Personalized Medicine Universe 3 (2014) 42–45

Contents lists available at ScienceDirect

Personalized Medicine Universe

journal homepage: www.elsevier.com/locate/pmu

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The ethics of personalized medicine

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ARTICLE INFO

Article history:
Received 21 January 2014
Received in revised form
27 February 2014
Accepted 7 March 2014

Keywords:
Personalized medicine
Ethics
Genetic sequencing
DNA

ABSTRACT

Personalized medicine is that branch of medicine whereby a patient's treatment and prognosis are based on his genes. Recent genetic research explains the variations and similarities between humans, their diseases, and their responses to various treatments. Because governments and universities have not set strict standards, there are numerous tests and kits available to detect genetic problems. But are these kits accurate? The validity of some biomarkers is suspect.

The ethics of personalized medicine became an issue when some laboratory tests resulted in women incorrectly having been told that they have a high risk of breast or ovarian cancer when they did not. Ethical issues are not confined to the utilization of genetic information, but can be raised with the acquisition of human material for the advancement of knowledge. Whose genes are these? Who owns your DNA?

In the US, patients are given prenatal genetic advice upon which they can decide for themselves how to proceed. But in Russia, patients have no choice. The state makes most decisions. Selective breeding would be unacceptable in western countries.

Imagine a 35 year old healthy woman who has completed her family thinking about her own health options in as much as her mother has just died from ovarian cancer and her older sister had died from ovarian cancer 8 years ago. She is now worried that in fact she might develop ovarian cancer. What should she do since any decision will affect her family, her health, and her privacy? Today we will discuss some of her options.

Personalized medicine is that branch of medicine whereby treatment and prognosis are based on a patient's genetic properties and pattern. Scientists, researchers, and clinicians are making strides in their study of genetics and personalized medicine, a field that is derived from the very essence of human anatomy, physiology, biochemistry, and pharmacology. Numerous genes have been identified which explain the variations and similarities between humans, their diseases, and their responses to these diseases and their treatments. Government agencies and universities have been focusing on the best ways to deliver this information to health care providers and to their patients because of the importance that these groups search and receive effective treatment. It falls on the shoulders of the government and universities to set the standards.

The National Institutes of Health (NIH) and the Food and Drug Administration (FDA) have been deliberating about the best way to develop new therapies and to direct that information to medical clinicians and to patients. For example, numerous tests or kits are already available to detect genetic problems in health care, but the question is: are these kits accurate? These government organizations collaborate with Therapeutics for Rare and Neglected Diseases (TRND) and examine promising medications for their effectiveness and safety. TRND develops and manufactures novel therapies, and performs clinical trials to ascertain the treatment of various diseases with human embryonic stem cells. The NIH is developing better evaluation tools such as biomarkers and assays. There has been a vast proliferation in the number of biomarkers, but so far there is insufficient evidence and analysis of the validity of some of the tests.

The ethics of personalized medicine has become an issue when some laboratory tests resulted in women having been told incorrectly that they had a high risk of breast cancer or ovarian cancer when in fact they may not have. Also some ovarian cancer tests were marketed before the NIH funded study was complete, which may have led to the unnecessary removal of women's ovaries. There are more than 2000 genetic tests available through the clinical laboratories, many of which have not been thoroughly tested. As a result, the NIH is organizing a voluntary registry, which hopefully

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http://dx.doi.org/10.1016/j.pmu.2014.03.001

will provide a reliable source of information about genetic variation, tests, and various therapies.

In addition to the registry, Dr. Gilean McVean of Oxford University and the staff in his department have sequenced the complete DNA material of more than 1000 persons from 14 population groups in Europe, Africa, Asia, and the Americas [1]. As progress is made in the field of genomics and personalized medicine, so, too, will numerous ethical questions emerge. For example, how are parents to react to a pregnancy when a genetic sequencing test shows a predisposition for a deadly disease without 100% certainty? What if the test on the pregnant patient shows that her expected baby may have a disease for which there is no cure? Do those who are known to have a genetic transferable disease have a responsibility not to procreate? Is there a right time to tell a child about the results of such a test?

The above listed problems may lead to an increase in the number of abortions performed, which in itself is an ethical problem. In the Jewish population, some embryos are routinely tested for Tay-Sachs because there is a high probability that these tests will be positive in this group. Whereas prenatal sequencing looks for all diseases, current tests look for specific genetic disorders in certain groups of people. Maybe the issue should not be whether or not testing is ethical, but rather does the sequencing make people healthier? [2].

Ethical issues are not confined to the use of the genetic information, but rather can be raised with the acquisition of blood and tissue for the advancement of knowledge. This particular issue deals with the definition of informed consent. The Havasupai Indian tribe in Arizona thought they were donating blood to a university for use in discovering the tribe's high rate of diabetes. In fact the Arizona State University researchers also used the blood to study the genetic causes of mental illness in the tribe's ancestry. According to the Indian tribe, this unauthorized study violated the tribe's values and they sued Arizona State University. The university paid the forty-one member group of the Havasupai tribe $700,000 to settle the case. In this case, there was a clash of interests: the Arizona State scientists wanted to pursue research and the Indians felt that they should be asked whether or not their body materials could be studied for other purposes. In addition to the need for a more specific informed consent, there has to be greater cultural sensitivity [3]. Sooner or later, the ethical issues related to genomics will interact with the privacy issues. Just as many people do not want to be tested for HIV for fear that their employer or insurance company would use that information in an adverse manner, so it is that many people do not want their genetic information to be on record. If the various genetic tests indicate that the patient might have the genes to develop amyotrophic lateral sclerosis or Parkinson's Disease, a company might not hire or retain that person for fear that the company would be responsible one day for the custodial and skilled care that person might require.

The nomenclature for the various human cancers has historically reverted back to the name of the offended and involved organ. For example, medical terminology referred to prostate cancer, ovarian cancer, and breast cancer. Now these tumors are referred to with the names of mutated genes deep within the tumors that caused the malignancy. The terms and the drugs used to combat these tumors are relatively new. The reason that there has been such a proliferation of these drugs is due to the declining cost of decoding DNA and the lure of obtaining exorbitant prices for these drugs that attack the molecules of cancer [4].

The web site My Cancer Genome lists the mutations in different types of cancer and also lists the drug therapies which are most likely to be of benefit in treatment. Once the type of mutation in the gene is identified, then a doctor can examine the various national and international drug trials aimed at these alterations. Hence, the mutation itself is used to search for the appropriate treatment. But before going to My Cancer Genome, a diagnostic test has to be employed to identify the relevant gene mutation. Foundation Medicine provides such tests, but these tests might cost up to $6000, which may or may not be covered by health insurance. This test analyzes a small piece of tumor, extracts the DNA and the sequencing genes, which are altered by the cancer. Then the alterations are matched with approved drugs or clinical trials. Genomic Health has developed a test to determine whether or not a breast cancer patient should or should not receive chemotherapy. Once it is known exactly what is inside a tumor causing it to grow, then this information can be matched with a specific drug, which targets that abnormality. Some call this precision medicine.

Ethical behavior is not limited to those validating tests, pharmaceuticals, medications, and research, but also includes those who interpret the genetic sequencing. For example, personalized medicine is based on bio-molecular mapping, monitoring, and tailored drug interventions. And yet besides that information, it is important to take into consideration the nature of human beings from a social and a cultural viewpoint [5]. Promoting good health means making wise decisions about public policy as well as wise decisions about the doctor patient relationship [6]. So it is that we opine on the Myriad Genetics Inc. case that has recently been argued in the US Supreme Court. The case in question is Association for Molecular Pathology et al. v Myriad Genetics Inc. et al-U.S. Supreme Court, No. 12-398. The ultimate question raised in this case is: Who owns your DNA? Whose genes are these? This is a contentious issue with ethical consequences for the future of gene-based medicine and for personalized medicine. A panel at the U.S. Federal Circuit Court of Appeals in Washington, D.C. upheld Myriad Genetics' right to patent "isolated" genes, which account for some inherited forms of breast and ovarian cancers. But this federal panel denied Myriad's effort to patent methods of "comparing" or "analyzing" DNA sequences. The ACLU Women's Rights Project's lawyer estimates that already 4000 of the 22,000 genes in the human genome have US patents. But the lawyers for Myriad Genetics argue that the denial of patent protection would significantly hinder research in personalized medicine, because the diagnostics and the therapeutics require large sums of financial resources and if there is no patent protection, then the investors will not be so forthcoming. Research and development for new pharmaceuticals costs millions of dollars and this estimated price may rise to tens or even hundreds of millions of dollars. A pharmaceutical company wants to know whether it could expect to recoup those costs, and in order to do that, they need to know the demographic profile of people with the genotype of interest. But critics of Myriad Genetics feel that it is unfair to give any company such a monopoly on people's genes. Specifically, this case concerns BRCA1 and BRCA2, which can be used to detect the risk of a woman's developing breast and ovarian cancer. And the critics of Myriad Genetics think that these patents are illegal, prohibit others from the clinical testing of BRCA1 and BRCA2 genes, and restrict and inhibit scientific research. In addition, Dr. James Watson, who helped discover the double helix structure of DNA, said "DNA's importance flows from its ability to encode and transmit the instructions for creating." [7] On June 13, 2013, the US Supreme Court ruled against Myriad Genetics and stated that no one can patent human genes.

Paul Root Wolpe of Emory University has underlined the ethical issues by examining differing areas [8]. The clinical issues include the reaction of over-the-counter medications given to different patients who may have dissimilar genetic profiles. Some drugs behave differently in a patient who is taking multiple medications. In addition, there is the problem of privacy especially with regard to false paternity tests. One of the important social issues deals with the willingness of pharmaceutical companies to do the research,