long-term consequences. In rodents, manipulating the microbial community structures that constitute the intestinal microbiota can impact body composition, but how this information may translate to humans is still unclear. The realisation that brown-like adipose tissue exists in humans has prompted provocative studies in animals demonstrating that adipose depots can be induced to carry out inefficient metabolism, a process that if translated to humans could alter energy balance to treat obesity and diabetes. A common obesity complication is type 2 diabetes, but obesity does not universally lead to diabetes, providing some support for the notion of ''healthy'' obesity. For those with obesity-associated diabetes, recent therapeutic options appear to decrease certain diabetes complications although the responsible mechanisms are poorly understood. Emerging evidence suggests that a combination of genetic and metabolic profiling could help guide management, but such an approach will also require behavioural and population-based strategies to address the failure of many providers and patients to utilise proven therapies.

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Increased intestinal permeability as a risk factor for type 2 diabetes in obesity

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Introduction: The interplay between the gut microbiota, intestinal permeability and chronic low grade inflammatory responses in the context of risk for obesity-associated disease continue to be of interest. A permeable intestinal mucosa is necessary to facilitate critical absorptive functions, but alterations in intestinal permeability have the potential to trigger Metabolic Endotoxaemia (ME) which may result in downstream activation of inflammatory signalling pathways and contribute to risk for disease. The aim of the study was to examine the associations between intestinal permeability and type 2 diabetes (T2D) using a derived risk score approach.

Methods: A total of 130 individuals with T2D (age: 57.5 ± 6.2 years (mean ± SD); BMI: 30.4 ± 3.2; 45% female) and 161 individuals without T2D (age: 37.4 ± 12.5 years; BMI: 25.1 ± 3.9; 65% female) were included in the study. Assessment of intestinal permeability included measurement of circulating lipopolysaccharide (LPS), LPS-binding protein (LBP) and intestinal fatty acid binding protein (iFABP) concentrations which were then used for calculation of a derived permeability risk score (PRS) based on quartile scoring of each individual measure. Associations between the PRS and T2D status were assessed using logistic regression models.

Results: LBP (~34%, $p < 0.001$), iFABP (~46%, $p < 0.001$) and the PRS (~24%, $p < 0.001$) were all significantly higher in the T2D affected individuals. Quantification of risk across PRS tertiles revealed that individuals with a PRS in the upper tertile were 5.07 times more likely (CI: 1.72—14.95; $p = 0.003$) to have T2D independent of age, sex and BMI.

Conclusions: These data support an association between intestinal permeability and risk for T2D. Consideration of intestinal permeability assessment as a potential tool for classifying individuals with Metabolic Syndrome as high or low risk for T2D development appears a logical progression of this work.

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Insulin transport and activity in the central nervous system

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Insulin acts within the central nervous system to alter numerous physiological outcomes including energy balance and glucose homeostasis. Insulin is transported into the central nervous system by a saturable-receptor mediated process that is proposed to be dependent on the insulin receptor. Transport of insulin into the brain is altered by numerous factors including diet induced obesity [1]. It has previously been observed that the