RESEARCH HIGHLIGHTS

Identification of novel breast cancer susceptibility genes by exome sequencing

To comprehensively assess the role of rare coding variants, we conducted a meta-analysis using 3 extensive whole-exome sequencing datasets, comprising 26,368 female cases and 227,673 female controls. Significant associations between protein-truncating variants and breast cancer were discovered for 6 genes at an exome-wide significance level (P < 2.5 × 10−6). ATM, BRCA1, BRCA2, CHEK2, PALB2, and MAP3K1. Additionally, associations were found for LQTR1, AT8, and BARB1 with P < 1 × 10−4 (Wilcox et al. 2022).

Genetic characterisation and clinical impact of 21 actionable pharmacogenes in the Spanish population

We analysed genetic data from 3,006 Spanish individuals to determine the allele frequencies for 21 actionable pharmacogenes. Our findings show that 98% of the Spanish population carries at least 1 allele linked to a therapeutic change. We translated this genetic data into clinical recommendations, suggesting an average need for therapeutic changes in 3.31 out of 64 associated drugs (https://cvc.clínicasinforsspa.es/) (Nuñez-Torres et al. 2023).

Novel genetic variants associated to susceptibility to SARS-CoV-2 infection and disease severity

We participated in the second updated genome-wide association study (GWAS) on COVID-19 severity and infection susceptibility to SARS-CoV-2 from the COVID-19 Host Genetic Initiative. A meta-analysis of up to 219,692 cases and over 3 million controls identified 51 distinct genome-wide significant loci – adding 28 loci from the previous data release (Pairo-Castineira et al. and Castro-Santos P et al. 2023).

Identification of anthracycline-induced cardiotoxicity (AIC) genetic risk markers by intermediate molecular phenotypes (IMPs)

AIC affects cancer patients, but we cannot predict who may suffer from this complication. We propose that levels of IMPs in the myocardium associated with histopathological damage could explain AIC susceptibility, so variants of genes encoding these IMPs could identify patients susceptible to this complication. We found genetic variants linked to these markers, and 2 genetic risk scores for paclitaxel and breast cancer patients were constructed (Gómez-Vecino A et al. 2023).