PerMed

AIM: To use all results obtained in the different projects to find the best treatment for each patient

EPHF / DFs / DMs

Recruitment → **Molecular Study**

Portuguese individuals with clinical criteria of **Familial Hypercholesterolemia (FH)**, **Rare Monogenic Familial Dyslipidemias (DFs)**, or **Monogenic Diabetes (DMs)**

Next Generation Sequencing (NGS)

Customised target gene panels with **Illumina NextSeq**

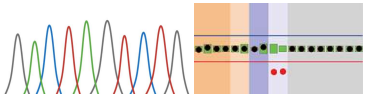
AIM: To identify the genetic cause of disease

FH
8 genes (*LDLR, APOB, PCSK9, LDLRAP1, ABCG5, ABCG8, APOE, LIPA*)

DFs
5 genes, low LDL (*APOB, PCSK9, MTTP, SAR1B, ANGPTL3*)
5 genes, low HDL (*ABCA1, APOA1, LCAT, CETP, SCARB1*)
9 genes, high TG (*LPL, APOC2, APOA5, GPIHBP1, LMF1, GPD1, APOC3, APOE, LIPA, LMNA*)

DMs
14 genes (*HNF4A, GCK, HNF1A, PDX1, HNF1B, NEUROD1, KLF11, CEL, PAX4, INS, BLK, ABCC8, KCNJ11, APPL1*)

Sanger / MLPA (variant confirmation)



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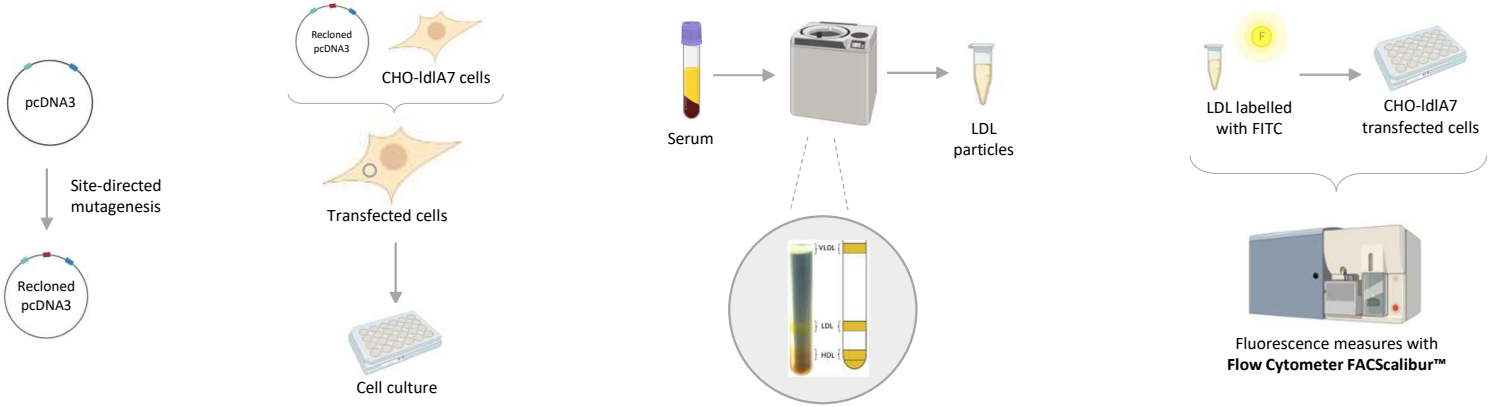
Variant Classification (ACMG guidelines)

- **Benign/ Likely benign** (Negative Report) → Research
- **Pathogenic/ Likely pathogenic** (Positive Report) → **Cascade Screening**
- **Variant of Uncertain Significance** (VUS) (Negative Result)

FunGen

Mutagenesis → **Transfection** → **LDL isolation by ultracentrifugation** → **Flow cytometry assays**



Functional Studies

AIM: To characterize the effect the variants have on protein function