



Application number/Title: 32974 - Rare, functionally validated, nonsense and missense mutations and human anthropometric and metabolic traits

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Keywords provided by the Applicant PI to describe the research project:
diabetes, dyslipidaemia, insulin-resistance, obesity

Application Lay Summary:

We know that some people carry rare mutations that disrupt the normal function of critical metabolic pathways, leading to conditions such as obesity and/or diabetes. Genome sequencing studies are increasingly identifying such rare mutations. Using knowledge about the precise structure and function of the proteins encoded by these genes and using experimental data generated in our lab we can predict which rare variants are likely to be disruptive. We plan to use the data from UK Biobank to examine the effects of carrying such mutations on measures such as body weight, body fat distribution, and metabolic measures such as glucose levels. We will enhance the understanding of genotype-phenotype relationships in important diseases such as obesity and Type 2 diabetes. We will identify through our own genetic and functional studies and through the literature, rare variants in genes thought to be important for control of energy balance and metabolism. We will sub-select rare variants on the basis of our knowledge of their functional adverse consequences and then interrogate the database as to whether such variants, singly and in aggregate, have any association with a relevant measure/phenotypes in Biobank. Full