OBJECTIVES:

To provide a basic overview of genetics, focusing on breast and ovarian cancer susceptibility mutations on BRCA1 and BRCA2.

DATA SOURCES:

Research and review articles and government internet sites.

CONCLUSION:

The advances in molecular biology has enabled health care providers to be proactive rather than reactive in predicting some cancers and offering prevention strategies to greatly reduce the risk of developing cancer. Our expanding knowledge base of genetics may one day provide tailored treatment, and predict recurrence rates for all cancers.

IMPLICATIONS FOR NURSING PRACTICE:

The science of genetics will impact every aspect of health care, from primary care to specialized care. Nurses are on the front line and will be expected to recognize patterns of disease that may indicate a possible genetic link, educate the family about the implications of a potential genetic susceptibility and refer the family for counseling. To accomplish this, each nurse should have a minimum basic knowledge of genetics, and formal education for those who educate and counsel.

KEY WORDS:

Cancer genetics, Genetic susceptibility, DNA microarray, Human genome sequencing, Cancer risk

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CANCER GENETICS

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THE language and knowledge of molecular biology have moved beyond the laboratory into the public arena. Today, many people may not understand the complexity of the DNA process, but are certainly familiar with the term. The scientific advances of the last decade have enabled us to predict susceptibility to developing breast, ovarian, and other cancers, specify more effective treatment modalities, and identify recurrence probability in a specific population of breast cancer patients. This article will discuss pivotal events in the history of genetics; basic science of cancer genetics; identifying, counseling and testing individuals at risk for a BRCA1 or BRCA2 mutation; new modalities in treatment; and discuss future directions.

HISTORICAL BACKGROUND

The history of modern genetics began with Gregor Mendel (1822–1884), a brilliant Augustinian monk and high school science teacher with a passionate love of nature. His work with cross-breeding peas and mice described laws of heredity that still stand today. His scrupulous records discussed inherited dominance, transmission of hereditary factors, and the numerical ratios of traits. These concepts actively initiated the quest to identify the biology of genetic information.[1] Another important milestone in the 19th century was the identification of the composition of nucleic acids, sugar, phosphoric acid, and nitrogen bases. After determining that sugars in nucleic acids can be ribose or deoxyribose, or RNA and DNA, the race to find the structure of DNA commenced. The helix shape had been proposed and demonstrated by scientists, namely Linus Pauling, from the California Institute of Technology and Maurice Wilkins and Rosalind Franklin, King's College, London. However, reproducibility problems remained. In 1953, Francis Crick and James Watson demonstrated that DNA did form a double helix, and one strand was the inverse of the other. They also demonstrated that each strand of the DNA molecule was a template that allowed separation during cell division to duplicate itself without a changing structure.[2,3] Their experimental data confirmed the helical structure that has been lauded by many as the most important biological work of the last 100 years.

CANCER GENETICS

The Human Genome Project began in 1990 with several goals; 1) identify all the genes in human DNA (20,000 to 25,000 estimated); 2) determine the pattern of the 3 million base pairs; 3)

store and share information in databases; 4) develop better tools for data analysis; 5) allow access to the private sector; and 6) focus on the ethical, legal, and social issues that will arise from the project.[4] This project was designed to be an international collaborative initiative of scientists, sponsored by the Department of Energy and National Institutes of Health and administered by the National Center for Human Genetics, within the National Institutes of Health.

Basic Genetics

The DNA alphabet is made up of four chemicals (A-adenine, T-thymine, C-cytosine, and G-guanine) that are repeated billions of times within a genome. This alphabet creates a template that is repeated in the nucleus of all the cells in our body. The genome template is expressed in the 23 pairs of chromosomes that determine our genetic makeup. The order of A, T, C, and G within a gene eventually governs physical appearance, organ functionality, growth and development, mental and motor skills, and potential for developing disease.

Chromosomes are composed of very tight coils of DNA and histones, the main proteins of chromatin. Histones participate in gene regulation and provide the structure around which DNA coils. The chemicals A, T, C, and G pair up to form bases that make the rungs of the DNA helix; sugar and phosphate molecules provide the backbone structure to support the helix. The chemicals always pair together with A pairing with T and C pairing with G.[5] When a gene "switches on," it eventually makes a protein, but it does not do so directly. First, the gene directs synthesis of a molecule called messenger RNA (mRNA). To transfer a gene's information from DNA to mRNA, base pairing is used. However, there is one change: an adenine base (A) in the DNA matches with a new base called uracil (U) in the mRNA. Messenger RNA travels from the nucleus into the cytoplasm to cell organelles called ribosomes. There it directs the assembly of amino acids that fold into a unique protein. The order of the chemicals in forming proteins is similar to letters forming words. The chemicals band together in sets of three to create the code for amino acids and the particular order will determine one of 20 amino acids. The amino acids are considered the building blocks that are arranged in numerous combinations to form specific proteins (Fig 1; color versions of all figures in this article are viewable on the journal's website at www.nursingoncology.com).[6]

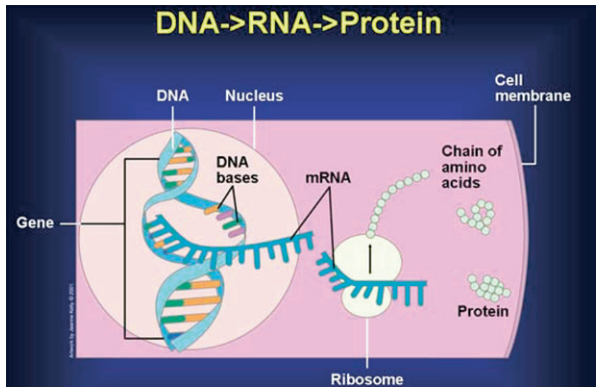

FIGURE 1. The process of creating a protein. (Image courtesy of the NCI.[6])

At normal conception, the mother and father donate one copy of their chromosomes to their offspring to produce 46 chromosomes that are arranged in 23 pairs. Pairs one through 22 are known as autosomes and the 23rd pair determines the sex characteristics of the individual. Women always donate an X chromosome as females have a pair of X chromosomes. Males carry an X and Y chromosome and can donate either X or Y chromosome (girl = XX; boy = XY). Figure 2 illustrates human chromosomes paired in numerical order.[7]

Patterns of Inheritance

Mutations that predispose an organism to disease can be acquired during a lifetime (known as somatic), or inherited at conception (referred to as germline) (Fig 3). Every individual has two copies of each gene that can determine a benign physical trait or potential for disease, depending on dissimilarity of each copy and the implication of the position of the dissimilarity on the gene. Mutations in genes that occur without consequence are known as polymorphisms. Polymorphisms are non-deleterious changes that are considered benign because although the chemical code varies from the normal code, the same amino acid is called in without altering the protein. Mutations that are considered deleterious change the structure of the gene by altering the protein. Missense mutations result from calling in a different amino acid that does not alter the length of the protein. Missense muta-