“FA” Gene Mutations in Familial Breast Cancer

The cancer susceptibility genes *BRCA1* and *BRCA2*, now also called *FANCS/BRCA1* and *FANCD1/BRCA2*, may be mutated in 10-20% of cases in which there is a strong family history of breast and/or ovarian cancer. These genes were originally identified as the most common genetic causes of the hereditary breast/ovarian cancer syndrome. In that disorder, only one of the two copies of the gene needs to be mutated to cause disease, because these genes can function in an autosomal dominant fashion, as is also the case for the *FANCJ/BRIP1* and *FANCN/PALB/2*. These genes are all part of a single DNA repair pathway known as FA/BRCA.

Thus, a woman with breast cancer may have one mutated gene copy in any of these 4 genes, for example, in *FANCN/PALB/2*, but her other copy of the *FANCN/PALB/2* gene is normal. This situation may occur in about 1-2% of cases with breast cancer and a positive family history. Families like this are at increased risk of breast and ovarian cancer, but they do not routinely develop FA.

This scenario is different from that of a child who is diagnosed with the inherited bone marrow failure syndrome Fanconi anemia, who has mutations in **both copies** of the same FA gene, and thus has no normal gene of that type.

Women with breast cancer who have a single mutation in one of the four genes listed above should seek advice from a geneticist, oncologist, or genetic counselor with expertise in familial/hereditary cancers, in order to understand how they and the members of their family should be evaluated and managed.