotyping the cohort

- Pancreatic β-cell function as a measurement of insulin secretion
  - Intravenous glucose tolerance test (ivGTT)

Study timeline: June 2016 – April 2017
Summarise *Early* data from the TOFI cohort

- **N = 365**
  - 206 Asian Chinese
  - 159 Caucasian

- **N = 70**
  - 36 Asian Chinese
  - 34 Caucasian

**Study timeline: June 2016 – April 2017**
## TOFI cohort: Summary of early results

<table>
<thead>
<tr>
<th></th>
<th>CAUCASIAN</th>
<th>CHINESE ASIAN</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Height (m)</strong></td>
<td>1.72 ± 0.1</td>
<td>1.66 ± 0.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>80.0 ± 15.7</td>
<td>75.9 ± 14.4</td>
<td>0.009</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>26.8 ± 4.6</td>
<td>27.4 ± 3.9</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Age (yrs)</strong></td>
<td>42.4 ± 16.</td>
<td>41.2 ± 13.3</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Total body fat (%)</strong></td>
<td>33.8 ± 10.2</td>
<td>35.0 ± 7.2</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Abdominal fat (%)</strong></td>
<td>36.9 ± 14.1</td>
<td>41.0 ± 9.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Mean ± SD**

**NOT AS TALL**
## TOFI cohort: Summary of early results

<table>
<thead>
<tr>
<th>Metric</th>
<th>Caucasian Mean ± SD</th>
<th>Chinese Asian Mean ± SD</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (m)</td>
<td>1.72 ± 0.1</td>
<td>1.66 ± 0.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>80.0 ± 15.7</td>
<td>75.9 ± 14.4</td>
<td>0.009</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.8 ± 4.6</td>
<td>27.4 ± 3.9</td>
<td>ns</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>42.4 ± 16.0</td>
<td>41.2 ± 13.3</td>
<td>ns</td>
</tr>
<tr>
<td>Total body fat (%)</td>
<td>33.8 ± 10.2</td>
<td>35.0 ± 7.2</td>
<td>ns</td>
</tr>
<tr>
<td>Abdominal fat (%)</td>
<td>36.9 ± 14.1</td>
<td>41.0 ± 9.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Mean ± SD

**N = 365**

206 Asian Chinese
159 Caucasian

- Weighed less
## TOFI cohort: Summary of early results

### Comparative Measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>Caucasian</th>
<th>Chinese Asian</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (m)</td>
<td>1.72 ± 0.1</td>
<td>1.66 ± 0.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>80.0 ± 15.7</td>
<td>75.9 ± 14.4</td>
<td>0.009</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>26.8 ± 4.6</td>
<td>27.4 ± 3.9</td>
<td>ns</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>42.4 ± 16.0</td>
<td>41.2 ± 13.3</td>
<td>ns</td>
</tr>
<tr>
<td>Total body fat (%)</td>
<td>33.8 ± 10.2</td>
<td>35.0 ± 7.2</td>
<td>ns</td>
</tr>
<tr>
<td>Abdominal fat (%)</td>
<td>36.9 ± 14.1</td>
<td>41.0 ± 9.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Mean ± SD

Although BMI values differ, they are similar.
**TOFI cohort: Summary of early results**

<table>
<thead>
<tr>
<th></th>
<th>CAUCASIAN</th>
<th>CHINESE ASIAN</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (m)</td>
<td>1.72 ± 0.1</td>
<td>1.66 ± 0.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>80.0 ± 15.7</td>
<td>75.9 ± 14.4</td>
<td>0.009</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.8 ± 4.6</td>
<td>27.4 ± 3.9</td>
<td>ns</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>42.4 ± 16.</td>
<td>41.2 ± 13.3</td>
<td>ns</td>
</tr>
<tr>
<td>Total body fat (%)</td>
<td>33.8 ± 10.2</td>
<td>35.0 ± 7.2</td>
<td>ns</td>
</tr>
<tr>
<td>Abdominal fat (%)</td>
<td>36.9 ± 14.1</td>
<td>41.0 ± 9.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Mean ± SD

**SIMILAR AGE**
## TOFI cohort: Summary of early results

**N = 365**  
206 Asian Chinese  
159 Caucasian

<table>
<thead>
<tr>
<th></th>
<th>CAUCASIAN</th>
<th>CHINESE ASIAN</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Height (m)</strong></td>
<td>1.72 ± 0.1</td>
<td>1.66 ± 0.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>80.0 ± 15.7</td>
<td>75.9 ± 14.4</td>
<td>0.009</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>26.8 ± 4.6</td>
<td>27.4 ± 3.9</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Age (yrs)</strong></td>
<td>42.4 ± 16.0</td>
<td>41.2 ± 13.3</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Total body fat (%)</strong></td>
<td>33.8 ± 10.2</td>
<td>35.0 ± 7.2</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Abdominal fat (%)</strong></td>
<td>36.9 ± 14.1</td>
<td>41.0 ± 9.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Mean ± SD  

**GREATER ABDOMINAL FAT**
TOFI cohort: Summary of early results

<table>
<thead>
<tr>
<th></th>
<th>CAUCASIAN</th>
<th>CHINESE ASIAN</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fasting plasma glucose</strong> (mmol/L)</td>
<td>5.1 ± 0.6</td>
<td>5.4 ± 0.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Hb(_{A1c})</strong> (mmol/mol)</td>
<td>33.3 ± 3.6</td>
<td>35.9 ± 4.1</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Established BLOOD markers for diabetes risk**

BOTH HIGHER in Asian Chinese
Established risk markers in the TOFI cohort

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

If anything Asian Chinese are slightly higher
Established risk markers in the TOFI cohort

Not surprising, fasting glucose levels are also significantly correlated with abdominal fat in both Ethnicities.

Again Asian Chinese are slightly higher.
**Novel (metabolomic) markers in the TOFI cohort**

Plot shows *novel blood metabolites* Caucasians (blue) and Asian Chinese (green)

Very interesting findings!

Partial least squares discriminatory analyses
Novel (metabolomic) markers in the TOFI cohort

Clear and robust separation between Ethnicities

Considerably different blood metabolite profiles between the two ethnic groups

Partial least squares discriminatory analyses
Very important that these studies are focused on Asian Chinese consumers

In line with Chinese regulatory requirements for validating health claims
TOFI-MRI cohort: Summary of early results

N = 365
206 Asian Chinese
159 Caucasian

N = 70
36 Asian Chinese
34 Caucasian

Study timeline: June 2016 – April 2017
TOFI-MRI cohort: Summary of early results

- Only scanned **women** so far
  - Due to gender differences in body composition

- **First analysis** of MRI scans
  - Undergoing review with **UK collaborators** – globally-leading research group for pancreatic fat MRI imaging & analyses

Study timeline: June 2016 – April 2017
TOFI-MRI cohort: Summary of early results

N = 70

36 Asian Chinese
34 Caucasian

Box plots showing median and interquartile range

Caucasian
Asian

Slightly younger

Caucasian
Asian

Slightly slimmer

Caucasian
Asian

Slightly higher
Fasting glucose

Caucasian
Asian

BMI (kg/m²)

Fasting plasma glucose (mmol/L)
TOFI-MRI cohort: Summary of early results

N = 70
36 Asian Chinese
34 Caucasian

Box plots showing median and interquartile range

**ORGAN FAT HIGHER in Asian Chinese women**

Despite being slightly younger & slightly slimmer
Caucasian female, 56 y
BMI 35 kg/m²

SAT 23%
Caucasian female, 56 y
BMI 35 kg/m²

Low Risk
Fasting glucose 4.96 mmol/L

SAT 23%
Pancreas 4% fat
Liver 3%
SAT: subcut fat

FAT IMAGE (3 mm)
Caucasian female, 56 y
BMI 35 kg/m²

Asian female
low BMI, TOFI profile

QL41227

FAT IMAGE (3 mm)
Pancreas

Liver 3%
SAT 23%
FAT IMAGE (3 mm)
SAT: subcut fat

Pancreas 4% fat

Asian Chinese female, 45 y
BMI 23 kg/m²

FAT IMAGE (3 mm)
Pancreas 10%

Liver 9%
SAT 13%
FAT IMAGE (3 mm)
SAT: subcut fat

9.6% fat

23%

13%

4%
Caucasian female, 56 y
BMI 35 kg/m²

Asian female, low BMI, TOFI profile

FAT IMAGE (3 mm)
Pancreas

9.6% fat

MRI SCAN

Asian Chinese female, 45 y
BMI 23 kg/m²

SAT 13%

Pancreas 10%

High Risk, TOFI

Fasting glucose
5.63 mmol/L

Liver 9%

FAT IMAGE (3 mm)
SAT: subcut fat
Individual women in the MRI cohort....

- Caucasian European
  - N = 34
- Asian Chinese
  - N = 36
(i) Women with high pancreatic fat (early data)

- Caucasian European: N = 34
- Asian Chinese: N = 36
(ii) Lean women with high pancreatic fat: who is TOFI?

Greater no. of TOFI women

Caucasian European
N = 34

Asian Chinese
N = 36
Are there Novel (metabolomics) risk markers for pancreatic fat?

Yes, strong correlations between some blood metabolites with high (green) and low (blue) pancreatic fat

Orthogonal Partial least squares analyses

$P = 3.41 \times 10^{-4}$
Are there Novel (metabolomics) risk markers for pancreatic fat?

Caucasian European

 ✓ Triglycerides, Phosphatidylcholines

 ✓ Primarily sphingolipids

Importantly, novel markers identified differed between the Asian Chinese and Caucasian women.

Orthogonal Partial least squares analyses
The early findings from *Novel* risk markers suggest...

There may be fundamental differences between the two ethnicities around biomarkers that represent high pancreatic fat.

Orthogonal Partial least squares analyses
Where to from here......

PANaMAH Phase I:
TOFI_Asia study

Phenotyping will continue

PANaMAH Phase II

Longer term F&B interventions

Collaboration with Nuku cluster

✓ European Caucasian
✓ Asian Chinese