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Utilising Multi-omics to Identify Novel Regulators of Cardiovascular Disease

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Despite there being a number of well established risk factors for coronary artery disease (CAD), such as hypercholesterolaemia and hypertension, one in four individuals that have a heart attack do not experience any of these traditional risk factors. Thus, other unknown genetic factors are proposed to contribute to this risk. Exploration of the genes involved in the development and progression of CAD provides an opportunity to uncover novel biology as well as potential therapeutic targets. Genome-wide association studies have paved the way in the identification of novel loci associated with CAD, however, a complementary approach is to use mouse genetic reference panels (GRPs), in which cardiometabolic diseases can be induced in genetically diverse strains of mice that undergo complex phenotyping. Using this approach, environmental variability can be minimised and pertinent tissues can be collected for cellular and molecular analyses. Here, we provide examples of the advantages of integrating mouse and human datasets to overcome some of the challenges seen with either dataset alone by (i) allowing the prioritisation of targets with clinical relevance; (ii) providing mechanistic insights into a target of interest and (iii) identifying conserved genes and pathways to improve confidence, together ensuring that those targets with the greatest translational potential are further explored. Furthermore, we discuss the application and integration of a range of datasets including GWAS, polygenic risk scores, proteomics and lipidomics, to identify novel metabolic changes and targets associated with CAD.