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Bile acid signaling and control of mitochondrial metabolism

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Abstract not available.

<https://doi.org/10.1016/j.orcp.2018.11.007>

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The novel designer cytokine IC7Fc protects against obesity-induced metabolic diseaseTamara Allen¹, Maria Findeisen², Mark Febbraio^{2,*}¹ *BakerIDI Heart & Diabetes Inst., Melbourne, VIC, Australia*² *Garvan Institute of Medical Research, Darlinghurst, NSW, Australia*

The gp130 receptor cytokines interleukin-6 (IL-6) and ciliary neurotrophic factor (CNTF) can improve obesity and insulin resistance in mice and humans. However, due to the known pro-inflammatory effects of IL-6 and the antigenic response in some patients to the clinically used form of CNTF (Axokine™), both proteins have limited, if any, therapeutic utility for treatment of type 2 diabetes (T2D). In an attempt to overcome these issues, we engineered a chimeric gp130 ligand, termed IC7Fc, where one gp130 binding site has been removed from IL-6 and replaced with the leukemia inhibitory factor receptor (LIFR) binding site from CNTF and then fused with the fragment crystallizable (Fc) domain of immunoglobulin G (IgG), creating a new cytokine with CNTF-like, but IL-6R- dependent signaling. We have demonstrated that IC7Fc significantly improves glucose tolerance and hyperglycemia and prevents weight gain and liver steatosis in diet-induced and genetically modified obese mice. In addition, IC7Fc improves glucose tolerance and is safe in non-human primates. In comprehensive human cell based assays, we have also shown that IC7Fc treatment results in no signs of inflammation or immunogenicity. Thus, IC7Fc is a realistic next generation biological for the treatment of obesity and T2D, disorders that are currently pandemic.

<https://doi.org/10.1016/j.orcp.2018.11.008>

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Hepatokines: linking fatty liver to diabetes

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Obesity is a risk factor for the development of secondary complications including dyslipidemia, non-alcoholic fatty liver disease, cardiovascular disease and type 2 diabetes. An accumulation of lipid in the liver, which is clinically known as hepatic steatosis, is a pathologic abnormality that is common in obese and type 2 diabetes patients. Hepatic steatosis occurs when fatty acid supply outweighs fatty acid demand and occurs in a time-course that usually precedes the induction insulin resistance and type 2 diabetes. This presentation describes how 'omics' approaches have been used to delineate the hepatocyte protein and lipid secretome in health and obesity, and unravelled unappreciated biology. Further,

we report on the pre-clinical validation of several liver secreted factors that either cause insulin resistance and disturbances in systemic metabolic homeostasis or enhance glycemic control in diabetes.

<https://doi.org/10.1016/j.orcp.2018.11.009>

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Emerging Roles of MAP kinase phosphatases in metabolic homeostasis

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Dietary interventions for adolescents affected by overweight and obesity—the evidence from randomised controlled trials.

<https://doi.org/10.1016/j.orcp.2018.11.010>

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The personal burden of stigma, bias and responsibility for obesity

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Abstract not available.

<https://doi.org/10.1016/j.orcp.2018.11.011>

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Diet as a shared risk factor for obesity and common mental disorders

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Mental illness including depression, anxiety, and bipolar disorder are a significant driver of global disability and a substantial social, economic and health burden. Treatment including pharmacotherapy such as antidepressants and psychotherapy such as Cognitive Behavioural Therapy avert less than half of the disease burden. Novel strategies are needed to prevent and treat mental disorders.

There are now consistent mechanistic, observational and interventional data to suggest diet quality and the microbiome may be a modifiable risk factor for mental illness. This presentation aims to overview of the nutritional psychiatry field. It includes a discussion of the neurobiological mechanisms such as inflammation likely modulated by diet, and focusses on the use of dietary, microbiome and nutraceutical interventions in mental disorders.

Potential biological pathways influenced by diet and potentially related to mental disorders include inflammation, oxidative stress, the gut microbiome, epigenetic modifications and neuroplasticity. Epidemiological data, particularly in depression, suggests an association between diet quality and mental health, across multiple populations and age groups; these do not appear to be explained by reverse causality or other demographic or lifestyle factors. Our treatment trial provides now replicated clinical evidence that dietary interventions in clinically diagnosed populations are feasible and can provide significant clinical benefit. Nutraceutical approaches including omega-3 fatty acids, folate, S-adenosylmethionine, N-acetyl cysteine and probiotics, amongst