junctions and endosomes, suggesting a role in endocrine function. This was linked to changes in hepatic expression of several genes linked to glucose homeostasis and lipid metabolism. The primary effect of PKCε on glucose homeostasis is, therefore, not exerted directly in the liver as currently posited. However, PKCε activity in adipose tissue modulates glucose tolerance and is involved in crosstalk with the liver.

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Lipidomic profiling reveals early-stage metabolic dysfunction in overweight or obese humans

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Advances in mass spectrometry and lipidomics techniques are providing new insights into the role of lipid metabolism in obesity and its metabolic sequelae. However, human lipidomic studies have produced inconsistent results, owing in part to the use of indirect proxy measures of obesity and insulin resistance and the relatively limited coverage of the lipidome. Here, we explored the relationship between the plasma lipidome and metabolic profiles using direct gold-standard measures of adiposity, insulin sensitivity, and insulin secretion, in addition to comprehensive lipidomic profiling (>450 species) and measurement of inflammatory cytokines and adipokines. We present new evidence showing a strong and independent positive correlation between the lysophosphatidylinositol (LPI) lipid class and insulin secretion *in vivo* in humans, supporting the insulinotropic effects of LPI demonstrated in mouse islets. Dihydroceramide, a sphingolipid precursor, was independently and negatively correlated with insulin sensitivity, indicating a possible upregulation in sphingolipid synthesis in obese individuals. We also show that phosphatidylethanolamine and its vinyl ether-linked (plasmalogen) derivatives correlate negatively with body fat, while dihexosylceramide correlates positively with interleukin-10. Together, these lipid classes may signify early pathogenesis toward type 2 diabetes and could serve as novel therapeutic targets or biomarkers for identification of high-risk individuals.

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Insights into type 2 diabetes susceptibility and resilience: TOFI_Asia study

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Predicting rate of progression and identifying those most at risk of adverse metabolic health is difficult and often associated with environmental, lifestyle, and dietary factors. Importantly site of lipid deposition, including ectopic 'overspill' into key organs, increases metabolic risk. We investigated susceptibility to type 2 diabetes (T2D) in healthy and prediabetic Asian Chinese ($N = 209$) and European Caucasian ($N = 156$) adults resident in Auckland, enrolled in the TOFI_Asia Study; within the Peak Nutrition for Metabolic Health (PANaMAH) program, one of four priority research platforms in the New Zealand National Science Challenges (NSC).

Phenotypic characterisation of the 2 ethnicity cohorts, using anthropometry, body composition (dual energy X-ray absorptiometry, DXA) and blood biochemistry revealed that although of similar age and body mass index (BMI), Chinese (Mean ± SEM, 42 ± 1 yrs; 27.4 ± 0.3 kg/m^2) had significantly greater abdominal fat (42.0 ± 0.6% vs 37.0 ± 1.1%, $p < 0.01$) than Caucasian (43 ± 1 yrs; 26.9 ± 0.4 kg/m^2) with correspondingly higher fasting plasma glucose (FPG) concentrations (5.4 ± 0.04 mmol/l vs 5.0 ± 0.04 mmol/l, $p < 0.001$) and glycated haemoglobin, Hb_{A1c} (36.0 ± 0.3 mmol/mol vs 33.0 ± 0.3 mmol/mol, $p < 0.05$). In addition, pancreatic and liver fat were quantified, using magnetic resonance imaging (MRI) and spectroscopy (MRS), in a subset of 36 Chinese (41 ± 2 yrs; 26.9 ± 0.7 kg/m^2) and 34 Caucasian (48 ± 3 yrs; 28.0 ± 0.7 kg/m^2) women from the cohort. These overweight, younger Asian Chinese had significantly lower MRI-determined abdominal and subcutaneous fat ($p < 0.05$) but pancreas (4.3 ± 0.3%) and liver (11.0 ± 1.7%) fat matched that, or tended to be higher than, Caucasian (pancreas: 4.1 ± 0.3%; liver: 8.1 ± 1.7%). Importantly, fat in pancreas (Chinese: $R^2 = 0.10$, $p = 0.09$; Caucasian: $R^2 = 0.28$, $p = 0.001$) and liver (Chinese: $R^2 = 0.12$, $p = 0.04$; Caucasian: $R^2 = 0.11$, $p = 0.05$) were positively correlated with FPG. The **T**hin on the **O**utside **F**at on the **I**nside 'TOFI' profile observed in this Asian Chinese cohort, may contribute to their greater risk of poor metabolic health compared to Caucasian counterparts even in individuals of the same BMI and younger age.

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