are notable. Improving health outcomes through pricing strategies is likely to require a broader selection of targeted foods, the deployment of higher subsidies/taxes and the use of well-designed complementary strategies. The feasibility, sustainability and acceptability of such approaches would need to be considered by remote food suppliers.

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Invited talk: IC7: A novel therapy for the treatment of metabolic disease

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We have previously shown that the gp130 cytokines interleukin-6 (IL-6) and ciliary neurotrophic factor (CNTF) can improve obesity and insulin resistance in both mice and humans [1,2]. However, due to the known inflammatory effects of IL6 and the antigenic response in some patients to the clinically used form of CNTF (Axokine), both proteins have no therapeutic utility. In an attempt to overcome this issue, we have designed a chimeric gp130 ligand, termed IC7, where one gp130 binding site has been removed from IL6 and replaced with the LIFR binding site from CNTF. This 'module swap' creates a new cytokine with CNTF-like, but IL-6R dependent activity. In a series of experiments, we have shown that IC7 has similar positive metabolic effects as CNTF, but may overcome the negative effects experienced by Axokine. Specifically, IC7 significantly improved glucose tolerance and hyperglycaemia and prevents weight gain and liver steatosis in obese mice. In addition, we have shown efficacy and safety in a study in non-human primates (*Macaca fascicularis*). In addition, in comprehensive human cell based assays, we have demonstrated that IC7, unlike Axokine, results in no signs of immunogenicity. Thus IC7 is a realistic and viable next generation biological for the treatment of obesity and T2D, disorders that are currently pandemic.

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Invited talk: Obesity in diabetes: Friend or foe?

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We associate obesity with poor clinical outcomes, including in people with type 2 diabetes. Compelling evidence links obesity in early life to higher risks of diabetes and death, justifying population-wide prevention efforts. However, obesity has been associated with improved rather than poorer diabetes outcomes and we lack good evidence that weight loss prevents diabetes complications and death. Obesity in diabetes might also confer health benefits in terms of enhancing beta-cell mass and maintaining bone health. These paradoxical findings will form the basis of discussion about the therapeutic role of weight loss in diabetes.

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Invited talk: Walt Whitman, Herman Melville, and the Challenges of obesity and diabetes

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Worldwide prevalence reports for obesity and diabetes over recent decades suggest that the chronic management of metabolic disease will dominate health care for the foreseeable future. Feeding behaviours contributing to obesity have been recognised for nearly a half-century, many of the key molecular mediators of central nervous system appetite control have been identified, and novel pharmacological agents have been introduced to treat obesity. However, less than robust results from medical management have promoted the pursuit of alternative clinical and scientific approaches. Anatomical interventions including bariatric surgery are gaining acceptance despite uncertainties about patient selection and

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