Breast cancer is the most common cancer in adult human females and one in every ten women will develop breast cancer in her lifetime. There are different factors that can increase a person's risk for developing cancer (i.e. environmental factors, hormones, obesity), but the main factor is family history [1]. Between 5-10% of breast cancer cases are due to a hereditary component.

In 1990, researchers discovered the first gene associated with breast cancer. This gene is known as BRCA1, and it is located on chromosome 17 [2]. In 1994, further studies linked another gene, designated BRCA2, to familial breast cancer. This research demonstrated that genes other than BRCA1 could be linked to breast cancer.

When functioning properly, both BRCA1 and BRCA2 are tumor suppressor genes. These genes regulate cell growth and cell death. Mutations of this gene can lead to both abnormal cell growth and uncontrolled cell death. Every person has two BRCA1 genes (one on each chromosome 17) and two BRCA2 genes (one on each chromosome 13). When there is a mutational change in one copy of either the BRCA1 or BRCA2 gene, a person's risk for developing various types of cancer rises dramatically, although both copies of the gene must be mutated before a person develops cancer [2]. Mutations in the BRCA1 or BRCA2 genes increase the risk for developing breast and ovarian cancer 10-20 fold [1]. Alterations or mutations in the BRCA1 or BRCA2 gene are only some factors in cancer development; several mutations in different growth regulator genes can also cause cancer formation.

Mutations that become prevalent in a specific ethnic group are usually attributed to the founder effect [3]. The founder effect is caused by a limited group of ancestry being isolated from an original population. If this separation continues, disease producing alleles present in the founders will become more frequent in the following generations. The 185delAG mutation within the BRCA1 gene was identified in about 1% of the Ashkenazi population, causing the Ashkenazi Jewish population to be considered a high risk group for breast and ovarian cancer [4]. This mutation, found in a high percentage in Ashkenazi Jews, has been coined the ‘Ashkenazi mutation’ [5]. A study conducted in Israel found that all tested Ashkenazi mutation carriers displayed the same allelic (alternative form of a gene) pattern, suggesting a common ancestor and the involvement of a founder effect [5].

Even though this mutation is associated with Ashkenazi Jews, it is not as specific to Ashkenazi Jews as was once thought. There has been evidence that this mutation is also present in Sephardi Jews. Researchers in Israel conducted a study regarding the 185delAG BRCA1 mutation that expanded the study group to other Jewish non-Ashkenazi groups: Moroccan, Yemenite, and Iranian [5]. The researchers found the 185delAG mutation in the non-Ashkenazi groups that they examined. Therefore, the researchers concluded that this mutation was not unique to Ashkenazim, but is present in other Jewish groups, both in individuals with breast and/or ovarian cancers as well as in the general population. They also found that 37.5% of the individuals studied shared the common Ashkenazi genetic markers while 25% of them had a pattern that was only slightly different with these same markers. These findings support the belief of a common ancient founder for this mutation in the Jewish population of different ethnic origins. Traditional historic accounts relate that the Jewish population was exiled several times throughout history, with the last exile occurring in 70 A.D. After the destruction of the Second Temple, the Jewish people were dispersed, leading to the Jews settling in Eastern Europe (Ashkenazi Jews), Iraq (Mizrachi Jews), and North Africa (Sephardic Jews). These Jewish populations remained geographically and culturally separate from each other [5]. The discovery of the 185delAG mutation in Ashkenazi, Mizrachi, and Sephardic Jews is evidence for a common ancestor, and also leads scientists to suspect that this mutation had arisen before the destruction of the Second Temple and the separation of Jewish communities.

Another study found a repeated occurrence of this mutation in Iraqi cancer-prone families. This further illustrated that this mutation was not unique to Ashkenazi Jews. Through genetic analyses of several genetic markers, the researchers identified common origins for Ashkenazi, Iraqi, Iranian, and Libyan Jews. They also concluded that this mutation may be part of the “ancient Jewish genetic pool” dating back to the Second Temple era [4].

This mutation was also identified in groups of questionable Jewish ancestry. A study of self-identified Latinos with breast and ovarian cancer from San Luis Valley, Colorado led researchers to find a repeated occurrence of the 185delAG mutation. Out of the seventeen Spanish families with the 185delAG mutation, three of them were Spanish-Gypsy, one was of Jewish ancestry, and one was of Sephardic Jewish heritage. Haplotype analysis on thirteen of these families showed that all but one had the common Ashkenazi Jewish haplotype. The study concluded that the 185delAG mutation was common in families with breast and ovarian cancer who originate from the San Luis Valley [6]. After this study was published, Harry J. Long, a medical oncologist at the Mayo Clinic, said that there is “a high probability that these people are descendants from Marranos or Spanish Jews who pretended to convert to Christianity during the inquisition” [7].

In 1492, King Ferdinand and Queen Isabella of Spain forced all Jews in the country to convert or leave, causing the emigration of over 100,000 Jews [7]. Some Jews fleeing Spain travelled to present-day California and New Mexico, which would indicate that the Latino group with the 185delAG mutation could possibly be descended from Spanish (i.e. Sephardic) Jews from that era. This would further strengthen the belief that 185delAG mutation exists among Sephardic, in addition to Ashkenazi, Jews.
Another study was performed in Ecuador and again in Colorado where a dominant presence of 185delAG mutation was found. While performing Y chromosome mapping and other genetic analyses, genetic signatures of Sephardic ancestry were identified in these communities. This suggested that the mutation in these two communities may have a Jewish origin. This finding showed that the Hispanic population and Latin American population may have a “certain degree of cryptic Jewish ancestry” [8].

Breast cancer is the most commonly diagnosed cancer in Hispanic women, so it is unsurprising that the 185delAG mutation has also been identified in the Hispanic population [9, 10]. “With the exception of Ashkenazi Jewish subjects, Hispanics had the highest rate of BRCA1 mutation (10.8%) among women younger than 65 with breast cancer and with a family history of cancer” [10]. Researchers also found this mutation in a non-Jewish Chilean family. They identified in this family a haplotype that was identical to that of the Ashkenazi Jewish population. This family was of Spanish descent and had been living in South America for at least four generations. The researchers noted that “it is possible that the crypto Jews of Sephardic origin carried this mutation to the new world” [11]. They speculated that the identification of the 185delAG mutation in this non-Jewish Chilean family suggests that other Chileans carry this mutation as well and are descendants of Jews.

The presence of the 185delAG mutation in Sephardic Jews as well as non-Jews points to the fact that this mutation is not solely an Ashkenazi mutation. This mutation likely arose during the Second Temple period, before the exile of the Jewish people. Since some Sephardic Jews carry this mutation, we can speculate that these genetic mutations were carried by Marranos who came to the Americas and transmitted this mutation to their offspring, resulting in the presence of these mutations in present-day Hispanic and Latin-American populations.

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References: