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Nutrigenetic effects in metabolic syndrome – A cornerstone for individualized therapy

Nutritional therapy is the basis of antidiabetic treatment. It allows early remission, preserves residual metabolic functions beyond glycemic control, counteracts polypharmacy and saves monetary resources.

The effectiveness of nutritional therapy is currently limited – due to moderate compliance with respect to many dietary approaches and lack of continuous consulting support under real-world conditions, but also due to sparse knowledge about high-risk phenotypes and possibilities of response prediction. One of the most prominent levers to improve the effectiveness of nutritional therapy are nutrigenetics. Several recent publications have demonstrated, that a specific dietary intervention may elicit extraordinary effects in certain genetic subgroups of patients. These findings cover the entire range of disorders within the Metabolic Syndrome: overweight and obesity (TCF7L2,[1–3] FTO,[4] DRD2[5,6]), glucose intolerance, insulin resistance and hyperinsulinemia (ACE,[7] FABP2,[8] TCF7L2[9]), hypertension (ACE[10]), hyperuricemia (SLC2A9[11]), hypertriglyceridemia (AT1R,[12] APOE,[13] FABP2[14]), dyslipidemia (FABP2,[15,16] FABP4[17]), elevated free fatty acids (FABP2[18]) and hypercholesterolemia (PPARGC1A,[19] ADRB2,[20] APOE[21]). There is even evidence for nutrigenetic effects on possible long-term outcomes such as impaired cognition (VEGF, GLUT1[22]) and all-cause mortality (OGG1[23]). However, only few studies are interventional, limiting their reproducibility in controlled settings, which ensure compliance to a very specific dietary pattern.

The following publication adds another piece to the huge puzzle of nutrigenetics, presenting a dietary RCT in a larger, well-selected cohort, capable to answer a nutrigenetic hypothesis. The paper indicates that carriers of the rs670 ApoA1 A+ polymorphism – covering about 30% of the subjects – primarly show higher HDL levels. Additionally, they not only preserved, but increased their HDL levels by almost 10%, when undergoing a low-fat diet. The effect is specific to HDL and is not accommodated by possibly detrimental effects on other cardiometabolic parameters.

By comparison of low-fat and low-carb diet, the authors are able to demonstrate the relevance of this finding in the wider context of prediabetic dyslipidemia. In the hypocaloric setting, low-carb diets often result in stronger improvements of triglyceride levels, similar benefit with respect to LDL and better preservation of HDL. This well-known pattern is replicated in the present trial, weakening the global relevance of HDL increase under low-fat conditions as the concomitant LDL improvement was limited. However, given the plethora of metabolic and behavioral patterns in subjects with prediabetes or overt T2DM, the present finding is a necessary step to individualize dietary recommendations. Subjects with the ApoA1 A+ genotype and with personal preference for a low-fat diet or contraindications for a low-carb approach (gout, renal impairment, chronic inflammatory disease) could benefit from increasing HDL without parallel impairment of other parameters.

A single SNP won't make a huge difference, but further investigations in the field of nutrigenetics need to be stimulated in order to provide wide-range knowledge on the interaction of genes and specific dietary interventions beyond mere weight loss. As this paper is the first nutrigenetic publication on rs670 in ApoA1 and one of the first on HDL, replication studies are needed. However, there are plenty of dietary RCTs in the literature, which may easily facilitate confirmatory results.

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Editorial to: Role of rs670 variant of APOA1 gene on metabolic response after a high fat vs. a low fat hypocaloric diets in obese human subjects

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