In the Unit we implement high-throughput methods for detection of genetic variation (single nucleotide variants, indels, structural variants) and methylation analysis using DNA microarray and next-generation DNA sequencing technologies. Complementarily, research focused on identifying predictive biomarkers for precision medicine is undertaken.

“Our aim is to identify predictive biomarkers in cancer patients in order to implement precision medicine in clinical practice.”

**OVERRVIEW**

Novel predictive genetic markers for adverse drug reactions in breast cancer (BC) patients. Persistent chemotherapy-induced alopecia (pCIA) and capecitabine-induced hand-foot syndrome (CiHFS) are 2 common adverse drug reactions in cancer treatment. pCIA occurs in its most severe form in up to 10% of BC patients treated with docetaxel-based therapies, having a profound psychological impact on them. CiHFS is a dermatological toxicity affecting around 30% of patients, and the main cause of dose reductions and chemotherapy delays. By GWAS, we identified a regulatory variant associated with pCIA appearance in patients; this finding was validated in the replication cohort (ORCombined 4.05; 95% IQR. 2.46-6.67; P=3.946 x 10-4). This variant affects ABCB1 mRNA expression, being the risk allele associated with decreased expression. The ABCB1 gene encodes P-glycoprotein, an efflux pump responsible for the elimination of docetaxel, and lower expression could cause decreased drug elimination and thus its intracellular accumulation. Carriers of the risk allele would experience high drug exposure in the hair follicle and alopecia may become permanent, owing to the destruction of hair follicle stem cells. In addition, we discovered and replicated a cluster of 4 variants associated with decreased levels of CDH4 mRNA and the protein it encodes, R-cadherin, which localises in the granular layer of the epidermis. This resulted in reduced expression of involucrin, a protein of the cornified envelope, an essential structure for skin barrier function.

**PUBLICATIONS**