

The complex genetics of Familial Hypercholesterolaemia (FH): from monogenic to polygenic disease

Dr. Marta Futema, research associate

Centre for Cardiology in the Young, University College London, United Kingdom

Familial Hypercholesterolaemia (FH) is the most commonly inherited disease of high LDL-cholesterol (LDL-C) that leads to premature coronary heart disease (CHD). In its classical monogenic form FH is caused by mutations in LDLR, APOB or PCSK9 genes. Mutations in these genes are found in ~75-80% of definite FH cases. Further ~13% have polygenic disease due high burden of common LDL-C-rising alleles. The cause of FH in the remaining ~12% remains unknown.

Genetic testing for FH can provide crucial information for cost-effective family screening and enables early intervention. Polygenic risk score can differentiate between the monogenic and polygenic hypercholesterolaemia. Genetic diagnosis leads to a different care pathway for monogenic and polygenic FH patients, a paradigm example of the use of an individual's genotype in Precision Medicine.