2022FHML_Langie_Repairing obesity
DNA repair deficiency as key player in the development of obesity and the subsequent cancer risk

Priority: 基础研究 / Basic Research and 人类健康与疾病的生物学基础 / Biological Foundations of Human Health and Diseases
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Key words: base excision repair (BER), cancer, genotype, mitochondria, obesogenic environment

The number of obese people is increasing and this cannot be explained solely by excessive consumption and/ or reduced physical activity. Research indicates that weight gain is influenced by interactions between our genes and our environment. In addition, various studies showed positive associations between BMI and cancer risks. Indeed, obesity and cancer share common characteristics; including enhanced production of reactive oxygen species, inflammation, DNA damage accumulation and impaired mitochondrial (mt) function. DNA repair may thus be a mechanistically overlooked link to explain the relation between obesity and cancer. Interestingly, mice lacking DNA repair-related genes show obesity and features of metabolic syndrome. In humans; carriers of low-activity variant (LV) alleles in DNA repair-related genes showed a higher risk of weight gain and related metabolic disorders.
Therefore, we **hypothesize** that these LVs in DNA repair genes can load the gun, but exposure to obesogenic environmental stressors (increased caloric intake, low physical activity) will pull the trigger of a vicious circle, leading to obesity and subsequently carcinogenesis.
The **objectives** are to study if individuals carrying LVs in DNA repair genes are more prone to gain weight, accumulate fat and develop obesity, and have an increased subsequent cancer risk. We will use sequencing data available from UK-Biobank participants to compare LVs in controls, overweight, obese and morbid obese. In addition, multivariate analyses will assess associations of genetic variants, defined as "at risk" BER genotype, with exposure (obesogenic environment) and effect data (obese phenotype). These data will subsequently be confirmed in a separate population. This research will give crucial new insights in the role of DNA repair in the development of obesity and cancer risk.

Techniques include: exome sequencing, bioinformatics, biostatistics, sample processing, DNA isolation, etc.

Related publications of the group:

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