Apolipoprotein E gene in the Metabolic Syndrome

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Country

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Apolipoprotein E gene in the Metabolic Syndrome

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Research Abstract

Metabolic Syndrome (MetS) is closely linked to disturbances in lipid and glucose metabolism and increases the risk of developing cardiovascular disease and diabetes. One-fourth of the adult European population has the MetS and a further increase is anticipated because a greater prevalence of obesity in the future. Apolipoprotein E (APOE) associates with lipoproteins and mediates theirmetabolism. In humans, the APOE gene is polymorphic and has three alleles, APOE*2, APOE*3 and APOE*4. Carrying the APOE*4 allele has been associated with an increased cardiovascular risk, predisposition to develop Alzheimer's disease and insulin resistance. Recently, APOE*4 has also been linked with MetS. However, the mechanisms whereby this association occurs are not clear. The objective of this
project is to investigate the role of APOE in metabolic syndrome. We hypothesize that APOE*4 presence determines a less flexible metabolism; i.e. an inability to effectively switch between lipids and carbohydrates for fuel and the subsequent carbohydrate intolerance.
For our Work Package 1 we will employ mice whose endogenous Apoe gene has been replaced by the human APOE*3 or APOE*4 allele. We will investigate the energy substrate handling of

these “humanized” mice at the whole body level by using metabolite tracers and diverse “-omics”, which will reveal why the energy generating pathways differ with apoE-isoform presence. At the population level, Work Package 2 will identify human APOE*4 carriers and investigate new APOE genetic variants to determine whether the association between APOE-isoform and metabolic syndrome is diet-dependent in the participants of the Aragon Workers Health Study, an ongoing longitudinal study targeted to study the appearance and progression of cardiovascular risk factors.
By translating basic science into human studies, this project will provide new targets to prevent or treat the onset of MetS and its associated morbimortality in European populations

Further information available at:

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