2011 Presidential Address: From Classroom to Courtroom to Clinic—Closing the Gaps in Human Genetics Education[1]

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In this address, I will talk about some current gaps in human genetics education. I will focus on two quite different areas in which we need to improve the knowledge of our fellow professionals and the general public: the use and interpretation of genetic testing and the understanding and appreciation of the science of evolution. I will conclude with an example in which these and other gaps are being closed through an educational program for the judiciary.

Our field has seen tremendous progress during the past two decades. The number of Mendelian conditions for which a molecular basis has been identified has increased from fewer than 200 in 1990 to more than 3,000 in 2011.[1] This in turn has led to progress in the identification of disease-causing mutations, genetic testing, and the diagnosis of genetic disease. The number of diseases for which genetic testing is available has increased from about 100 in 1993 to nearly 2500 today (see Web Resources).

This explosion of information has produced an education gap among health-care professionals. A recent survey of 10,000 U.S. physicians showed that nearly all of them agreed that genetic variation influences drug therapy.[2] Yet only 26% reported that they had education in the use of genetic testing. Only 10% felt that they were able to put pharmacogenetic testing to good use. This gap in understanding is accentuated by the rise of direct-to-consumer testing, in which consumers can receive information about ancestry, disease-associated variants, and possible risk of disease for more than 400 health-related conditions.[3] They can learn about potential sensitivity to drugs such as Warfarin, Clopidogrel, and Abacavir. Information is also available about approximate relative risks for developing diseases such as age-related macular degeneration or type 2 diabetes. Increasingly, health-care professionals are being asked to interpret these results for their patients.[4]

To better understand the results of genetic testing, we might find it useful to make some comparisons. A loss-of-function mutation in *APC* can confer a lifetime risk of colon cancer of virtually 100%, compared with a population risk of approximately 5% (Figure 1).[5] In contrast, a variant in *TCF7L2*, which has the strongest known association with type 2 diabetes risk, increases the relative odds of developing diabetes by roughly 50%[6] but increases the absolute risk by only a few percent. This distinction must be communicated clearly to health-care professionals, consumers, and payers. It is also important to realize that risk results, especially for common diseases, are often based on association studies that have not been consistently replicated.[7] Furthermore, these results can vary significantly among populations.[8] In fact, the great majority of genome-wide association studies have been carried out on populations of European ancestry, and their results cannot necessarily be extrapolated to other populations.[9]

Another important issue is the sensitivity and specificity of genetic tests. For common diseases in which most of the genetic causation is presently unknown,[10] the sensitivity of a genetic test is necessarily low. In many cases, the associated variants are also common in the general population, and thus the specificity is not very high either (Figure 1). Health-care professionals, as well as consumers, need to

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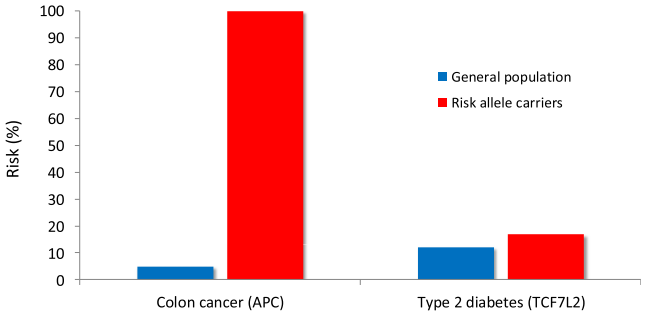

Figure 1. Risk of Developing Colon Cancer or Type 2 Diabetes for Individuals Who Carry a Disease-Causing Variant in *APC* or *TCF7L2*, Respectively
Risk (%) for variant carriers is compared with risk in the general population.

be aware of the limitations, as well as potential benefits, of genetic testing.

It is interesting that new technology, such as genetic testing, is often overrated, whereas accepted science is often underrated and under-recognized. The latter is certainly true of the science of evolution. A well-known survey, conducted in 34 different countries, reported the proportion of the public who accept the science of evolution.[11] Although acceptance is quite high in many European countries, it remains low in the United States. Another recent survey showed that 58% percent of Americans believe that evolution *and* creationism should be taught together in our public schools.[12] And 38% think that creationism should be taught *instead* of evolution in our public schools.

These rather alarming statistics can be attributed, at least in part, to several common myths about the science of evolution. I'd like to examine and deconstruct each of these myths.

One is that evolution is not testable or falsifiable. This myth itself can be falsified by considering the age of the Earth. If our planet were only six thousand years old (or only ten million years old), there wouldn't have been enough time for evolution to do its work, and the theory would be falsified. Charles Darwin was well aware of this. In his characteristically careful prose, he stated, "I am greatly troubled at the short duration of the world according to Sir W. Thompson [Lord Kelvin], for I require for my theoretical views a very long period *before* the Cambrian formation" (Charles Darwin, in a letter to James Croll, 31 January, 1869). We now have abundant evidence, of course, that the Earth is old enough to accommodate the evolution of life in its many forms. Many other such examples can be cited. Evolutionary theory has been tested rigorously, over and over again, using the fossil record and genetic evidence. The evidence has consistently and overwhelmingly supported the theory of evolution.

We can also test a competing theory, the theory of "intelligent design" (formerly known as creation science). Intelligent design hypotheses are readily falsified by many features of the human body itself.[13] Our lower backs, for example, are notoriously prone to pain and failure. This is inconsistent with intelligent design but easily explained as a consequence of evolution for bipedal locomotion. The circuitous path of the mammalian vas deferens, ascending from the testes and looping around the ureters before descending back to the penis, is a vivid and rather comical example of unintelligent design. But it can be explained by evolutionary opportunism as it became necessary for the testes to migrate outside the body to maintain a cool temperature in warm-blooded mammals. Nature abounds with similar examples in which we observe not the purposeful signature of an intelligent designer, but instead the opportunistic, and sometimes even whimsical, process of evolutionary tinkering.[14,15]

Another common myth is that we humans have stopped evolving. In fact, genetic studies provide abundant evidence of ongoing human evolution: rapid evolution of malarial resistance, convergent evolution of hereditary lactase persistence in African and European herding populations, evolution of genes that affect skin pigmentation, and the evolution of genes that affect adaptation to high altitude.[16] As our ability to scan whole human genomes for adaptive variation increases, we will doubtless discover many additional examples of the continuing evolution of our own species.

A third myth is that the theory of evolution is controversial among scientists. In a 2006 opinion poll, 28% of Americans responded that scientists disagree seriously about evolution; 10% were "not sure."[12] A former US president stated just several years ago, "Well, the jury is still out on evolution." This myth is especially concerning because of its obvious corollary that we should be "teaching the controversy" in our schools. So what do scientists (the jury) actually think about evolution? A 2009 AAAS survey of more than 2,500 scientists showed that 97% agree that "humans and other living things have evolved over time." This level of agreement in the scientific community is unusual, to say the least. The jury, in fact, is "in," and the verdict is unanimous.

A final myth is that the study of evolution has no practical value. In fact, evolutionary principles have a wide variety of practical applications. We use them in the management of wildlife populations; they are used in the forensic genetic analysis of thousands of criminal cases each year. Evolutionary principles are also critical in the analysis of genomic data. They figured prominently in the designs of the 1000 Genomes Project,[17] the International HapMap Project,[18] and in countless genome-wide association studies. Evolutionary principles such as cross-species conservation (to identify functional variants in sequence data) and linkage disequilibrium (to design association studies) are applied routinely. And evolution is used directly in designing vaccines and drugs. For example, aptamers are created by mutating sequences and then subjecting them to rounds of in vitro selection (SELEX; systematic evolution of ligands by exponential enrichment). By mimicking the process of natural selection, this process has led to a number of drugs that are in phase II and phase III trials, as well as at least one FDA-approved drug for the treatment of eye disease.[19]

All segments of society can benefit from education about these and many other aspects of human genetics. Many or most ASHG members have participated in these educational endeavors, and I will conclude with a brief description of an area in which I and many ASHG colleagues have devoted some effort: the education of our judiciary. Much of this work has been done through a non-profit organization, ASTAR (Advanced Science and Technology Adjudication Resource Center). In two- to three-day training sessions, judges learn about a variety of genetic topics relevant to their profession: DNA and forensics, genetic testing, genetically modified foods, gene patenting, evolution and creationism, stem cells and cloning, and behavior genetics.

This last topic has generated substantial interest among judges, in part because of recent studies that appear to show, at least under some circumstances, an association between antisocial behavior and variation in genes that encode monoamine oxidase A (MAOA) and the serotonin transporter.[20,21] Genetic test results for these loci have been introduced as evidence of diminished capacity in more than a dozen murder cases in the United States.[22,23] In a high-profile case in Italy, an appeals court reduced the sentence of a convicted murderer in part because of his MAOA and serotonin transporter genotypes.[24] These developments present significant concerns to judges, who are required increasingly to act as the gatekeepers of courtroom evidence. They need to understand at least the basic principles that underlie the genetic evidence presented to them. Although our efforts in judicial education are necessarily brief and incomplete, they do help to demystify our science and to make it more accessible.

Explaining our science clearly to lay audiences is a challenge, but it presents an opportunity to educate, to enlighten, and sometimes even to inspire. In doing so, we will help to close the gaps in human genetics education.

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Web Resources

The URL for data presented herein is as follows:

Gene Tests: http://www.ncbi.nlm.nih.gov/sites/GeneTests/

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