Dr. M. Nedwidek-Moore/Stuyvesant H.S. Jonathan Quang

Assignment #4 / Due 2/12/16 SBS11QHG Period 10

Screening of BRCA-1 and BRCA-2 Genes

There are two genes in humans that are found to increase the risk of breast and ovarian cancer if these two genes are mutated. These are the BRCA-1 and BRCA-2 genes. According to the National Cancer Institute, " BRCA1 and BRCA2 are human genes that produce tumor suppressor proteins. These proteins help repair damaged DNA and, therefore, play a role in ensuring the stability of the cell’s genetic material," (NIH). Instability in genetic material may eventually lead to cancer.   
 There are numerous ways BRCA-1 and BRCA-2 are scanned for. According to Kumaravel Somasundaram in " BRCA1 and BRCA1 Genes and Inherited Breast and/or Ovarian Cancer: Benefits of Genetic Testing," " Some of the techniques which are commonly used are single-strand conformation polymorphism (SSCP), restriction endonuclease fingerprinting (REF)-SSCP, conformation-sensitive gel electrophoresis (CSGE)... and denaturing high performance liquid chromatography (DHPLC)" (Somasundaram). Going over all of the techniques would be redundant, so focus will be placed on the DHPLC method. The DHPLC method requires polymerase chain reaction (PCR) to generate more of the sample DNA. According to the Cold Spring Harbor laboratory, the genes for BRAC1 and BRAC2 are located on chromosome 17 and 13 respectively.   
 The portion of DNA that is to be tested is to be placed into a vial containing DNA polymerase, small sequences of DNA called primers, and the four nucleotide bases, adenine, thymine, cytosine, and guanine. The vial is then placed into a machine that heats up the vial for a set amount of time to break the hydrogen bonds in the DNA. Once that time is over, the vial is allowed to cool so that primers may attach to both strands of DNA. The temperature of the vial then rises to the optimal temperature for DNA polymerase to work in. This effectively duplicates the DNA.  
 The first step of DHPLC is heating and cooling of the DNA sample and the DNA without the mutation. This causes the DNA to denature and reform. Homoduplex's, matching pairs of two DNA strands will be more stable against heating while heteroduplex's, DNA strands that have places where they do not match, will be less stable against heat. A column of styrene - divinylbenzene is hydrophobic and has neutral charge. DNA has negative charges along its phosphate groups. Ammonium ions can be used to introduce interaction between the DNA and the column. When the column is washed, heteroduplex's, being weaker, will be washed away first. This fact is exploited by having a UV detector.   
 The accuracy for this method is very high. In " Diagnostic Accuracy of Methods for the Detection of BRCA1 and BRCA2 Mutations: a Systematic Review," it states, " Sensitivities were reported to be [about] 100% for ... denaturing assay, high-performance liquid chromatography (DHPLC) ," (Gerhardus, Schleberger, Schlegelberger, Gadzicki). Any testing done with DHPLC is likely to be accurate with such a high sensitivity. This means that any patients that choose to get themselves tested for mutations in BRCA1 and BRCA2 with this method will most likely get an accurate answer.   
 The American Society of Human Genetics released a recommendation stating "Adolescents should be encouraged to defer predictive or pre-dispositional testing for adult-onset conditions until adulthood because of the complexity of the potential impact of the information at formative life stages." This statement stands true, so long as there is no reason to perform any procedure to prevent the issue during adolescence. With BRCA1 and BRCA2, the treatment is to perform a mastectomy and/or removal of the ovaries. The ovaries are crucial to growth, and they should not have any problems during adolescence. No body parts really have to be removed until the child is an adult because breast and ovarian cancer is unlikely to occur until then.   
 There is also the psychological aspect to consider. If an adolescent is told that they are likely to have a life changing, potentially deadly, problem in the future, they will not be able to live their lives normally. They will have the mental burden of worrying about future surgeries and death. This matter is only made worse with tests such as DHPLC, which has a nearly 100% accuracy. There is very little room for doubt.

Bibliography

"BRCA1 & BRCA2: Cancer Risk & Genetic Testing." *National Cancer Institute*. National Cancer Institute, 1 Apr. 2015. Web. 12 Feb. 2016. <http://www.cancer.gov/about-cancer/causes-prevention/genetics/brca-fact-sheet>.

Gerhardus, A., H. Schleberger, B. Schlegelberger, and D. Gadzicki. "Diagnostic Accuracy of Methods for the Detection of BRCA1 and BRCA2 Mutations: A Systematic Review." *National Center for Biotechnology Information*. U.S. National Library of Medicine, 7 Mar. 2007. Web. 12 Feb. 2016. <http://www.ncbi.nlm.nih.gov/pubmed/17342152>.

Somasundaram, Kumaravel. "BRCA1 and BRCA1 Genes and Inherited Breast And/or Ovarian Cancer: Benefits of Genetic Testing." *Indian Journal of Surgical Oncology*. Springer-Verlag, 3 Sept. 2010. Web. 12 Feb. 2016. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3244237/>.

Xiao, Wenzhog, and Peter J. Oefner. "Denaturing High-performance Liquid Chromatography: A Review." *Wiley Online Library*. Medline, 25 May 2001. Web. 12 Feb. 2016. <http://onlinelibrary.wiley.com/doi/10.1002/humu.1130/abstract>.