[3]. Transplantation of bone marrow from wild-type or *Gpr21*$^{-/-}$ animals into irradiated wild-type animals fed normal chow (13.5% fat), or high fat diet (HFD; 60% fat) for 27 weeks, revealed no improvement in glucose homeostasis, but an improvement in insulin sensitivity and a decrease in immune cell infiltration into eWAT. Furthermore, a decrease in the migratory ability of isolated CD11b^{+} bone marrow monocytes from *Gpr21*$^{-/-}$ mice compared to wild-type in response to monocyte chemoattractant protein-1 (MCP-1) was observed. These data were confirmed using a PKH26 monocyte tracking study. RNAseq analysis of CD11b^{+} monocytes from *Gpr21*$^{-/-}$mice revealed an overall significant effect on genes involved in inflammation and cell migration, including *Il6*, *Ccl2*, *Cxcl2* and members of the TLR family, supporting the reduced functional response. Significant changes in genes involved in atherosclerosis was also observed, including *Apoe* and *Nr4a1*. These data indicate that GPR21 is involved in the chemotaxis of specific immune cells. Targeting this receptor may prove beneficial for the treatment of T2DM and its complications.

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https://doi.org/10.1016/j.orcp.2018.11.162

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Stabilization of beta catenin in hypothalamic cell lines

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Beta-catenin is a signalling molecule in the Wnt-signalling pathway, which has typically been associated with embryogenesis and tumorigenesis. More recently, new lines of evidence suggest that it may also be involved in the pathogenesis of type-2 diabetes. In its active form, beta-catenin acts together with the transcription factor T cell-specific transcription factor-7-like 2 (TCF7L2) to activate target genes of the Wnt-signalling pathway. Impairment in this signal transduction pathway in the pancreas may contribute to the development of type-2 diabetes. The role of the hypothalamus in controlling glucose homeostasis is becoming well-recognized, and we have recently found that Wnt signalling is activated in the hypothalamus in response to feeding-related hormones. To investigate possible mechanisms of feeding-induced stabilization of beta-catenin, we have used adult mouse hypothalamic cell lines that express the phenotype for various metabolic neuropeptides and receptors involved in central regulation of metabolism. We surveyed a variety of potential hormone factors that can simulate the effect of feeding: forskolin, exendin-4 and MTII (an α-MSH analogue). After treatment, we firstly measured NPY and AgRP secretion. Treatment with these factors did not affect the secretion of either neuropeptide. After applying KCl to depolarise the cells, however, there was significantly greater release of both AgRP and NPY from treated cells compared with vehicle-controls, indicative of an effect on synthesis or vesicle trafficking. We next treated these cell lines with forskolin and discovered that in one of the cell line, all the Wnt-responsive genes analyzed were markedly up-regulated. In addition we found an increase in total beta-catenin protein expression following treatment with either forskolin, exendin-4 or MTII. These data suggest that the treatment has increased the pool of neuropeptide available for release. These results are consistent with the role of beta-catenin in regulating a feeding response through a central mechanism.

https://doi.org/10.1016/j.orcp.2018.11.163

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Glycoprotein acetyls (GlycA) associate with BMI and co-morbidities in childhood obesity

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Introduction: Childhood obesity is a pro-inflammatory state associated with metabolic and cardiovascular complications. In adults, glycoprotein acetyls (GlycA), a newly described inflammatory marker, is associated with cardiovascular disease and all-cause mortality, but there are few paediatric data. In a cohort of children attending a tertiary paediatric obesity clinic, we investigated the relationship between GlycA and obesity-related cardiometabolic co-morbidities.

Methods: Participants were enrolled in COBRA (Childhood Overweight BioRepository of Australia) between 2009–2017. Study site was at the Royal Children's Hospital, Melbourne. Data collected included demographic (age and sex), anthropometric (weight, height, BMI, pubertal stage) and clinical (blood pressure) measures. An 8-hour fasted blood sample was collected for liver function (to assess for non-alcoholic fatty liver disease, NAFLD) and GlycA. An OGTT revealed the status for impaired glucose tolerance (IGT), insulin resistance (IR) and type 2 diabetes mellitus (T2DM). Hypertension (HTN) was determined according to current guidelines. GlycA was analyzed by NMR spectroscopy of serum. Binomial regression modeling, adjusted for age, sex, BMI and pubertal stage, assessed the relationship between GlycA and each of the dichotomized outcome variables (IGT, IR, T2DM, NAFLD and HTN).

Results: 216 participants were included (52% females, mean age 11.9 years (SD ± 3.1), 35% post-pubertal). The mean value for BMI *z*-score was 2.49 (SD ± 0.24), and for GlycA 1.103 mmol/l (SD ± 0.123). GlycA was associated with BMI (pearsons $\rho = 0.29$; $p < 0.001$). Comorbidity prevalences were: IGT:36%, IR:55%, T2DM:2%, sHTN:49%, dHTN:26%, NAFLD:38% and hyperlipidaemia:25%. In fully adjusted models, GlycA was associated with hyperlipidemia ($p < 0.0001$), IR ($p < 0.05$) and NAFLD ($p < 0.05$), but not with IGT, systolic or diastolic HTN.

Conclusion: Increased GlycA, indicative of chronic inflammation, was associated with BMI and its co-morbidities in obese children. Longitudinal studies are warranted to define its role as