

Teaching with single nucleotide polymorphisms: Learning the right lessons

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The identification of gene variants associated with an increased risk for specific medical conditions has accelerated over the past 5 years and with it the hope that genomic tests will offer expanding opportunities to improve clinical care. To the extent that they do so, health care providers must be prepared to use them appropriately. Accordingly, medical geneticists are concerned to ensure that medical students, residents, and physicians in practice are appropriately prepared for the growing role of genomics in clinical practice.

A potentially engaging and informative strategy that has captured the attention of many educators is classroom use of the genomic profiling tests now being offered directly to consumers by several companies. In this issue, a multidisciplinary faculty group at Tufts describe their experience developing this idea.¹ They envisioned a program in which medical students had the opportunity to undergo genomic profile testing, the results of which would then be used as instructional tools. This approach was seen as a way to introduce medical students to both the excitement and the complexity of emerging genomic testing. But the faculty also wanted to identify and address ethical concerns in a prospective manner; their article in this month's issue reports their effort to do so, and how their educational program changed as a result.

Preliminary discussions by the faculty with their Institutional Review Board indicated that the use of personal genomic profiles would be viewed as human subjects research, requiring informed consent of participating students. This judgment took into account the experimental nature of the testing process, the unknown risks and benefits, and the vulnerability of students offered a testing program by their teachers. To avoid the complication of informed consent, the plan was changed to a course using anonymous personal genomic data, provided by one of the companies offering direct-to-consumer (DTC) testing. The course plan also incorporated discussion of certain ethical concerns associated with personal genomics, including the potential for psychological harm from risk information, issues of privacy and confidentiality, and the family implications of some test data.

In parallel to the medical student course, several faculty accepted an offer of free genomic profiling from the same company that provided the anonymous test data. This process revealed some of the potential outcomes of such testing: one faculty member received results that had implications for family members, another received results indicating he is at increased risk for glaucoma. In the latter case, the faculty member consulted a glaucoma specialist, who is described as lacking “the

education to translate testing results into improved clinical practice.” Applying general clinical reasoning, the specialist suggested that the faculty member undergo annual glaucoma screening.

Although the article describes a commendable effort to devise a genetics course that is timely, exciting, and ethically informed, the glaucoma example points to a problem that seems to have been overlooked by the course instructors: the reality that there is no established clinical utility for information about genetic risk for glaucoma. We lack the outcome data to know when such information is clinically beneficial or how it might be used to improve health. Indeed, the US Preventive Services Task Force found little evidence that early detection of glaucoma (much less identification of increased risk for the condition) reduces vision impairment.² Moreover, as a recent investigation by the Government Accountability Office elegantly demonstrated,³ the same DNA sample sent to different purveyors of DTC genetic testing returns wildly different risk results, demonstrating the field's current inability to combine results to determine an individual's net risk of disease, undermining claims of clinical validity.

The anticipated benefits of personal genomics are based on the assumption that benefits of screening or other early interventions will be greater in people with a higher a priori risk—but empiric data are needed to establish such recommendations. A test that is of questionable clinical validity and no demonstrated clinical utility in the general population may perform equally poorly when applied to various risk-stratified subsets of that population. That is, a useless test may simply be a useless test. The glaucoma consultant did not lack education; rather, she lacked evidence and had the wisdom to perceive that fact. Her choice to recommend annual glaucoma screening is logical and reflects a physician's instinct to respond when presented with risk information. However, as she was undoubtedly aware, the increased screening could result in higher medical costs (in the broadest sense of the term) without discernible medical benefit. The medical concern here is the uncritical assumption of a test's potential utility in the absence of any evidence in support of its use and the corollary that test use in these circumstances represents a waste of health care resources. The ethical concern is with the use of tests lacking clinical utility as pedagogical tools. Making such a test the focal point of a course is likely to be viewed by students as an endorsement of testing. This approach may interfere with the difficult task of getting students to focus on evidence and develop the (often counter-intuitive) critical analytic skills they will need throughout their careers in assessing medical innovation.

Interestingly, the authors report negative feedback from their students' regarding the inclusion of a course lecture taught by someone with a financial interest related to personal genomic testing. The course directors were right to disclose this salient conflict; as they note, the subsequent feedback underscored the importance of providing students with ample time for the full discussion of such issues. However, it is worth noting that another conflict of interest—arguably more important—was not addressed in planning the course. The course benefitted from the

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complimentary provision of anonymous test results from a company with a commercial interest in selling tests. Seven faculty members also received free testing. The authors noted that educating future physicians is part of the company's business plan but apparently did not note the uncomfortable similarity to the deployment of drug representatives. In medical schools around the country, drug detailing is now raising concern. Both the American Association of Medical Colleges and the Institute of Medicine have recommended sharply curtailing student contact with drug company representatives,^{4,5} because of the questionable message it sends to students, and many medical schools have enacted policies limiting such contact.⁵ The same concern applies to DTC genetic tests.

Medicine and the for-profit world are inexorably intertwined, producing both benefits and problems. On the positive side, the profit motive can harness entrepreneurial fervor, spur innovation, and generate efficiencies, all in the ultimate service of patients. However, if not properly channeled and made transparent, inherent commercial conflicts of interest can divert focus from the unbiased application of medicine, to our patients' detriment. In this context, medical educators have an obligation to ensure that medical students do not confuse information (or products) provided to support a business interest from material developed solely to enhance their education. To the extent that educators see a need to include DTC personal genomics in the medical genetics curriculum, they may want to seek help from colleagues with expertise in medical marketing and evidence-based medicine to ensure a balanced presentation.

Ultimately, the idea of using personal genomics as a focus for medical education raises arguments against "genetic exceptionalism." In our understandable impatience to apply exciting genomic technology to the care of patients, spur interest among students in our field and prepare them to practice "genomic medicine," we must hold genetics to the same high standards—both ethical and clinical—that we expect of any medical discipline. And we should start with our training obligations. The best lesson medical students can learn about personal genomics is that it, like all innovative medical technology, must be rigorously assessed to determine its benefits and harms, and that responsible physicians must require such evidence in pursuit of their ultimate goal of serving their patients.

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