Our work focuses on deciphering the genetic bases of hereditary and sporadic breast and ovarian cancer and other rare tumours. During 2020, we contributed to the definition of the main bona-fide breast cancer (BC) susceptibility genes through our substantial participation in an ambitious international collaboration (BRIDGES, a European project).

In addition, we obtained funding to develop two new projects focussed on breast and ovarian cancer genetics. We have also been exploring the currently unknown genetic basis of testicular cancer. More recently, we started a study to elucidate the common genetic origin of different autoimmune endocrinopathies, such as chronic gastritis atrophy, thyroiditis, diabetes, or arthritis, and we identified several genes that open a new scenario for diagnosis and treatment. Finally, we found interesting results suggesting a synthetic lethal interaction between BRCA1 and OGG1 and a synergistic effect between OGG1 and PARP1 inhibitors.

“In 2020, we contributed to determining the most relevant genes in BC susceptibility, we found several candidate genes explaining the possible common origin of autoimmune endocrinopathies, and we identified a synergistic effect between OGG1 inhibitors and PARP1 inhibitors.”

RESEARCH HIGHLIGHTS

Hereditary breast and ovarian cancer

Deciphering the role of rare variants in BC

The first publication reporting results obtained by the European project BRIDGES, to which we made a major contribution, was released this year. Thirty-four confirmed or putative BC susceptibility genes were sequenced in 60,466 cases and 53,461 controls. Nine genes were confirmed as bona-fide BC susceptibility genes, and the risk conferred by their mutations to develop the disease was refined. These results, published in the New England Journal of Medicine (Dorling et al., 2020), are highly relevant to improving the genetic diagnosis, counselling and follow-up of BC patients and their families. In addition, we participated in the largest collaborative international study evaluating the risk conferred by mutations in the RAD52 and RAD51D genes to develop breast and ovarian cancer (Yang et al., 2020).

Identification of 14 new candidate BC susceptibility genes

As a complementary approach to the large collaborative projects, we are conducting a study using next-generation sequencing (NGS) technologies in a few, very well selected families, to identify new BC susceptibility genes. This approach led to the identification of RECQL5, a member of the RECQL-helicases family, as a new BC susceptibility candidate (Taveras-Tapia et al., 2019). Besides RECQL5, we identified 13 additional candidate genes that are extremely interesting because of their function, the potential deleteriousness of the variants, and their rarity in the general population. We developed an NGS panel containing this set of genes and will evaluate their role in BC by sequencing a large set of 3000 Spanish BC families.

Modifier genes in BRCA1/2 genes

We continue to play an active role in the CIMBA consortium (Consortium of Investigators of Modifiers of BRCA1 and
**Publications**


- Virchows Arch 476, 195-207.

**Human Cancer Genetics Program**

**Human Cancer Genetics Group**

**Figure**

![Image](image.png)