PhD Project Proposal
(Epidemiology / Health Data Science)

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Title	Association of diet quality, food intake, nutrition and subcutaneous adipose tissue gene expression in humans
Background / description	Obesity is an established risk factor for many chronic diseases, including cardiovascular diseases, diabetes, and certain types of cancer.[1] We know today that not only the amount of body fat, but also its distribution play as crucial role for disease risk. Thus, numerous studies have shown that abdominal adiposity is more strongly related to health risks than peripheral adiposity.[1] In line with this observation is evidence that visceral adipose tissue (VAT, which is the major compartment that determines abdominal adiposity) is metabolically more active than subcutaneous adipose tissue (SAT, which is the major determinant of peripheral adiposity). SAT might even have protective effects.[2] Maintaining a healthy diet protects against metabolic diseases, and there is also increasing evidence from population-based studies that dietary factors, nutrition, and diet quality is are not only related to obesity but also to body fat distribution.[3,4] Yet, our understanding of the pathways that may link diet and nutrition with obesity and body fat distribution beyond the role of energy intake is unclear. We recently identified novel genes whose gene expression in subcutaneous adipose tissue has an effect on body fat mass (BFM) and body fat distribution (BFD).[5] The analysis identified 625 genes associated with adiposity, of which 531 encode a known protein and 487 were novel candidate genes for obesity. Enrichment analyses indicated that BFM-associated genes were characterized by their higher than expected involvement in cellular, regulatory and immune system processes, and BFD-associated genes by their involvement in cellular, metabolic, and regulatory processes. Mendelian Randomization analyses suggested that the gene expression of 69 genes was causally related to BFM and BFD. Six genes were replicated in UK Biobank. Thus, we identified novel genes for BFM and BFD that are BFM- and BFD-specific, involved in different molecular processes, and whose up-/downregulated gene expression may causally contribute to obesity. Yet, it is unclear to what extent dietary factors, nutrition, or diet quality may have an effect on expression of these or other genes in adipose tissue. Identification of such effects may point to potential mechanisms to strengthen the causal evidence. The aim of this project is, therefore, to examine the association of habitual diet, nutrition, and diet quality with gene expression in subcutaneous adipose tissue in a population-based setting. The project will be based on a study for which we have gene expression data from subcutaneous adipose tissue available and

	information on diet and other factors. For a subset, information on visceral and subcutaneous adipose tissue volume, determined by magnetic resonance imaging (MRI) is also available.
	<u>References</u>
	1. Nimptsch K, Konigorski S, Pischon T. Diagnosis of obesity and use of obesity biomarkers in science and clinical medicine. Metabolism 2019;92:61-70. (Review) (In eng). DOI: 10.1016/j.metabol.2018.12.006. 2. Porter SA, Massaro JM, Hoffmann U, Vasan RS, O'Donnel CJ, Fox CS. Abdominal subcutaneous adipose tissue: a protective fat depot? Diabetes Care 2009;32(6):1068-75. DOI: 10.2337/dc08-2280. 3. World Cancer Research Fund/American Institute for Cancer Research. Continuous Update Project Expert Report 2018. Diet, nutrition and physical activity: Energy balance and body fatness. (dietandcancerreport.org). 4. Fischer K, Pick JA, Moewes D, Nothlings U. Qualitative aspects of diet affecting visceral and subcutaneous abdominal adipose tissue: a systematic review of observational and controlled intervention studies. Nutr Rev 2015;73(4):191-215. DOI: 10.1093/nutrit/nuu006. 5. Konigorski S, Janke J, Patone G, et al. Identification of novel genes whose expression in adipose tissue affects body fat mass and distribution: an RNA-Seq and Mendelian Randomization study. Eur J Hum Genet 2022. DOI: 10.1038/s41431-022-01161-3.
Tasks	Development of study objectives, hypotheses, and analysis plans, data analysis and interpretation, publication of results
Prerequisits	Strong interest in epidemiology and in biomedical research questions, preferably a master degree in epidemiology and in a biomedical field (nutrition, medicine, biology, biochemistry). Strong knowledge in biostatistics and statistical analysis programs (SAS).
Number of available positions	1