Application number/Title: 29256 - Study of gene-environment interaction and Mendelian randomization of obesity and cardiometabolic risk

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Keywords provided by the Applicant PI to describe the research project:

G×E, MR, obesity, cardiometabolic risk

Application Lay Summary:

1a: Obesity and cardiometabolic risk are the major threats to the public health worldwide, determined by genetic susceptibility, environmental risk factors, and their interactions; however, it is still a lack of evidence of G×E interaction and unconfounded estimates of a modifiable exposure. This project is expected to (1) examine whether diet, lifestyles, and early life exposures may interact with the genetic variations in relation to obesity and cardiometabolic risk, and to (2)test the causal effect of a modifiable exposure on the outcomes (e.g. hypertension, insulin resistance, dyslipidemia, type 2 diabetes) using Mendelian randomization analysis.

1b: Sufficient sample size in UK Biobank and its extensive information on diet, lifestyle, early life factors, and genetics enable us to explore G×E interaction and causality of different risk factors in the pathogenic mechanisms underlying obesity and cardiometabolic disorders. The findings will eventually contribute to the improvement of the prevention, diagnosis, and treatment of common complex diseases.

1c: In the G×E interaction analysis, we will create different types of genetic predisposition scores for each participant, and examine whether early life, diet, and lifestyle risk factors may interact with the genetic scores in relation to obesity and major cardiometabolic disorders. As for Mendelian randomization (MR) analyses, genetic proxy markers for well-understood effects on modifiable exposures will be used to evaluate the causal effects on the outcome.

1d: We plan to use the full cohort.