Personalized Medicine & Race-Based Drug Development:
Addressing Minority Health Care Disparities in an Ethically
Charged Area

Michael B. Losow Esq.
PERSONALIZED MEDICINE & RACE-BASED DRUG DEVELOPMENT: ADDRESSING MINORITY HEALTH CARE DISPARITIES IN AN ETHICALLY CHARGED AREA

MICHAEL B. LOSOW, ESQ.*

Thank you. I would like to start by saying that any of the nice slides you see in here I owe directly to Doctor Francis Collins, who has just recently done a similar speech and lent me his slide show. One of the things you learn in law school is that you are supposed to be prepared, but, as you see, as I go through the slides that I put together, they are not really well designed, and I did not have quite enough time to put background time in that I was hoping to do. So, whenever you see something nice, I will probably refer to Doctor Collins again.

Before even getting into my speech, I could probably spend all my time talking about Doctor Jesty's presentation because there are so many ethical issues that are raised therein, and the FDA issues have all been in the news. Last summer an issue hit the news: the race-based development of drugs. I am going out of order of my speech now, but I do want to give you the background of how I started working on this and why this issue has become so important. Last July, one of BIO's companies, NitroMed,
was doing a clinical trial on a product called BiDil® that was geared for African Americans with heart failure. The trial was stopped because the FDA considered it unethical to give people a placebo when the product was so good. Forty three percent of the African American people using the product were recovering from heart failure, but not just surviving heart failure: they were recovering and living normal lives, being able to go back to work and do things. This was extraordinary because, in general, most heart failure products did not help African Americans. That drug was the first drug of its category to help African Americans with heart problems. When news of this hit the public, the response was not: “Wow, this is fantastic, we’re going to save more than ten thousand lives of Americans every year.” It was, “How can a company make a product for a single race?” So, that is when I started getting involved with this issue and started looking at several things. I want to address several things, including the following questions. What is race? What is race to the scientist? What is race and how do we deal with it? NitroMed’s trial, in particular, was based on probably the worst definition of race, yet they had scientific grounds for using race as a basis.

I also am going to apologize. I am going to read some of this which is the way I dislike to give presentations most of all. Maybe I should give you some disclosure. I am not just the president of this hair club for men, but I am also a member. I am a cancer survivor who was saved by biotechnology and hence I am a strong believer in this stuff. Anyway, one of the side results of chemotherapy is that my recall is not what it used to be, so that is why I am going to be relying on my notes.

We know that minorities are disproportionately affected by heart disease. They are disproportionately affected by major disease areas, for instance, heart disease, cancer, diabetes, HIV.4 We also know that timely, appropriate treatment is not often provided to minorities. I believe that biotechnology will lead the scientific revolution to identifying the best scientific treatments without regard to race, culture or socioeconomic conditions. There should be no scientific rationale for health care treatment

---

4 See Public Health: GSK, ABC Radio, and DHHS to Improve Health Among Communities of Color, AIDS WKLY., June 30, 2003, at 31 (noting that racial and ethnic minorities are disproportionately affected by HIV/AIDS, cancer, heart disease, diabetes, and asthma).
disparities. As personalized medicine becomes the norm, we must ensure that science and research include the widest range of genetic diversity that will lead to better treatments for everyone. In fact, we are at the dawn of an age of science and medical treatment where the old social constructs of race will have no place and no meaning. Different treatment can be eliminated in the practice of medicine as a result of what we are learning from genetics and the development of biomarkers, which are biological molecules that indicate a particular disease, a particular disease state or indicators of a response to treatments.

Before going into more detail, I would like to lay some groundwork, define some terms for you, and the next five slides will kind of lay out the background of some of the disparities. African American women are twice as likely to die of cervical cancer as are white women. African American women are also more likely to die of breast cancer than are women of any age or other racial or ethnic group. African American seniors are almost four times less likely than Caucasians to receive coronary bypass surgery, and African Americans are two and a half times more likely to die from heart failure than Caucasians. HIV prevalence in African American women is twenty four times that of white women, and African American men are eight times as likely as white men to be diagnosed with HIV. Latinos, Native Americans, African Americans, and certain Asian Pacific Islander groups all have rates of diabetes far exceeding Caucasians, and Hispanic Latino Americans are one and a half times more likely to have diabetes than non-Hispanic whites.

5 See Patricia Guthrie, Cancer Project Aims to Save Women’s Lives, ATL. J.-CONST., Aug. 13, 2004, at 1B (noting that “[lack of access to quality health care and private health insurance, along with other poverty-related factors, diet, lifestyle and exposure to environmental toxins are cited as possible reasons for the black-white cancer disparity”).

6 See Breast Cancer: Women Focused on the Present are Less Likely to Have Mammograms, WOMEN’S HEALTH WkLY., Sept. 18, 2003, at 38 (suggesting that learning why African-American women delay receiving a mammography might lead to more effective measures to overcome statistical disparity).

7 See Are Drugs Color Blind?, TIME, Nov. 22, 2004, at 100 (commenting that “superficial differences like skin color explain far less than was once thought”).


African American seniors are nearly two times less likely to receive treatment for prostate cancer.  

So, those statistics show clearly that disparities exist concerning race and disease. You generally hear of it and have a sense for it, but there are so many statistics out there. This is a major problem, and there are many reasons for disparities and I will get into that later as well.

What I would also like to do now is define some terms. First, personalized medicine is kind of the rage — what people are talking about. BIO, the Biotechnology Industry Organization, just had an investor's conference in New York City the past three days. At nearly every session the two issues discussed were personalized medicine and drug safety in light of the Vioxx® issues. I would also like to say, to distinguish biotechnology, that BIO is a trade association. We represent nearly a thousand biotech companies. Those include the big pharmaceutical companies, such as Pfizer and Merck, but also, small companies like NitroMed.

We like to think of biotechnology products, in general, as novel products that have a major impact. Most of our companies that have products out there started with orphan products, or drugs for diseases of less than two hundred thousand people. These are products that save lives; for instance, children with Cystic Fibrosis used to die before age ten; the average life span now is mid thirties and is ever-increasing. Another example is Gaucher’s Disease, which used to be a killer; however, there is now a product that keeps children with said disease alive to adulthood and living near normal lives. So, these are groundbreaking products. They are not kind of a Vioxx® compared to an aspirin. These are new and novel products.

So, what is personalized medicine? Let me first tell you what it is not. It is not you going into your doctor, who comes up with a specific drug to treat just you, although in certain instances there might be something similar to that. There are researchers

10 See Hon. Elijah E. Cummings, Life and Death in America’s Health Care System: Giving our Private Sorrows a Stronger Public Voice, BALT. AFRO-AMER. NEWS, March 30, 2003 (asserting that African American seniors are more likely to have lower limbs amputations due to diabetes).

11 See Expensive Drugs for Rare Illnesses Increase Pinch for State Aid Pediatric Health Care, OBESITY, FITNESS & WELLNESS WEEK, Mar. 12, 2005 (noting that median life expectancy of cystic fibrosis is thirty three years old).
looking at cancer vaccines that will take your cancer tumor and turn it into a vaccine that they put back into you, which will then kill the tumors in your system. But that is not really what most personalized medicine is about. According to Personalized Medicine Coalition, \footnote{Personalized Medicine Coalition, \url{http://www.personalizedmedicinecoalition.org} (last visited Nov. 16, 2005) (detailing mission as benefiting patients by advancing understanding of personalized medicine).} personalized medicine uses new methods of molecular analysis to better manage a patient’s disease or predisposition toward a disease. It aims to achieve optimal medical outcomes by helping physicians and patients choose the disease management approaches likely to work best in the context of a patient’s genetic and environmental profile. The question is: why do we need personalized medicine? Currently, fifteen to thirty five percent of blood pressure patients receive no benefit from blood pressure medicine that exists.\footnote{See generally Barry Meier, \textit{Health Groups Urge More Drug Reviews}, \textit{Int'l Herald Trib.}, Dec. 30, 2004, at 15 (discussing ongoing struggle of doctors to determine which drugs provide effective treatment for patients, including those targeting blood pressure).} Twenty to fifty percent of patients who need anti-depressants receive no benefit from the anti-depressants that are out there.\footnote{See generally Mark Hovit, \textit{A Shadow of Doubt: Medical Schools Give Too Much Control to Drug Firms When Testing Medications, Critics Say}, \textit{Fort Worth Star-Telegram}, Jan. 16, 2005, at A1 (suggesting that drug firm control over medication testing often minimizes results indicating that antidepressants do not work).} Doctors will not know until they give it to you whether you are going to receive a benefit from that drug being administered to you. If there is a way to identify the people who will benefit from a drug, you can then only give the appropriate drug to the appropriate person. This shows what personalized medicine can do.

Biotechnology is using newfound knowledge in genetics to produce new approaches to therapies and cures. In the not-so-distant future, our genetic profile will be a major component of health assessment and care. One key here is risk prediction. We can read your genetic profile to determine your risk for certain diseases and then give you an idea of what to do. So, you can do a colonoscopy starting at age forty; if you have a high risk for colon cancer, you can specifically avoid a high fat diet from that point on. Second, we have the phenomenon of pharmacogenomics. Under this, a doctor can provide a dose to a patient based on a particular genetic profile. So, again, for an
anti-depressant, if you know someone’s genetic profile, a doctor can give that person the right drug and the right amount of it. And we can develop new therapies, for example, gene based drugs for therapy for cancer or for heart disease.

Biotechnology seeks to understand the genetic factors of disease which can dramatically change health outcomes, while freeing us of ethnicity-based categories of evaluating risks. This is supposed to be about race-based development, but it also can dramatically change health outcomes generally. Such approaches include genetic screening programs that more precisely diagnose diseases or help physicians select the type and dose of medication best suited to certain groups of patients.

Biotechnology is developing better and targeted medical treatment opportunities. Even today, when the FDA approves a product, it is not really approving a product for everybody in that category. One example is lymphoma; there are now many types of lymphoma, so when a product is approved, for example, a radiopharmaceutical, it is radiation treatment that’s carried through a monoclonal antibody, that is a drug that goes through the system, and the radiation attacks just the tumor. It avoids full body radiation that people have had in the past and all the side effects that go with it. But it is only approved for certain types of lymphomas.

Through genetics and advances in biotechnology, we will develop drugs that are more effective to segments of the population. Drugs will be targeted toward sex and gender, recognizing differing responses to treatments. Drugs will be targeted toward race, but hopefully down the road, not race in the current social context of skin color, but in a more real meaning, geographical ancestry type of context. For example, people with East African ancestry tend to be slower metabolizers of drugs. Personalized medicine is the way we manage a patient’s disease or predisposition to a disease.

Biotechnology is using pharmacogenomics and pharmacogenetics. Pharmacogenomics is the study of all the

---

genes to determine drug behavior.\textsuperscript{16} Pharmacogenetics is the study of inherited differences in drug metabolism and your response.\textsuperscript{17} With genetic screening, we will be able to more precisely diagnose diseases and sub types. From what we learn, we will utilize a patient’s genetic and environmental profile to select the treatment in the drug therapies including the type and dose of medication. While we are decades away from a fully realized world of personalized medicine, we are already seeing the benefits.

Genetics play a role in the response to drugs as well. Oncologists now use a genetic test to determine which children with leukemia are likely to have a potentially fatal reaction to the standard dose of commonly used chemotherapy, and adjust the dose accordingly. They can test women with breast cancer to determine which patients are likely to respond to a chemotherapy drug called Herceptin\textregistered. Herceptin\textregistered is used for patients who over express the HER-2 gene. With the product Herceptin\textregistered, there is a diagnostic test that is given first, and again, the doctor can determine, only patients that over-express HER-2 will get Herceptin\textregistered.

Similarly, we have already seen gene markers that predict colon cancer and the treatment and the response for that as well. We have seen remarkable progress in preventing diseases with direct genetic links. Over the last three decades, the number of Tay Sachs cases has been slashed by more than ninety five percent thanks to genetic screening in those of Eastern European Jewish descent. Tests for liver enzymes, for liver enzyme variations critical to the metabolization of many drugs are on the way. These variations, some of which are more prevalent in Asians, other more prevalent in Caucasians, can result in overdoses and toxic reactions to common drugs.

Researchers are also looking for genetic markers that makes many African Americans more likely to respond to this experimental heart failure drug. These and other products in the


\textsuperscript{17} See Studies Have Investigated Genetic Variants and Response to Statin Therapy: \textit{Coronary Heart Disease}, HEART DISEASE WKLY, Mar. 13, 2005 (describing pharmacogenetics as “exploring genetic polymorphisms that influence response to drug therapy”).
pipeline will help healthcare providers deliver the right drug to the right patient in the right dose. So, the benefits of personalized medicine are providing people with products that will provide relief only if it's good for them. For those where it will not have any impact, you would save a lot of time, you save a lot of money, and you protect the patient from all the side effects because there is no drug that is effective that also does not have some side effects.

Before I go into the issue of race based drug development anymore, I want to give a little background on some of the industry and the impact of personalized medicine on biotechnology product development. From start up until the product is, approved, that is from the time a company submits an independent new drug application, it takes between ten and fifteen years to get approval from the FDA.18 On average, the cost of a new product is a half a billion to—a fairly recent Tufts University study said—as much as almost nine hundred million dollars to develop a new product.19 From the time that you file your IND with the FDA, your patent is running. Generally, and although everybody has twenty year patent life for any product, whether it is a widget or a drug, until your drug is approved, your patent time is running out. So, there is very limited time, between five and seven years,20 for a company that invests all this time and money to get back its money on a drug product as well as make money—as most corporations are there to do.

The new motto of biotechnology or drug development, really, is "biology over chemistry." Prior to the genome sequencing in 2000, there were five hundred proteins, enzymes, and biochemical compound targets that our companies looked at and tried to have an impact on. Since 2000, there are now ten thousand targets.

The old business model for the drug industry was creating a blockbuster drug, and then to get rich off of that. The new model is targeting or tailoring products to a specific patient group. Treatments, these drug companies hope, will cover ninety percent of the disease based on genetic profiles and ten percent will be tailored to specific patients. But we are talking about smaller and smaller subsets of the population, so you are not talking blockbuster drugs anymore that can be used on everyone. So, the question is how do you build economies of scales for these smaller markets? And, getting now into our discussion, will personalized medicine actually increase or decrease disparities for minorities?

Here, I would like to again address the race issue. How do you define race? And when you are doing drug development, in general, do you include minorities in your trials? The reality is most companies have done race-based drug development without calling it that, because minorities generally are not included in clinical trials. So, we are doing drug development for the white population – even if it is unintentional. Most of the time it is unintentional because of the high cost of clinical trials; that is one of the most costly, if not the most costly part of developing a drug product. It takes a long time to get people into clinical trials. It costs companies a lot of money to find people to do clinical trials. For a variety of reasons, minorities do not generally like to participate in clinical trials, so it costs the drug companies even more to go out and recruit them. There is also an economic disincentive because companies know that there is a difference in metabolization based on race. For example, on the classification of skin color, basically, African Americans with certain ancestry will metabolize drugs slower. The drugs might not have an impact on African Americans.

Frankly, with most heart drugs, there is even a sex-based difference in response to drugs. Most heart drugs that have been developed really do not help women, and until the 1990’s, there was no requirement that such drugs be tested on women. In fact, it was often intentionally done that women were not included in clinical trial studies. This is why we do not have the data on the value of a lot of those earlier drugs for women. But if a company knows that they are going to include minorities in drug trials, this inclusion may devalue the end result because it will have
less of an impact on the whole group that they are looking at. Then a company might worry that the FDA will not approve the drug because it will not be statistically significant enough for the FDA to approve. This is opposed to, as I mentioned before, BiDil® where forty-three percent of the African Americans saw actual life-saving improvement from the heart drug. Forty-three percent is an enormous percentage which is why the FDA stepped in and said this is something really good. They are still going through the process and that drug will be up for approval this June, actually.

So, these two women, Doctor Royal and Doctor Dunston, from the Howard University Human Genome Project, stated that knowledge from the human genome project and research on the genome variation increasingly challenged the applicability of the term “race” to human population groups, raising questions about the validity of inferences made about race in the biomedical and scientific literature.21 And, again, most of what they are referring to is skin color race as we define in society when we walk down the road. We notice, “Oh, that person is Asian, that person is Black,” and they’re categorized in that race.

As background, Howard University has had its National Human Genome Center22 investigating and sharing their DNA sequence variation findings and the implication for treatment of diseases common in African Americans. They are creating a database of genetic material that they hope will eventually include seventy-five hundred individuals. Just as an aside, as we look at genetics and as we do research, one of the reasons Howard decided to do this was to make sure that African American genetics were profiled. Because of the industry and the government requirements in Japan, we do know at least there will be a fair amount of profiling of Asian genetics, but


22 See National Human Genome Center at Howard University, Vision Statement, available at http://www.genomecenter.howard.edu/intro.htm (last visited Nov. 16, 2005) (detailing mission “to explore the science of and teach the knowledge about DNA sequence variation and its interaction with the environment in the causality, prevention, and treatment of diseases common in African American and other African Diaspora populations”).
there was no source collecting this kind of data on African Americans. In fact, before you hear about the issue of stem cells being developed, you are going to hear a lot more about stem cells and the lines approved by President Bush, the sixty some odd lines that were approved for federal funding of research. Within those sixty some odd lines, not one of them had been developed from minorities; therefore, one of the concerns that folks at Howard had is that we get to know the total variants of human diversity.

So, "race," as most people think of it, is a social construct. It is skin color, but from a scientific perspective, the true genetics really needs to be more geographical ancestry. So, East Africans are known to be slower metabolizers. There is a community in Utah of very religious Catholics who were exhibiting diseases of Eastern European Jews. A genetic and genealogical study was done, which found that most of those families there actually had Jewish roots because their families had converted to Catholicism during the Inquisition. Such history of conversion was never passed along through the families, and it was not until they all got sick with these diseases here in Utah, that they were able to go back and find that there was a genetic link; again, it is a geographical basis.23

There are many causes for health care disparities. Many of you may know of the Tuskegee syphilis studies,24 which lead to strong distrust of science, scientists, and the government. This is also one of the major reasons why African Americans do not participate in drug trials. Culture, diet, socioeconomic status, poverty and unemployment lead to healthcare disparities, access to healthcare, exposure in the environment, education, and discrimination. When minorities go to doctors, even minority doctors, they often find that there is discrimination in the approach and treatments. Stress is a major factor and, in fact, studies have shown that those who live with discrimination on a

---


regular basis live with higher levels of stress. That adds to more health care disparities.\(^{25}\)

Dr. Loberg, who is the head of NitroMed, had told me that he had a very hard time with his study on African Americans for BiDil\(^{\circ}\). He had over a thousand people in the trials. This was the largest trial on any heart failure drug for African Americans. Prior to this, the largest number of minorities in a cardiology clinical trial was seventy in a trial of six thousand patients. In this case, with the help of many other groups, including the Association of Black Cardiologists,\(^{26}\) the National Medical Association,\(^{27}\) which represents black doctors, even the Congressional Black Caucus,\(^{28}\) the NitroMed trial was able to enlist over a thousand patients and they did not lose one of them. There was one hundred percent compliance.

So, the question is, with the human genome knowledge, can we eliminate disparities? Yes so long as we focus on complex diseases of the least healthy groups, and that study provides insights into the causes of disparities, and that the benefits are shared with the vulnerable populations. The message then goes out to the minorities that science and medicine values the human variation as an instrument of self-discovery. If we do not do that, according to Dunston and Royal, we will exacerbate these disparities. The benefits will be realized for only the affluent; research is only for medical treatment of rare diseases. The message becomes distorted and tells the minority groups that they are inferior. Also, the science and the genetic knowledge will just exacerbate the disparities, if used to further an image of a single physical ideal of the typical white patient.

\(^{25}\) See David Williams, Discrimination, Oct. 1998, http://www.macses.ucsf.edu/Research/Psychosocial/notebook/discrimination.html\#Top (last visited Nov. 16, 2005) (indicating correlation between stress levels experienced by minority individuals and negative physical and mental reactions including increased blood pressure levels).


There are other public policy and ethical issues. There is a genetic non-discrimination bill that passed the Senate,\textsuperscript{29} and that will probably not pass the House. And I will end with a quote from Dr. Collins just as a way of thanking him for his slides: "Genetics is teaching us that there is no scientific basis for drawing sharp boundaries around ethnic or racial groups. At the DNA level, we are all ninety nine percent the same, all of us."\textsuperscript{30}

\textsuperscript{29} See Kate Dalke, \textit{Genetic Nondiscrimination Bill Passes U.S. Senate}, available at http://www.genomenewsnetwork.org/articles/10_03/s1053.shtml (last modified Oct. 15, 2003) (reporting that Senate unanimously passed the bill).

\textsuperscript{30} See Lauren Crowley, Woodrow Wilson International Center for Scholars, \textit{Human Genomics: Our Shared Inheritance}, http://wwics.si.edu/index.cfm?topic_id=1414&fuse action=newsitem&news_id=2150 (last visited Nov. 16, 2005) (discussing summary of Dr. Collins's speech about genomics at the Wilson Center Director's Forum, noting that human DNA is 93.9% the same from person to person).