Personalized Medicine, Genomics, and Pharmacogenomics: A Primer for Nurses

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Personalized medicine is the study of patients’ unique environmental influences as well as the totality of their genetic code—their genome—to tailor personalized risk assessments, diagnoses, prognoses, and treatments. The study of how patients’ genomes affect responses to medications, or pharmacogenomics, is a related field. Personalized medicine and genomics are particularly relevant in oncology because of the genetic basis of cancer. Nurses need to understand related issues such as the role of genetic and genomic counseling, the ethical and legal questions surrounding genomics, and the growing direct-to-consumer genomics industry. As genomics research is incorporated into health care, nurses need to understand the technology to provide advocacy and education for patients and their families.

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Genetics and genomics are rapidly changing health care by making it more personalized than ever before. Medical genetics is defined as the study of how individual genes can be identified and used for medical applications, including as markers for targeted drug therapies, to identify disease or the predilection for disease, and for tailoring treatments (Offit, 2011). In 2003, the first human genome was completely mapped, cataloging all of a person’s genes (National Institute of General Medical Sciences, 2013). In the years since the advent of medical genetics, researchers have found that many factors other than the presence or absence of single genes predict disease; medical genomics is a study of all genes and other factors (e.g., epigenetic influences, environmental influences) that contribute to inheritance patterns and how medical care can be tailored to individual genomes. Pharmacogenomics is the study of how a person’s genome affects his or her reaction to medicines (National Institute of General Medical Sciences, 2013). Personalized medicine employs applications from genetics, genomics, and pharmacogenomics, as well as the analysis of environmental factors, to individualize health care to an individual’s specific needs. Personalized medicine represents a major change in the way health care will be delivered, and nurses need to stay informed about its science, clinical use, ethics, economics, and social impact. Because cancer is fundamentally a genetic disease, advances in genetics and genomics have profound implications for oncology, and patients will be looking to their healthcare providers—including nurses—for guidance (Riley et al., 2012).

Background

To understand the nursing implications of genomics, one must first understand the underlying science. Although the idea of inheritance has been studied since ancient times, the era of modern genetics began in 1865 when Mendel explained the concept of discrete dominant and recessive genes and described how traits can be passed down from generation to generation, sometimes skipping a generation (Lorentz, Wieben, Tefferi, Whiteman, & Dewald, 2002). Not long after, genetic material (DNA) and chromosomes were discovered. In 1953, Watson and Crick described the double-helix structure of DNA and later showed that DNA codes for ribonucleic acid (RNA), which then codes for the production of proteins in the body (Lorentz et al., 2002). With the exception of sperm and egg cells, each human cell contains 23
pairs of chromosomes (46 total) composed of DNA. The DNA is arranged in sequences of bases, and the total sequence is unique to each individual. Each chromosome can be broken down into discrete segments of DNA called genes, and these genes tell the cell what to do (American Cancer Society, 2011). With the completion of the human genome project in 2003, the nearly 21,000 genes in a human cell were cataloged (Stratton, Campbell, & Futreal, 2009).

The study of genetics has revealed that DNA mutations cause variations in the displayed characteristics of organisms, with mutations sometimes leading to abnormal, unchecked proliferation of cells or cancer. Most cancer mutations involve oncogenes and tumor suppressor genes. Oncogenes function to regulate cell growth but can mutate to instead enable abnormal cell growth. A mutation in the RAS family of oncogenes is present in about one-third of all tumors, including lung, colon, and pancreatic cancers (Virshup, 2010). Tumor suppressor genes normally help turn off abnormal cell growth, repair DNA, or cause cells to die (American Cancer Society, 2011). Germline mutations, which cause 5%-10% of all cancers, are inherited. BRCA1 and BRCA2 are examples of germline tumor suppressor genes; mutations in these genes are implicated in hereditary breast and ovarian cancers. Much more common than germline mutations, somatic mutations occur during a lifetime (Riley et al., 2012). Somatic mutations occur by various means (e.g., exposure to radiation, toxins, certain viruses), but the majority do not cause cancer. The mode of mutation varies widely and can involve substitutions, insertions, or deletions of DNA bases; gene duplication; and chromosomal rearrangement.

Cancer development and proliferation is usually polygenic, involving multiple gene mutations that accumulate over a lifetime—cancer is usually a disease of the genome rather than any one specific gene. Cancer-promoting genetic mutations accumulate over time; four to seven specific mutations are usually necessary for cancer to arise (Virshup, 2010). Many of these mutations are specific to certain cancers (Stratton et al., 2009). For example, the translocation of material between chromosomes 9 and 22 (the Philadelphia chromosome) is associated with chronic myeloid leukemia (Lorentz et al., 2002; Stratton et al., 2009). With this knowledge, imatinib mesylate was developed to effectively target cells with this chromosomal mutation and induce cell death (An et al., 2010). By analyzing patients’ DNA for specific genes (genetics) and for certain genes in combination with certain expression (genomics), healthcare providers can identify the risks for developing disease, diagnose specific diseases, offer more accurate prognoses, tailor individualized treatment plans, and prescribe targeted drugs. This is the future of personalized medicine in oncology.

Genetic cancer risk assessment is an interdisciplinary process that should be employed when clinicians suspect significant familial risk. Familial risk factors include early onset of cancer (e.g., breast cancer before age 45, colorectal cancer before age 50); individuals having multiple, different primary cancers; cancer in multiple generations of a family; and certain cancers occurring together (e.g., breast with ovarian, pancreatic with melanoma) (Weitzel, Blazer, MacDonald, Culver, & Offit, 2011). The risk assessment process is complex, involving a family history, physical examination, genetic counseling, and genetic and/or genomic testing. By combining that data, overall risks for different cancers can be estimated. Specific genetic tests are usually ordered for suspected familial cancer syndromes, such as testing for BRCA1 and BRCA2 in breast cancer syndromes, MSH2 and MLH1 in Lynch syndrome (i.e., hereditary nonpolyposis colorectal cancer), APC in familial adenomatous polyposis, and MEN1 and RET in multiple endocrine neoplasia types 1 and 2. The U.S. Centers for Disease Control and Prevention (CDC) and the National Cancer Institute have websites with information about the different hereditary cancer syndromes and which patients are appropriate for additional testing based on health histories (see Figure 1).

In the arena of diagnosis, genomics is increasingly used to differentiate subtypes of cancers. Whole-genome sequencing of a patient’s cancer can reveal all the mutations that contributed to oncogenesis, allowing clinicians to diagnose specific subtypes of cancers vulnerable to specific treatments. Applications include mapping the genomic characteristics of pediatric acute myeloid leukemia and testing for gene expression subtypes of breast cancer (e.g., HER2-positive subtype) (Stratton et al., 2009). As genomic sequencing becomes faster and more accurate, cancer genome sequencing will become more prevalent in clinical diagnostic use (Welch et al., 2011).

Genetic and genomic testing also is influencing cancer prognosis and treatment. Genomics testing can be used in determining disease severity and outcomes, such as in breast cancers and various lymphomas (Bertucci et al., 2011). Treatments and pharmacogenomics applications are numerous, including using medicines that target specific mutations in cancers. For example, trastuzumab is a drug that binds to HER2 receptors on susceptible breast cancers and induces antibody-dependent tumor cell death (Squassina et al., 2010). Another important application is genomic testing for individual variations in drug metabolism. Testing can demonstrate patients’ genomic expression of liver enzymes, particularly those within the cytochrome P450 family, a group of liver enzymes that breaks down many classes of drugs including warfarin, clopidrogel, and some chemotherapy agents (National Human Genome Research Institute, 2013). Therefore, clinicians can predict how well a patient will metabolize specific drugs and then prescribe effective drugs at the best doses.

Personalized medicine offers the promise of treating diseases or predispositions identified in the individual genome with specific, targeted pharmacogenomic medicines dosed for the individual’s unique metabolism. In addition, genetic testing can determine whether side effects are likely, leading to fewer side effects for patients. Genetic testing is a rapidly evolving field and much research is still needed, particularly in regard to testing clinical use (Offit, 2011). Although a lack of efficacy data exist, oncology, in particular, shows significant evidence

Applications of Genetics, Genomics, and Personalized Medicine

Personalized medicine has evolved for many years. For decades, personalized medicine included consideration of family traits and environmental influences on the individual. As the science of genetics and genomics has progressed, these newer understandings are being incorporated into medicine and pharmacology, affecting risk assessment, diagnosis, prognosis, and treatment.
of use. Trastuzumab is highly effective against susceptible breast cancers (Artac et al., 2010). Other drugs have shown clinical effectiveness and have been approved by the U.S. Food and Drug Administration (FDA), including erlotinib and gefitinib for lung and other cancers. These drugs target cells with genetic mutations, causing epidermal growth factor receptor overexpression. Certain antileukemic drugs are metabolized by the thiopurine methyltransferase (TPMT) enzyme. Genomic tests for inherited TPMT deficiency allow clinicians to prescribe effective and safer doses of drugs for managing acute lymphoblastic leukemia (Artac et al., 2010). More research is needed to determine the clinical use of many genomic therapies, as well as the economic return for the required investments.

Genomics Implementation Considerations

As the science of genomics continues to be translated into healthcare practice, important concerns remain. Most importantly, patients need to be protected from proven genomic science with unproven clinical use. Other important issues to consider are the vital role of genetic and genomic counseling, the ethical and legal questions surrounding genomics, and the growing direct-to-consumer (DTC) genomics industry. While genomics is being adopted into practice, nurses will be vital as patient advocates and educators.

Genetic and genomic counseling is an invaluable component of genomic healthcare. According to the National Society of Genetic Counselors, a referral for genomic cancer counseling is appropriate for those with a personal and family history that suggests an increased risk for cancer (Riley et al., 2012). In the United States, certified genetic counselors have Master’s degrees in genetic counseling and must pass a board certification examination (National Society of Genetic Counselors, n.d.). Counseling should include, at minimum, a personal and family medical history (including a three- to four-generation pedigree), psychosocial assessment, risk assessment, pretest counseling, a rigorous informed consent process, and, if indicated, a blood draw and revealing of results (Vig & Wang, 2012). Post-test psychosocial counseling is sometimes indicated, as determined by the counselor or the referring practitioner. Counselors and practitioners must work together closely with the patient because risk assessments and genomic results can influence treatment plans. For example, Angelina Jolie made headlines when she decided to have a prophylactic double mastectomy after discussing her estimated 87% lifetime risk for breast cancer with practitioners and counselors (Grady, Parker-Pope, & Belluck, 2013). Genomic counselors help patients make difficult treatment decisions that are individually appropriate given that patient’s unique lifetime risk and risk tolerance.

The ethical issues surrounding genomic health care are complex. Genomic testing can have potentially life-altering implications not only for the patient, but also for the entire family. For example, a genomic cancer risk profile that suggests an increased risk of cancer also can suggest that family members share this risk, but no clear ethical or legal guidelines exist pertaining to the duty to warn family members of risk (Offit, 2011). Increasing patient autonomy in healthcare decisions has been an ongoing trend in the industry, and this tenet is central to genomic counseling (Hawkins & Ho, 2012). However, healthcare workers must balance a patient’s right to autonomy and information with the duty of non-maleficence (i.e., to do no harm). Some genomic results can have profound implications for patients, and a proven potential exists for severe and clinically relevant psychological distress, particularly without proper post-test counseling (Offit, 2011). In addition, most information revealed by genomic testing is not clinically actionable, such as one’s risk

Nursing Resources

- American College of Medical Genetics and Genomics
  This website has information about current genetic/genomic tests, as well as educational resources for all aspects of genetic and genomic healthcare.
  www.acmg.net
- Centers for Disease Control and Prevention (CDC)
  An informational page on all aspects of genomics health care, including evidence-based recommendations for testing.
  www.cdc.gov/genomics
- Evaluation of Genomic Applications in Practice and Prevention
  A website for an independent, multidisciplinary group commissioned by the CDC to provide information on the clinical usefulness and evidence of various genetic and genomic tests and interventions. It also provides up-to-date recommendations.
  www.eqppreviews.org
- National Cancer Institute Fact Sheet on Hereditary Cancer Syndromes
  This site lists common hereditary cancer syndromes, their associated genetic mutations, and recommended testing.
- National Cancer Institute
  This website contains information on a broad range of topics regarding human genomics and cancer genomics.
  www.cancer.gov/cancertopics/understandingcancer/cancergenomics
- National Human Genome Research Institute
  This website contains information specifically for health professionals regarding genomics, including patient management, competencies, and policy and ethics issues.
  www.genome.gov/27527599
- National Society of Genetic Counselors
  This is a resource for healthcare providers and patients with information about genetic health, genetic counseling, and finding a genetic counselor, and contains tools for monitoring one’s family and genetic health.
  www.nsgc.org

Patient Resources

- American Cancer Society
  This website offers information about familial breast cancer testing— is it appropriate? What is involved?
- National Cancer Institute
  This is a reliable resource for patients about understanding cancer and genomics.
  cancergenome.nih.gov/cancergenomics/whatisgenomics/whatis
for developing Alzheimer disease. Therefore, a very thorough informed consent process is a crucial part of the genomic counseling process (Hawkins & Ho, 2012). Debate continues about the ethics of disclosing (or not disclosing) non-actionable, yet serious, genomic risks discovered incidentally during other testing (National Public Radio, 2013).

The rapidly changing technology has introduced other ethical concerns. Genome sequencing technology is constantly evolving and is not always entirely accurate. False-positives and false-negatives remain a real possibility and may alter patients’ future health-maintenance behaviors. Counselors and nurses need to educate patients about the limitations of the technology and the need to continue with preventive screenings despite any reports of low lifetime risks for developing specific cancers.

Discrimination based on genetic and genomic information is another concern. Federal and state laws are in place that protect patients and have reduced the risk of discrimination based on genomic testing results (Artac et al., 2010). For example, the Health Insurance Portability and Accountability Act protects a person’s genetic information (National Institute of General Medical Sciences, 2013). Despite the evidence, a remote possibility of discrimination remains from employers as well as from health, life, long-term, and disability insurance companies for patients and their families.

Another area of concern is the growth of the DTC genomics industry. Until recently, DTC companies, most notably 23andMe, Inc., advertised widely and offered genomic health profiles to the public without prescription. In November 2013, the FDA ordered 23andMe to halt offering genomic analyses until it could provide additional validation of the information (Steele & Gold, 2014). These companies offered genetic trait analysis and risk profiles on various diseases, with tests ranging from male-pattern baldness trait to risk of developing Alzheimer disease. Although DTC companies argued that they were simply providing consumers with access to their genetic data, the FDA’s decision demonstrates that the boundaries between the public, the healthcare community, and regulators are unsettled regarding access to genomic information (Hawkins & Ho, 2012; Steele & Gold, 2014).

All of the legitimate concerns about genomic testing are magnified when genomic profiles are offered directly to consumers without medical supervision. No standardized, regulated, or required genetic counseling exists in DTC genomics, and the process may lack an adequate informed consent procedure (Riley et al., 2012). Interpretation of genomic results is critical, and DTC genomic testing lacks a standardized post-test counseling. Without proper counseling, genomic results with questionable validity and use increase the possibility of falsely alarming or reassuring clients who may then alter their health-maintenance behaviors or suffer psychological distress (Offit, 2011; Udesky, 2010). In addition, most genomic information is currently not clinically actionable and, without proper counseling, may cause more harm than good (Offit, 2011). After a year-long investigation, the U.S. General Accounting Office concluded that DTC genomic testing results were “misleading, and of little or no practical use” (Udesky, 2010, p. 1,377). For these reasons, the FDA issued its directive to halt DTC genomic testing, at least for now. As this issue is settled, nurses should stay informed of changing regulations and should warn patients and family members about the dangers of DTC genomic testing without proper physician supervision, prescription, and genomic counseling.

The science and technology behind genomic testing is evolving so rapidly that healthcare clinicians are having trouble keeping pace. Research has begun to show that genomic markers with proven validity may still fall short of meeting evidence-based standards of clinical usefulness (Offit, 2011). Recognizing the need for systematic, evidence-based recommendations for genomic testing, the CDC launched the Evaluation of Genomic Applications in Practice and Prevention (EGAPP), 2009 working group in 2004. EGAPP produces evidence-based recommendations for or against specific genomic tests. Nurses can use this information to educate patients about the proper interpretation of test results.

Looking Forward: Genomics and Nursing

Nurses will play an important role in how this technology is implemented; their unique role as patient advocates and educators will be immensely important in this healthcare transformation. Because the ethical ramifications of genomic medicine are still being worked out, nurses will act as patient advocates to protect their interests as policies are developed. Premature translation of this technology from research into practice leads to real risks of patient harm, and nurses in academia and in practice will be counted on to advocate for patients’ protection. Nurses will also play a role in educating patients and families about genetics and genomics and, more importantly, educating patients about what to do with findings. Even the most valid genetic or genomic tests will not be useful to prevent disease in susceptible individuals unless patients change their behaviors. Testing that reveals a high lifetime risk of colorectal cancer, for example, should be followed by nursing reinforcement of education to reduce environmental risks, such as reducing consumption of processed foods and red meats. Patients will look to nurses for education in the interpretation of genetic and genomic results. Although certified genetic counselors are best suited and trained to interpret test results, nurses can guide patients in the implications and uses of those results.

Implications for Practice

- Increase knowledge of basic science because cancer is a genetic disease and will be increasingly addressed with genetic and genomic medicine.
- Use genomic analysis to understand how patients will metabolize specific drugs.
- Help patients understand the risks and benefits of these new technologies and explain the ethical ramifications.

Conclusion

The era of personalized medicine and genomic health care is now. In the future, more genomic information will be collected and analyzed, and personalized medicine should allow clinicians to accurately identify risks, diagnose diseases, determine effective treatments and doses, and develop targeted
effective drugs. Nurses will be expected to understand genetic and genomic medicine and advocate for patient interests. The future of personalized medicine, particularly in oncology, is exciting but uncertain, and patients will look to nurses for expert guidance.

References


