FANCONI ANEMIA: NEW GENES, NEW PARTNERS AND NEW SYNDROMES

Jordi Surrallés

Genetics Service, Hospital de Sant Pau, Department of Genetics and Microbiology, Universitat Autònoma de Barcelona, and CIBER on Rare Diseases, Barcelona, Spain.
Jordi.Surralles@uab.cat

The biomedical relevance of genome maintenance is illustrated by the severe clinical consequences of mutations in DNA repair genes. A clear example are genes involved in the repair of DNA interstrand-cross links and double strand breaks by homologous recombination (HR), such as BRCA1, BRCA2, PALB2, BRIP1, or RAD51C. Mutations in these genes cause familial breast cancer and Fanconi anaemia (FA) in monoallelic or biallelic carriers, respectively. Furthermore, the proteins encoded by many of these genes are crucial for the modulation of the response of cancer cells to chemotherapeutics, including cisplatin and PARP inhibitors. Therefore, the identification of additional components of this DNA repair pathway is of extreme biomedical importance. By using whole exome sequencing and interactomics we have recently identified and functionally studied novel components of this pathway and uncovered their association to Fanconi anemia and breast and colon cancer susceptibility. Functional studies of variants identified in these novel genes are of critical importance to understand their role in cancer predisposition or FA-related bone marrow failure and to correlate the genetic variant with the clinical outcome. Newly acquired knowledge about FA/BRCA pathway promises to provide a cure in the near future.