Generation of CRISPR edited cell lines for studying human genetic variations regulating coronary artery disease and thrombosis.

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Abstract

Cardiovascular diseases (CVD) are the major cause of death worldwide, in which genetic risk factors may have a profound influence in the onset and the final outcome. Hence, understanding the contribution of genetic variants in the development of CVD is a key step in order to find new molecular targets to fight against disease. Today, genome based new technologies may help us to find new genetic variants, including single nucleotide polimorfisms (SNPs) associated with specific pathologies, thus, we can study in depth, how changes in specific loci could modify the expression and/or function of genes so far unexplored, bringing the opportunity to develop more precise preclinical models of disease in order to fill the gaps between basic research and clinical practice faster. In this project we studied two different genes that had been found as candidates in two different GWAS (Genome Wide Association Study), an approach used to associate specific genetic variants with particular diseases. The first GWAS was done by the Charge consortium evaluating changes in the levels of Von Willebrand Factor (VWF) in a population of 46354 individuals, detecting eleven loci associated with changes in the expression of VWF, focusing on Ras-related protein Rab-5C (RAB5C), for its relevance in thrombosis. The second GWAS, associated to coronary artery disease, identified RE1-silencing transcription factor (REST) as a potential target for the disease. Here, we present our first methodological approach to obtain cells lines deficient for these specific genes.

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