Cytogenetics: Oncology Nurses in Advanced Practice
Decipher del(13q14) and t(14:16)

Stephanie Jacobson, RN, BSN, FNP-C, OCN®, Julie Eggert, PhD, GNP-BC, AOCN®, Kelly Smith, MS, FNP, BC, and Thomas Rosenzweig, MD

Advances in genetics related to the diagnosis and treatment of cancer have transformed the oncology specialty into one with more promising outcomes. Because of the Human Genome Project, the association between genetics and cancer is more clearly defined and healthcare professionals need to be prepared to integrate new genetics knowledge into clinical practice. This article reviews basic genetic information essential for oncology nurses in advanced practice. Application of genetic guidelines uses the model of multiple myeloma. Multiple myeloma is an example of a disease in which cytogenetics has become increasingly important for diagnosis, prognosis, and treatment. As the basis of knowledge in genetics continues to expand, oncology providers are transitioning to a paradigm in which cytogenetic elements carry more weight in diagnosis and treatment.

All forms of cancer are related to inherited or acquired genetic mutation. Since the launch of the Human Genome Project in 1990, the science of genetics and awareness of the role it plays in malignant transformation, growth, and treatment has grown exponentially (Human Genome Project Information, 2011). As knowledge increases about genetics and how it influences malignancies, oncology nurses in advanced practice must understand the evolving needs of patients related to new diagnosis and treatment discoveries in cancer using genetics (Jenkins, 2011).

A working knowledge in genetics assists those nurses in the identification and management of hematologic malignancies. Multiple myeloma (MM) is a malignancy of the plasma cell, affecting its ability to produce immunoglobulins, which alter the body’s ability to fight infection by producing insufficient amounts or by producing dysfunctional immunoglobulins (Tariman & Estrella, 2005). The diagnosis of MM is confirmed with bone marrow biopsy results that detect specific genetic mutations like additions, translocations, or deletions, which may affect the prognosis. Serial biopsies monitor disease progression and evaluate treatment effectiveness. The goal of the current article is to provide genetic information that oncology nurses in advanced practice should know, using the model of MM. The synthesis analyzes cytogenic results from bone marrow testing and teaches clinical use.

Chromosomes

Cytogenetics is concerned with the study of the structure, function, and abnormalities of chromosomes (Genetics Home Reference, 2012). Analysis includes G-banded chromosomes or other banding techniques, as well as fluorescence in situ hybridization (FISH) and comparative genomic hybridization (CGH) (Genetics Home Reference, 2012) (see Table 1). Chromosomes in the nucleus of cells contain genetic material. Each chromosomal gene codes for a specific protein (National Human Genome Research Institute, 2011a, 2011b). Proteins are essential to the structure and function of the body’s tissues and perform most of the body’s work. Scientists have estimated that each individual...
TABLE 1. Common Cytogenetic Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Reason for Use</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comparative genomic hybridization</td>
<td>May not be informative in detecting balanced translocations; Better for use in detecting losses or gains</td>
<td>High sensitivity; Can do a genome wide screen; simultaneous view of multiple genes; Does not require in-vitro culture</td>
<td>Technically involved; Requires metaphase preparation</td>
</tr>
<tr>
<td>Fluorescence in situ hybridization</td>
<td>Performed to detect smaller abnormalities; Probes matching normal DNA are used to detect aberrations.</td>
<td>Used in conjunction with classic cytogenetics; High sensitivity; Faster results</td>
<td>Probes are numerous and lengthy; need to know what abnormalities may be present in sample and order those specific probes</td>
</tr>
<tr>
<td>Karyotype&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Most widely used technique; Detects large aberrations</td>
<td>Oldest form of cytogenetic testing; Best for detecting large defects (e.g., translocations, deletions, trisomies)</td>
<td>Cells must be in metaphase to count the chromosomes; Growth in culture media required; results make take several days.</td>
</tr>
<tr>
<td>Polymerase chain reaction</td>
<td>Used to detect smaller abnormalities</td>
<td>High-resolution capability; High sensitivity for detecting minor mutations; Get results quickly</td>
<td>Very technically involved; Genome wide screen unavailable; Chance for false-positive results</td>
</tr>
</tbody>
</table>

<sup>a</sup>Special karyotype: chromosomes in color

Note. Based on information from the National Human Genome Research Institute, 2011a, 2011b; Stolzfus et al., 2001.

has 20,000–25,000 genes along their chromosomes (U.S. National Library of Medicine, 2012). Most individuals have 22 pairs of autosomes and two sex chromosomes for a total of 46 chromosomes (U.S. National Library of Medicine, 2012).

Structure

The process of cell division, when two identical daughter cells are formed, is called mitosis. Chromosome pairs in the nucleus can be seen only under a microscope during the metaphase cycle of mitosis when a cell is undergoing division (U.S. National Library of Medicine, 2012). During metaphase, the chromosomes are condensed and become distinguishable as they align at the center of the cell, yielding the diagnostic tool known as a karyotype. Each pair has a point of constriction known as the centromere. The centromere divides the chromosome into a short “p” arm and a long “q” arm (U.S. National Library of Medicine, 2012).

The location of a gene on a chromosome is described using a standardized method of mapping to identify the locus of a specific chromosomal band (see Figure 1). When chromosomes are stained during metaphase, an intricate pattern of banding is visible along the arms. The band, or locus, on the arm of the chromosome indicates where the mutation can be found (Eggert, 2011). For example, chromosome 13 abnormalities can be visualized in 10%–20% of patients with MM, with the most common mutation, in this case a deletion, described as del13q14 (Terpos, Eleutherakis-Papaikouvoû, Dimopoulouû, 2006). A deletion is when a piece of a chromosome breaks off and genetic material is lost (U.S. National Library of Medicine, 2012). In del13q14, the first number represents the chromosome being described (U.S. National Library of Medicine, 2012). In del13q14, the 14th locus on the “q” arm of chromosome 13 (i.e., 13q14) (Terpos et al., 2006).

Aberrations

Chromosomal abnormalities, or aberrations, can be large or small. An example of a large chromosomal aberration is aneuploidy, the addition or deletion of chromosomes. The two most common forms of aneuploidy are monosomy (the loss of a chromosome pair leaving only one copy) and trisomy (the presence of an extra chromosome where a chromosome would normally have two copies) (U.S. National Library of Medicine, 2012). Hyperploidy is noted when an individual has 47 or more chromosomes instead of a normal set of 46 chromosomes; this trait is found in 55%–60% of MM cases (Jagannath, 2008). Partial monosomy describes the loss of only part of a chromosome, such as the loss of a “p” arm (U.S. National Library of Medicine, 2012). Chromosomal aberrations also occur in the chromosome structure with individual nucleotides or sequences of DNA that are lost or rearranged. Like other forms of genetic mutation, these can have either no effect on the individual or can manifest as major medical problems (U.S. National Library of Medicine, 2012). The two most common forms of structural mutations are translocations and deletions (U.S. National Library of Medicine, 2012). Translocations and deletions can involve an entire “q” or “p” arm of a chromosome and be easy to detect, or only involve sequences located in loci of the chromosome, making detection much more difficult (U.S. National Library of Medicine, 2012).

Translocations

Translocations occur when pieces of a chromosome detach and reattach to a different chromosome (U.S. National Library of Medicine, 2012). Nomenclature used to identify translocations may be depicted as t(14;16), where “t” indicates that the mutation is a translocation and the numbers in the parentheses represent the two chromosomes involved. In some cases, a
more specific location of the translocation is needed, and the nomenclature would be depicted as t(14;16) (q32;q23), noting that the translocation is between the 32nd loci of the “q” arm on chromosome 14 and the 23rd loci of the “q” arm on chromosome 16 (O’Conner, 2008). That translation may be seen in some patients with MM (Avet-Loiseau et al., 2011).

Deletions

Deletion can occur at any point along the chromosome (U.S. National Library of Medicine, 2012). Nomenclature used to depict a deletion might be del(17p), indicating the deletion is on the “p” arm of chromosome 17. A more detailed description of the deletion location is del(17p13), with the deletion on the 13th loci of the “p” arm of chromosome 17. That deletion is associated with a poor prognosis in patients with MM (Lode et al., 2010). Another deletion associated with a poor prognosis in patients with MM is del(12p13.31). This nomenclature indicates that the deletion is found at loci 13.31 of the “p” arm on chromosome 12 (Avet-Loiseau et al., 2009).

Tumor Suppressor and Oncogenes

Mutations can activate or inactivate genes leading to continued cancer proliferation. Proto-oncogenes and tumor suppressor genes are located in all normal cells, primarily to regulate or suppress cell division (U.S. National Library of Medicine, 2012). Proto-oncogenes are normal proliferation genes that assist in maintenance and initiation of cell proliferation. Once mutated, the proto-oncogene is no longer capable of turning off (U.S. National Library of Medicine, 2012). Conversely, tumor suppressor genes act as a brake to control cell division. Therefore, when the gene mutates, cell proliferation is uncontrolled (U.S. National Library of Medicine, 2012).

Cytogenetics Applied to Multiple Myeloma

Environmental influences, such as tobacco or pollution, as well as family history, combine to affect an individual's body and its genetic makeup, leading to multiple genetic mutations and changes over time (National Cancer Institute [NCI], 2010). The majority of chromosomal changes are not detrimental to the health of an individual; however, for a third of the U.S. population, those genetic changes may lead to cancer in their lifetime (NCI, 2010).

Cytogenetic Model

Diagnosis of MM is characterized with a “classic triad” of presenting factors including greater than 30% plasma cell proliferation, osteolytic lesions, and the presence of either serum or urine M protein (Tariman & Estrella, 2005). FISH analysis along with CGH can detect chromosomal abnormalities in 80%–90% of patients diagnosed with MM (Faiman, 2007).

MM is considered incurable, with a 40% five-year survival rate (Decaux et al., 2008). To improve survival rates, genetic profiles have been developed that identify genetic abnormalities including those associated with poor prognosis (Decaux et al., 2008). Current clinical trials report the importance of cytogenetic profiles to accurately stage MM in patients; however, the International Staging System (ISS) for MM does not include evaluation of cytogenetics (Avet-Loiseau et al., 2007).

Waheed et al. (2011) compared the ISS to cytogenetic abnormality analysis in patients with MM and found that, although the tools are useful for prognosis individually, the two prognostic measurements were most beneficial if used in conjunction. Waheed et al. (2011) later developed a 17-gene prognostic model for diagnosis and treatment of MM. Avet-Loiseau et al. (2009) conducted a study that used single-nucleotide polymorphism arrays to identify genetic lesions that could be associated with MM prognosis. Using the molecular karyotypes for 192 MM samples and 10 normal samples, Avet-Loiseau et al. (2009) developed a prognostic model based on genetic abnormality frequency. Results identified five highly significant genes with prognostic capability: ILF2, ADAR, ALDH9A1, UBAP2L, and CD27. The CD27 gene is associated with very poor outcome and disease progression (Avet-Loiseau et al., 2009).

Aneuploidy

According to Terpos et al. (2006), aneuploidy is frequently seen in patients who have MM. Hyperploidy, such as trisomy of chromosomes 6, 9, or 17, is associated with male patients older than 55 years, who have MM with a more positive prognosis. The extra genetic material may preserve normal tumor suppressor genes, offsetting the negative impact of hyperploidy (Terpos et al., 2006). Hyperploidy of chromosomes 3, 5, 7, 9, 11, 15, 19, or 21 is found in 50%–60% of patients and also indicates a more positive prognosis (Avet-Loiseau et al., 2009). Hypoploidy, having fewer than 46 chromosomes, is commonly found in MM on chromosomes 6, 13, 16, and 22, and is associated with a poorer prognosis (Terpos et al., 2006).

Translocations and Deletions

Fifty percent of patients with MM have a deletion in chromosome 13 (Avet-Loiseau et al., 2009). Avet-Loiseau et al. (2007) studied 983 patients with MM, 48% with del(13), and found that del(13)
TABLE 2. Helpful Resources for Genetics Information

<table>
<thead>
<tr>
<th>Organization</th>
<th>Web Site</th>
<th>Resource</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetic Alliance</td>
<td><a href="http://www.geneticalliance.org">www.geneticalliance.org</a></td>
<td>Provides educational materials for patients</td>
</tr>
<tr>
<td>International Society of Nurses in Genetics</td>
<td><a href="http://www.isong.org">www.isong.org</a></td>
<td>Focuses on genetics in nursing and professional growth and education as it relates to genetics</td>
</tr>
<tr>
<td>National Cancer Institute</td>
<td><a href="http://www.cancer.gov">www.cancer.gov</a></td>
<td>Conducts cancer research; provides nurse training in cancer diagnosis and education for patients</td>
</tr>
<tr>
<td>Oncology Nursing Society’s Cancer Genetics Special Interest Group</td>
<td><a href="http://cancergenetics.vc.ons.org">http://cancergenetics.vc.ons.org</a></td>
<td>Provides resources and information related to genetics, as well as community for discussion among other oncology nurses with interest in genetics</td>
</tr>
</tbody>
</table>

had prognostic capabilities, particularly if associated with t(4;14) and del(17p). The median overall survival for patients with del(13) and t(4;14) was 41 months versus 22 months for patients with del(13) and del(17p) (Avet-Loiseau et al., 2007). However, a separate retrospective study by Avet-Loiseau et al. (2011) (N = 1,003) determined that t(14;16) is a rare abnormality among patients with MM (occurrence of 3.2%) and not statistically significant as a poor prognostic factor.

Treatment

The genetic profile of a patient with MM affects response to specific chemotherapies. Terpos et al. (2006) indicated that patients with chromosome 13 deletions had a worse prognosis, responded less to treatment, and relapsed more frequently. In addition, patients with chromosome 13 deletions had a better survival with tandem autologous stem cell transplantations (SCTs) versus autologous SCTs (Terpos et al., 2006). The researchers also suggested patients with that deletion should be treated with higher doses of thalidomide, a common immunomodulatory agent used to treat patients with MM. Conversely, the study reported a longer overall survival rate with a t(11;14) translocation (Terpos et al., 2006).

The National Comprehensive Cancer Network ((NCCN), 2011) provides guidelines for basic diagnostic and treatment approaches for cancer diagnoses. Cytogenetic profiling has been moved from the category “useful under some circumstances” to “initial diagnostic workup” in patients suspected of having MM. FISH abnormalities included in this initial diagnostic workup for MM target del(13), del(17), t(4;14), t(11;14), t(14;16), and 1q21 amplification (a cellular process where multiple copies of a cell are produced) (NCCN, 2011).

Implications for Practice

Nursing organizations such as the International Society of Nurses in Genetics and the Oncology Nursing Society have recognized and continue to emphasize the importance of genetics education in nursing and clinical practice. For oncology nurses in advanced practice, new expectations related to genetics are being developed, including the need for knowledge gained from taking complete family histories, cancer genetic risk counseling, and basic understanding of genetics (American Nurses Association, 2009; Greco, Tinley, & Seibert, 2012; Oncology Nursing Society, 2007). In addition, the American Nurses Credentialing Center (2008) has incorporated genetic content into their “Essentials” at the baccalaureate and graduate levels. The American College of Surgeons (2012) also has reinforced the importance of advanced practice oncology nurses’ knowledge in genetics by requiring certification if working in high-risk cancer genetics.

Despite the addition of genetic content to core curriculum in graduate nursing programs, studies have shown that advanced nursing knowledge regarding genetics is insufficient (Tomatir, Sorkun, Demirhan, & Akdag, 2006). Bancroft (2010) defined the issue as a gap among scientific discovery and clinical practice. Understanding cytogenetics is paramount in oncology, particularly for areas specializing in hematologic malignancies. Bone marrow biopsies that evaluate multiple cytogenetic abnormalities are the basis for diagnosis and the continuous monitoring progression for patients with hematologic cancer (Tariman & Estrella, 2005).

After the patient and family’s initial shock of a cancer diagnosis, oncology nurses frequently are asked to answer questions related to pathology and bone marrow biopsy results that guide treatment options. Oncology nurses in advanced practice can empower patients to be competent in their own care by educating them about novel therapies for cancer and helping them to make informed decisions about treatment and clinical trial options (Tariman & Estrella, 2005). By understanding the role genetics play in diagnosis and management of cancers, oncology nurses in advanced practice serve as a reliable resource for patients. Table 2 provides resources for nurses interested in learning more about genetics information and its relation to oncology.

Conclusion

Genetics content was not available in high school textbooks until the late 1970s, emphasizing the potential lack of knowledge among oncology nurses in advanced practice about how genetics affects the care of patients with cancer undergoing tumor treatment (Eggert, 2011). According to Jenkins (2011), genetics and genomics are being added to competency expectations for all nursing levels, including advanced practice roles in oncology. Patients expect that advanced practitioners have an understanding of their disease and are capable of explaining that disease, its processes, and the laboratory test results that are relevant to care and longevity. Oncology nurses in advanced practice need to know how to interpret and incorporate genetic information as it relates to cancer treatment and progression.
Implications for Practice

- Oncology nurses in advanced practice will now be expected to have basic knowledge of genetics and how it relates to cancer. Nursing curricula are beginning to incorporate genetics based on the recommendations of nursing organizations.
- Patients often look to advanced practice nurses for answers, so they must be prepared to give concise and accurate information.
- Advances in research have shown that genetic profiling can assist with determining prognosis of disease. This knowledge can help providers choose targeted treatment that will give patients the best chance at survival.

References


