

# Commentary: To Genotype or Not to Genotype? Addressing the Debate Through the Development of a Genomics and Personalized Medicine Curriculum

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## Abstract

As technologic innovation helps broaden and refine our knowledge base of genetic associations, a growing interest in translating these genetic discoveries to clinically useful laboratory tests has given rise to the potential of personalized medicine. To fully realize this potential, medical schools must educate trainees on genetic and genomic testing in clinical settings. An emerging debate in academic medical centers is not about the need for this education but, rather,

the most effective educational models that should be deployed. At Stanford School of Medicine, several proposals to offer personal genotyping in the educational curriculum argued that learning genetics and the attendant cutting-edge molecular techniques would be more powerful and sustained if students were applying their knowledge to their personal genotypes. Given the complex ethical, legal, and social issues involved in implementing such a

program, a schoolwide task force was formed to evaluate the risks and benefits of offering personal genotyping to students and residents. In this commentary, the authors discuss the salient issues raised by the task force and describe the safeguards adopted into the ultimate approval and implementation of the course, which included the opportunity for students to analyze their own genomes.

The successful completion of the Human Genome Project,<sup>1</sup> followed by the International HapMap Project<sup>2</sup> and the ongoing 1,000 Genomes Project,<sup>3</sup> have provided a map of the human genome accompanied by an expanding catalog of human genetic variation. Much of this progress can be attributed to the development of DNA microarrays designed to interrogate hundreds of thousands of single-nucleotide polymorphisms (SNPs) across the genome. Although SNP arrays have powered nearly 1,000 genome-wide association studies of approximately 150 traits to date, they offer a relatively low-resolution view of variation in the human

genome, focusing almost exclusively on common variants in the population. Even though this approach has yielded thousands of novel genetic associations, the proportion of heritability explained by these loci remains low for most traits (i.e., less than 10% for most complex traits<sup>4</sup>). In hopes of explaining more of the heritability of common disease, recent focus has been directed toward the investigation of rare variants,<sup>4,5</sup> where platforms for targeted sequencing and whole-genome sequencing are poised to supplant SNP arrays as the dominant technology. These high-resolution technologies also allow the study of structural variation in the genome, such as copy number polymorphisms and inversions, which may account for a substantive fraction of missing heritability. Still, additional determinants of heritability, such as epigenetic alterations, remain largely overlooked in studies performed to date.

As technologic innovation helps broaden and refine our knowledge base of genetic associations, a growing interest in translating these genetic discoveries to clinically useful laboratory tests has given rise to the potential of personalized medicine. Although challenges still remain in the interpretation and application of single-gene tests, the incorporation of personal genomes into clinical medicine is emerging.<sup>6</sup> Already,

several companies offer direct-to-consumer (DTC) genotyping, and the affordability and resolution of these technologies continue to increase. At the same time, the potential widespread availability of DTC genotyping raises a number of ethical, legal, and social issues.<sup>7-9</sup> These issues have prompted recent deliberations by the Food and Drug Administration (FDA) and the United States Congress, as well as a report by the Government Accountability Office concluding that some DTC genomics companies have been providing misleading results to their customers.<sup>10</sup>

Despite current uncertainty about the regulatory landscape for commercial genetic testing, physicians must equip themselves for a future that includes a panoply of genetic laboratory tests and an increasing number of inquiries from patients about the interpretation of personal genetic information. Medical and health sciences education programs must prepare health care workers for the continuing deluge of scientific publications and anticipated questions from the public, including whether such testing should be pursued and how results should be interpreted.<sup>11</sup> An emerging debate in academic medical centers is not about the need for this education but, rather, the most effective educational models that should be deployed.<sup>12</sup>

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At Stanford School of Medicine, this debate was precipitated in the summer of 2009 by several proposals to offer personal genotyping in the core curriculum for our medical students, graduate students, and internal medicine residents. The principal rationale for including personal genotyping in the curriculum was an assumption that learning genetics and the attendant cutting-edge molecular techniques would be more powerful and sustained if students were applying their knowledge to their personal genotypes. However, numerous faculty leaders, after becoming aware of plans to offer personal genotyping to students, expressed concern—not about the educational value of participatory learning, but about a wide range of ethical conundrums. Some of these are relevant to anyone who elects to undergo personal genotyping. However, the vulnerability of students—including the unintended coercion that might result from peer pressure or student perceptions of faculty expectations—raised additional questions and concerns. We recognized that it was critical to engage in more discussion and debate about the potential benefits and risks of the proposed curricular strategy before moving forward with its implementation.

The dean of the School of Medicine (P.A.P.) therefore put on hold the plans for education-related genotyping in 2009 and appointed the senior associate dean for medical education (C.G.P.) to chair a schoolwide task force made up of basic science and clinical faculty, including psychiatrists, biomedical ethicists, genetic counselors, legal counsel, and medical students. The principal charge to the task force was to evaluate the risks and benefits of offering personal genotyping to students and residents, as part of any course offered at the School of Medicine. Over the course of a year (2009–2010), the task force engaged in a spirited debate regarding the specific issue of student genotyping. Issues were raised about how anonymity and confidentiality could be ensured, and the potential inadvertent impact of the results of student testing on family members was discussed. The task force also discussed the need for genetic counseling (along with the resources to cover this service) for individuals receiving news that might add to the already-considerable stress many students experience by the very nature of their work and study demands. Task

force members also expressed concerns about real or perceived conflicts of interest because some of our faculty have relationships with two California-based companies involved with genotyping (23andMe and Navigenics).

The task force then focused its deliberations on a course that was proposed by one of our current MD students who completed his PhD in genetics (K.S.). The proposed eight-week course was designed for medical and graduate students and included the opportunity for students to analyze their own genomes. The overall objective of the course was to provide students with an appreciation of the scientific underpinnings of genomics and its relevance to the future of medicine. Course work also was designed to reflect on the accompanying scientific, ethical, legal, and policy limitations and challenges. Learning formats included lectures, journal clubs, and hands-on workshops where students would perform data analysis exercises on their own genomic sequence data to explore associations with disease, drug response, and ancestry. Curriculum details are available online at <http://gene210.stanford.edu>. In this commentary, we discuss the salient issues raised by the task force and describe the safeguards adopted into the ultimate approval and implementation of the course.

## Weighing the Issues

### Coercion

Task force members were concerned that students, legally considered a “vulnerable population,” might feel coerced into undergoing personal genotyping because they might deduce that refusal to do so could adversely affect their performance evaluation. We took several measures to mitigate this concern. The course was designed as an elective rather than a required medical school class. Genetic testing was optional for those enrolled in the course. For classroom exercises, all students were given the opportunity either to use their personal genotype data, if available, or publicly available genotype data from any of 12 anonymous individuals. Finally, each student’s personal decision to undergo genotyping was confidential, and course instructors were “blinded” as to which students opted to be personally genotyped.

## Data confidentiality

The task force was determined to ensure that student genotype data remained confidential. Only information derived from the data (e.g., predictions of height, optimal warfarin dosing, or genetic ancestry) were shared and presented in aggregate to the class. Students’ genotype data, if available, were kept locally on personal laptop computers, and the students were specifically directed not to publicly disclose their genotypes.

## Informed decision making

Although personal genome scans are currently available directly to consumers, this service remains the subject of intense debate among stakeholders, including the FDA and Congress.<sup>7,8</sup> We felt it was critical to ensure that students were aware of this controversy and that they received a broad introduction to all the issues surrounding personal genotyping prior to deciding whether to undergo genotyping. The first three class sessions were dedicated to discussing the risks, benefits, uses, and limitations of personal genotyping, as well as attendant ethical, legal, and social issues. As part of this introductory information, students screened and discussed *In the Family*, a documentary chronicling a woman’s struggle to cope with her breast cancer genetic test results.

## Financial considerations

Despite the declining price of genotyping, the current cost (~\$400 per test) is still substantial on a student budget. We sought to provide financial support for students who elected to undergo genotyping, while at the same time avoiding the financial inducement of providing a “free” test. Accordingly, students who elected to be genotyped were required to pay \$99. This amount was chosen because companies had offered this level of discount to the public earlier in the year, and students had indicated their willingness to pay this amount in a survey previously administered at our institution.<sup>13</sup>

The task force also expressed concern that our school’s purchase of the service might be perceived as endorsement of the value of personal genotyping in general, and of the testing company specifically. Furthermore, given the possibility of some of our faculty having a personal or financial interest in

the selected company, concerns about conflicts of interest were raised. To mitigate any real or perceived conflicts of interest, we gave students the choice of purchasing services from either of the two companies licensed to offer such testing in California. Both companies had existing educational rates for their genotyping services, and the Department of Genetics paid that rate for each participating student, less the \$99 student co-pay. Finally, instructors in the course disclosed specific conflicts of interest, if any, at the start of each lecture.

### Counseling

Safely and effectively managing interpretation of the genotyping results, especially unexpected disease susceptibility and paternity findings, was a major concern expressed by task force members. The tendency of medical students to diagnose themselves with diseases they are studying, sometimes referred to as “medical studentitis,” is a recognized phenomenon.<sup>14</sup> How knowledge of personal predisposition to disease would affect student reactions is unknown. To address this concern, we provided robust personal genetic counseling and psychological support services. At the time of our course offering, one of the companies offered unlimited access to its in-house genetic counselors, before and after undergoing testing, at no additional cost; the other offered genetic counseling through a partnership with an independent genetic counseling provider.

To further minimize the risk of students experiencing undue anxiety from test results, several faculty from our Department of Psychiatry and Behavioral Sciences offered to be available to students for private counseling as an additional layer of support beyond genetic counseling. Counseling provided by all parties was confidential, and a student’s decision to seek counseling was private.

### Research

Although using “self-testing” as a technique to engage learners in the subject of their studies has been used in medical education,<sup>15–17</sup> offering medical students the opportunity to analyze their own genome sequence is a novel application of this technique.

Accordingly, formally evaluating the pedagogical effectiveness of this practice seems warranted. We thus obtained approval from our institutional review board to conduct two research studies. The first was a survey study administered before and after the course. The survey was designed to examine whether there are differences in educational outcomes between students who did or did not elect to be genotyped. The second research initiative used a qualitative case study design that explored whether student attitudes, expectations, and experience with personal genetic information changed over time and whether personal genotyping affects individual behavior.

### To Genotype or Not to Genotype? Beginning to Answer the Question

The discussion and debate carried out by our task force played a pivotal role in shaping the development and ultimate implementation of our course. Although some task force members remained opposed to the student genotyping option included in the course, the majority ultimately felt that the necessary safeguards had been incorporated.

We believe that it is imperative that medical students and other trainees are well educated about this rapidly emerging area of medicine and science. As the cost of genotyping and whole-genome sequencing continues to decline, the era of the affordable personal genome will likely become a reality. Patients will have access to these technologies through commercial vendors or their medical providers. As educators, we must educate our students and the medical community about the interpretation, limitations, and impact of genetic data in clinical settings. This field will continue to develop and evolve, and we must ensure that our students understand how their patients and their families could profoundly benefit—or suffer—from such information.

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