the potential of HCC to have wide-spread impact by changing the expectations around healthy food provision.

Conclusion: This study shows engagement methods and potential challenges of the HCC, and provides lessons for other local governments in the UK and abroad considering similar actions to address the healthiness of food businesses in their community.

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Cellular energy sensing and metabolism: implications for treating obesity

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The survival of all cells is dependent on the constant challenge to match energetic demands with nutrient availability, a task which is mediated through a highly conserved network of metabolic fuel sensors that orchestrate both cellular and whole organism energy balance. A mismatch between cellular energy demand and nutrient availability is a key factor contributing to the development of obesity, thus understanding the fundamental mechanisms by which cells sense nutrient availability and demand may lead to the development of new treatments. Glucose lowering therapies such as caloric restriction, exercise, metformin and cold all induce an energetic challenge that results in the activation of the cellular energy sensor AMP-activated protein kinase (AMPK). Activation of AMPK in turn suppresses lipid synthesis and inflammation while increasing glucose uptake, fatty acid oxidation and mitochondrial function. In contrast, high levels of nutrient availability, suppress AMPK activity while also increasing the production of peripheral serotonin, a gut-derived endocrine factor which suppresses beta-adrenergic-induced activation of brown adipose tissue. Identifying new ways to manipulate these two ancient fuel gauges, by activating AMPK and inhibiting peripheral serotonin, may lead to the development of new therapies for treating obesity.

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What should we over-eat?

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Abstract not available.

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The diverse obesity phenotypes – Implication for treatment

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Over the past 30 years researchers described varied metabolic phenotypes in overweight and obesity with diverse disease outcomes. Well-conducted randomized large cohort clinical trials in individuals with overweight and prediabetes or type 2 diabetes suggest mixed response to caloric restriction or metformin, the first-line medication in type 2 diabetes [1]. In the Diabetes Prevention Program, 21% of individuals with prediabetes treated with metformin progressed to diabetes at 3 years [2]. Similarly, 55% of individuals with prediabetes in the Tubingen Lifestyle Intervention Program did not revert to normal glucose tolerance in response to energy restriction and moderate exercise intervention [3]. Using gold-standard phenotyping tools of hepatic and peripheral glucose regulation, we find different levels of insulin resistance in liver and muscle in individuals with obesity. Using latest-generation plasma metabolomic and lipidomic analyses combined with machine learning, random forest-based feature selection and classification we identified three plasma lipids that can classify subcohorts of liver versus muscle insulin resistance in obesity with remarkable accuracy. We propose that therapy guided by plasma biomarkers will be more therapeutically effective, have less side-effects, and be more cost-effective.

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Disruption of AMPK-glycogen binding in vivo reveals novel roles in whole-body and tissue metabolism

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The AMP-activated protein kinase (AMPK) and glycogen are essential for maintaining metabolic homeostasis. The energy-sensing AMPK heterotrimer contains a regulatory β subunit with a carbohydrate-binding module (CBM) known to bind glycogen. However, the physiological roles of AMPK-glycogen binding in metabolism *in vivo* are unknown. To determine the effects of disrupting AMPK-glycogen binding, two whole-body knock-in (KI) mouse lines were generated targeting tryptophan residues known to mediate glycogen binding in either the AMPK β1 (W100A KI) or β2 (W98A KI) subunit, predominantly expressed in liver and skeletal muscle, respectively. Whole-body, serum and tissue analyses were performed in male KI and wild type (WT) litter mate mice maintained on an *ad libitum* chow diet. Intraperitoneal glucose tolerance testing revealed normal glucose tolerance in W100A mice but impaired glucose handling in W98A mice (56% increase in AUC; $P < 0.05$) compared to WT, with no differences observed in fasting serum insulin. Body composition (determined from EchoMRI) showed normal whole-body fat and lean mass in W100A mice. Strikingly, W98A mice displayed a 42% increase in fat mass ($P < 0.05$) and 5% decrease in lean mass ($P < 0.05$) relative to WT. Metabolic caging demonstrated no changes in cumulative food intake, O_2