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**A SPECIFIC SERUM FATTY ACID (FA) COMPOSITION ACROSS MULTIPLE LIPID FRACTIONS UNDERLIES PATHOPHYSIOLOGICAL FEATURES OF TYPE 2 DIABETES IN THE CANADIAN PROSPECTIVE METABOLISM AND ISLET CELL EVALUATION (PROMISE) COHORT**

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**Background**: FA can positively or negatively influence metabolic function and could modulate risk for diabetes. Since FA within individual lipid fractions fulfill distinct physiological functions, a specific clusters of FA could be indicative of a greater risk for diabetes. Our aim, therefore, was to identify specific patterns in the composition of FA across multiple lipid fractions that underlie insulin sensitivity (IS) and beta-cell function.

**Methods**: Adults at risk for diabetes (n=477) had multiple blood samples during an OGTT. FA from triacylglycerol (TGFA), phospholipid, cholesteryl ester, and non-esterified (NEFA) fractions were quantified from fasting samples and the mole percent (mol%) of total lipids was calculated. Outcome measures included the Matsuda index (ISI) for IS and the Insulin Secretion-Sensitivity Index-2 (ISSI-2) for beta-cell function. Partial least squares (PLS) was used to identify underlying clusters in the FA composition, with FA from all lipid fractions included as the predictor variables and ISI or ISSI-2 as the response variables, in separate PLS models.

**Results**: The first two PLS components (C1 and C2) were extracted. These components explained 39.2% and 22.4% of the variance in the outcomes and explained 22.5% and 21.8% of the variance in the FA for ISI and ISSI-2, respectively. TGFA loaded heavily on C1, while NEFA loaded heavily on C2. Only specific TGFA contributed substantially to the variability in the outcomes (i.e. TG14:0, TG16:0, TG16:1n-7, TG18:0, TG18:1n-9, TG18:1n-7). A higher mol% of these specific TGFA associated with lower ISI and ISSI-2 values.

**Conclusions**: We identified a cluster of TGFA that had a strong relationship with lower IS and, to a lesser extent, beta-cell function. These TGFA (e.g. 16:1n-7) are reported to associate with refined or simple carbohydrate intake and have experimentally been shown to exhibit lipotoxic effects. Our results suggest that only a few FA from a broad spectrum of serum FA may underlie the association between lipids and glucose dysregulation, and that these lipids are possible mediators between the reported associations of carbohydrate intake and diabetes risk.

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