a predictive biomarker for adverse obesity-related outcomes in childhood.

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Lower prevalence of performance genes are linked with increased severity of obesity in youth

Christoph C.S. Saner[1,2,*], Brooke B.H. Harcourt[1,2,3], Markus M.J. Juonala[2,4], Kung-Ting K.T.K. Kao[1,2,3], Peter P.H. Houweling[2,3], Kathryn K.N. North[2,3], Matthew M.S. Sabin[1,2,3]

[1] *Department of Endocrinology, Royal Children's Hospital, Parkville, Victoria, Australia*
[2] *Murdoch Children's Research Institute, Parkville, Victoria, Australia*
[3] *Department of Paediatrics, The University of Melbourne, Parkville, Victoria, Australia*
[4] *Department of Medicine, University of Turku and Division of Medicine, Turku, Finland*

Introduction: Obesity mainly arises from an imbalance between activity and energy intake, although some children appear to carry a genetic predisposition for weight gain. The ability to sustain physical activity and effectively induce a favorable metabolic outcome is genetically predetermined. Candidate genes for fitness and muscle strength have been shown to influence muscle function and mass in response to exercise. We aimed to determine whether there is a genetic predisposition limiting effectiveness of training and substrate's utilization.

Methods: Children from the Childhood Overweight BioRepository of Australia (COBRA), presenting at The RCH Weight management Service, were clinically assessed, PBMCs were collected for DNA analysis ($N = 238$) and Actical-accelerometer was worn for 7-days. SNP analysis on a unique performance gene panel included; *ACTN3*-rs1815739, *CNDP1*-rs2887, *HIF1A*-rs11549465, *GALNT13*-rs10196189, *PPARGC1A*-rs8192678, *RPLP1_GEMIN8P1*-rs4776471, *CRHBP*-rs1715747. Correlation analyses were calculated between allele prevalence of fitness genes and BMI *z*-scores, body and truncal fat percentage, waist circumference, blood pressure and accelerometer data.

Results: Genotypes associated with fitness were less prevalent in the COBRA cohort than in reference population studies. A more pro-fitness genotype was associated with lower body weight ($p < 0.05$ for ACTN3,ZFYVE26 and CNDP1), decreased waist circumference ($p < 0.01$ for RPLP1_GEMIN8P1) and decreased body fat ($p < 0.05$ for IL15RA) in females and lower body fat ($p < 0.05$ for SHBG_GENE) for males. Increased daily physical activity was associated with pro-fitness genotypes ($p < 0.05$ for ZFYVE26,CNDP1,HIF1A,CRHBP and SHBG_GENE). Sex dependent variation was observed in blood pressure measurements between genotypes ($p < 0.05$ for UGT2B4 in females; for GALNT13 and PPARGC1A in males).

Conclusion: In an obese cohort, those with higher BMI are less likely to exhibit a favorable 'fitness genotype' and are less physically active which places them at greater risk of cardiometabolic complications. Knowledge about susceptibility for weight gain may identifies individuals at risk for increasing severity of obesity and complications.

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The impacts of cyanidin-3-O-β-glucoside and peptides extracted from yoghurt on glucose uptake and gene expression in human primary skeletal muscle cells from obese and diabetic individuals

Min Shi*, Xiao Q. Su, Andrew J. McAinch

Objective: Incidence of type II diabetes mellitus is rapidly increasing worldwide. This study aimed to investigate whether cyanidin-3-O-β-glucoside (C3G), or peptides with angiotensin converting enzyme (ACE) inhibitory activity, alone or in combination, alter glucose regulation in human primary myotubes derived from obese and obese diabetic individuals.

Research design and methods: In cells treated with 10 μM, 100 μM of C3G, 150 μg/mL, 1500 μg/mL of peptide and their combinations, [3H]-2-deoxyglucose uptake and mRNA expression of multiple genes related to insulin resistance and glucose metabolism were determined by 'real-time' PCR. Statistical analyses were performed using GraphPad Prism 7 (GraphPad Software, Inc, La Jolla, CA, USA). $P < 0.05$ was considered significant.

Results: In the obese group, both low and high concentration of peptides with ACE inhibitory activity and the combination of these peptides with high C3G concentration significantly enhanced glucose uptake in the presence or absence of insulin. However, only high peptide concentration increased glucose uptake in the absence of insulin in the diabetic group. In the obese group, high concentration of peptide alone and its combination with low C3G down-regulated the mRNA expression of angiotensin II receptor, type 1 (AGTR-1) and FOXO1, and up-regulated the mRNA expression of insulin receptor substrate 1 (IRS-1), GLUT1 and GLUT4. Furthermore, the expression of AGTR-1 and FOXO1 were decreased with high peptide and its combinations of C3G in the diabetic group. Only high peptide concentration increased IRS-1 mRNA expression in the diabetic group.

Conclusions: C3G and peptides with ACE inhibitory activity improve glucose uptake potentially via the regulation of AGTR-1 and insulin-dependent signalling pathway (with insulin-like properties) in human primary myotubes. This provides a potential novel approach for the regulation of glucose metabolism in obese and diabetic individuals.

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Peripheral NPY antagonism reduces HFD-induced adiposity and improves glucose tolerance in ageing mice

Yan-Chuan Shi[1,*], Kim Loh[2], Kailun Lee[1], Herbert Herzog[1]

[1] *Garvan Institute of Medical Research, Darlinghurst, NSW, Australia*
[2] *St Vicent's Institute of Medical Research, Melbourne, VIC, Australia*

The prevalence of obesity is the leading cause of metabolic syndrome in ageing people. The NPY system plays a critical role in controlling energy balance, centrally and peripherally, but its role in the development of obesity in ageing populations is not clear. To investigate this we treated 20 week-old wild type mice with high fat diet with/without the non-brain-penetrable highly selective Y1 receptor (Y1R) antagonist BIBO3304 (0.5uM) daily for 3 weeks and compared this also to a cohort of younger mice.