



**Application number/Title:** 23940 - Genome-wide searches for gene x life-style interaction for obesity phenotypes

**Applicant PI:** Prof. Iris Heid

**Applicant institution:** University of Regensburg, Genetic Epidemiology, Franz-Josef-Strauss Allee 11, Regensburg 93053, Germany

**Funding body:**

Internally funded by University of Regensburg

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

Genomewide association, Gene-Environment Interaction, Obesity

**Application Lay Summary:**

1a: A substantial contribution of genetic factors with >150 genetic loci for obesity phenotypes is identified. Modulating effects of age, sex, physical activity, or smoking (called gene-environment interaction, GxE) are documented. However, previous genome-wide searches to identify GxE for obesity phenotypes in consortium meta-analyses were conducted mostly based on stratifying by dichotomized exposure variables. There is little empirical work on how this can be improved by using more refined statistical approaches; the full spectrum of GxE effects on obesity phenotypes is not yet known. We aim to identify the best statistical approaches and to detect GxE for obesity phenotypes.

1b: Obesity is a severe and common risk factor for many chronic diseases like type 2 diabetes and cardiovascular disease. Classical intervention like restricted caloric intake or increased physical activity has been shown to be largely ineffective in the long run. By advancing the knowledge about GxE for obesity phenotypes and about the best statistical models to detect them, our research will contribute to an improved understanding of how genetic factors exert their effects on obesity and thus improve the understanding of mechanisms affecting this severe public health burden.

1c: We plan to apply various approaches (e.g. modeling exposure quantitatively or modeling interaction directly instead of stratified analyses) to

detect GxE for obesity phenotypes (Body-Mass-Index, Waist--Hip-Ratio) in the UK Biobank data as a single large data set without the restrictions implied by meta-analyses. We will compare approaches for various types of GxE interaction effects (i.e. whether life style factor enhances, attenuates or switches on/off the genetic effect).

1d: We require the full cohort with genome-wide imputed data to ensure the statistical power, but we will appreciate an update to the full 500,000 subjects with genome-wide imputed data as soon as available.