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DNATwist: A Web-Based Tool for Teaching Middle and High School Students About Pharmacogenomics

DS Berlin[1], **MG Person**[1], **A Mittal**[1], **MA Oppezzo**[2], **DB Chin**[2], **B Starr**[1,3], **TE Klein**[1], **DL Schwartz**[2], and **RB Altman**[1,4]

[1] Department of Genetics, Stanford University School of Medicine, Stanford, California, USA

[2] School of Education, Stanford University, Stanford, California, USA

[3] Tech Museum of Innovation, San Jose, California, USA

[4] Departments of Bioengineering and Medicine, Stanford University, Stanford, California, USA

Abstract

DnaTwist is a Web-based learning tool (available at http://www.dnatwist.org) that explains pharmacogenomics concepts to middle- and high-school students. Its features include (i) a focus on drug responses of interest to teenagers (e.g., alcohol intolerance), (ii) reusable graphical interfaces that reduce extension costs, and (iii) explanations of molecular and cellular drug responses. In testing, students found the tool and topic understandable and engaging. The tool is being modified for use at the Tech Museum of Innovation in California.

Over the past decade, we have amassed a staggering wealth of genetic data. In 2003, the Human Genome Project provided an essentially finished sequence of the 3 billion bases that compose the human genome. More than 17 million areas of interindividual DNA sequence variation have been identified.[1] Drawing on these discoveries, direct-to-consumer companies provide DNA scans of more than 600,000 genetic polymorphisms for as little as $400, and others sell targeted tests to assess specific disease risk or traits, predict drug response, or provide ancestry information. Several individuals have recently had their entire genome sequenced, including James Watson,[2] Craig Venter,[3] and Stephen Quake.[4] Sequencing costs have plummeted from the original $2.7 billion of the Human Genome Project. One company plans to launch a $5,000 human genome–sequencing service within the next year.[5] With a doctor's prescription, an individual can have his or her entire genome sequenced.[6] Health-care organizations such as El Camino Hospital and Palomar Pomerado Health (both in California) now offer their patients genetic testing services.

Updating genetics education for the twenty-first century

Given the powerful applications and implications of genetic testing, it is important to educate the public.[7] Current K–12 curricula cover only basic genetic background information such as Mendel's experiments with peas and the gene-driven inheritance of traits, the Central Dogma—genetic information flows from DNA to RNA to protein, and a little about the structure of these macromolecules. Although these provide an essential foundation, curricular materials should be extended to help students consider consumer

Correspondence: RB Altman (russ.altman@stanford.edu).

CONFLICT OF INTEREST

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genomics questions and opportunities, including the following: What are the risks and benefits of having a DNA scan? Should I have my entire genome sequenced? What do the results mean, and are they actionable? What are the implications for my family members? How private are my genetic data? What are the repercussions of voluntarily sharing my data with others?

Online tools: cost-effective and scalable

Drawing on our work on the database resource, the Pharmacogenomics Knowledge Base (PharmGKB; http://www.pharmgkb.org), we initiated DNATwist for genetics education. Pharmacogenomics is the study of how genetic variation influences drug response, and it provides a useful domain for introducing gene–environment interactions. Students' conception of genetics can be expanded beyond the simple mapping of a gene to a single physical trait or disease. When one considers the gene as one player out of many, it is easier to understand that the effects of one gene can be modulated by others, and that the environment also contributes to shaping an organism's phenotype. The "nature vs. nurture" debate morphs into the "nature and nurture" interaction, with both genetic and environmental factors contributing to the manifestation of phenotypes. Pharmacogenomics can introduce these ideas through such interesting and relevant examples as the genetic underpinnings of alcohol abuse.

DNATwist is an online resource that has the potential to reach many people at low cost. It emphasizes several "big ideas": (i) genetic differences can cause obvious variations (e.g., blond vs. black hair), but sometimes it takes interaction with the external environment to distinguish interindividual differences (e.g., differences in drug response that manifest following drug exposure), (ii) studying a gene product in its biochemical context interacting with other players, we can sometimes understand how genetic variation affects gene product function, resulting in differences in observable traits, and (iii) differences in the distribution of genetic variants help in the prediction of whether an individual from a particular population carries a given variant, with implications for the prediction of disease risk, drug response, and other traits. Although the ethical, legal, and social implications of genomics are also important, we currently do not address these directly.

Pedagogically, the DNATwist interface follows several design guidelines to engage and support learners, including (i) visual representations of scientific content, (ii) select process animations, (iii) interactivity with embedded goals, (iv) high-level simplicity with progressive deepening, and (v) navigation structures that reinforce levels of explanation. To provide users with the experience of using resources similar to those used by scientists, the software includes simplifications of the online tools and databases used by experts, such as the University of California Santa Cruz Genome Browser (http://genome.ucsc.edu/cgi-bin/hgTracks?org=human), the National Center for Biotechnology Information Map Viewer (http://www.ncbi.nlm.nih.gov/mapview/map_search.cgi?taxid=9606), and the Allele Frequency Database (http://alfred.med.yale.edu).

The design elements of DNATwist permit reuse for many instances, but the first instantiation focuses on the role of an aldehyde dehydrogenase 2 (*ALDH2*) variant, *ALDH2*2*, in causing alcohol-intolerance symptoms. Most students have heard of alcohol and its gross effects, in contrast to their lack of familiarity with many prescription drugs, and it is an interesting story. *ALDH2*2* shows a striking population-specific distribution, occurring only in individuals of Asian descent. Individuals who carry one or two copies of the loss-of-function *ALDH2*2* allele are alcohol-intolerant, with an inability to efficiently convert acetaldehyde, a toxic alcohol metabolite, into acetate, which is nontoxic and can be

cleared from the body (reviewed in ref. 8). The DNA sequences of the *ALDH2*2* allele (which encodes a nonfunctional protein) and the *ALDH2*1* allele (which encodes a fully functional protein) differ at only one nucleotide, resulting in a single amino acid substitution in the protein.

DNATwist comprises three linked "knowledge portals" to visually represent the scientific content: (i) the Chromosome Cruiser, (ii) the Pathway Portal, and (iii) Gene World. The Chromosome Cruiser locates the gene of interest on a visual layout of the human genome, pinpoints the genetic variant within the gene, and indicates the DNA and protein sequence of the alleles. Students gain a visual understanding of the specific difference between *ALDH2* variants and how they lead to differences in its protein product. The Pathway Portal (Figure 1) provides a "systems" view of the drug interaction with the human body, illustrating the passage of alcohol through the human body and the biochemical pathway through which the human body transforms alcohol. An interactive simulation shows how ALDH2*2 influences alcohol metabolism to produce alcohol intolerance. Gene World (Figure 2) illustrates the distribution of *ALDH2*2* in different populations around the world and shows how a genetic variation within a population can be correlated with the frequency of an associated phenotype.

Given its basic graphical interface, navigation, and pedagogical structure, DNATwist can be populated with additional pharmacogenomics instances. The Chromosome Cruiser and Gene World provide a stable graphical background and primarily require changing highlight locations and links to further resources. The Pathway Portal is more topic- specific. To illustrate the metabolism or mechanism of action of other drugs and the effect of genetic variants requires producing new graphics customized to the specific drug-target interaction and cellular location involved.

To assess its appeal and understandability, advanced-placement biology students in California used the system for about an hour in a pair of pilot studies, with 19 students in the first (PT-1) and 22 in the second (PT-2). Neither cohort had previously studied the topic of pharmacogenomics. In our evaluation, 90% of the students (36/40 respondents) reported that they found the scientific content comprehensible. On a follow-up test, the students averaged 80% on a quiz with either 17 (PT-1) or 19 (PT-2) questions that covered topics specific to the lesson. Perhaps more significantly, in the first pilot we asked students if they wanted to learn more about pharmacogenomics, and all 19 replied "Yes." To anticipate future developments, we asked students to rate interest in five possible pharmacogenomics topics. Students indicated "high interest" in learning about genetics and nicotine addiction (48%), a genetic variant and severe side effects in people taking a drug used to treat HIV (54%), and using genetics to predict pain-medication effectiveness (63%).

DNATwist is being adapted for the Understanding Genetics website of the Tech Museum of Innovation. To tailor the tool for middle-school students, the target age group of the Tech Museum, the exhibit has students play the role of a genetic counselor, using a linear storyline that takes students through the three portals as they follow the case of a couple who wish to learn about the likelihood that their child will be alcohol-intolerant. With 600,000 unique visitors per year to the Understanding Genetics website, the DNATwist Tech Museum adaptation has the potential to reach a very large audience.

In conclusion, DNATwist is one promising approach to updating genetics education. Pharmacogenomics is a highly relevant, engaging, and comprehensible entry point. Through new materials and simplifications of existing online tools, with modest pedagogical elements, it becomes possible to bring the expanding world of new science to the public.

Acknowledgments

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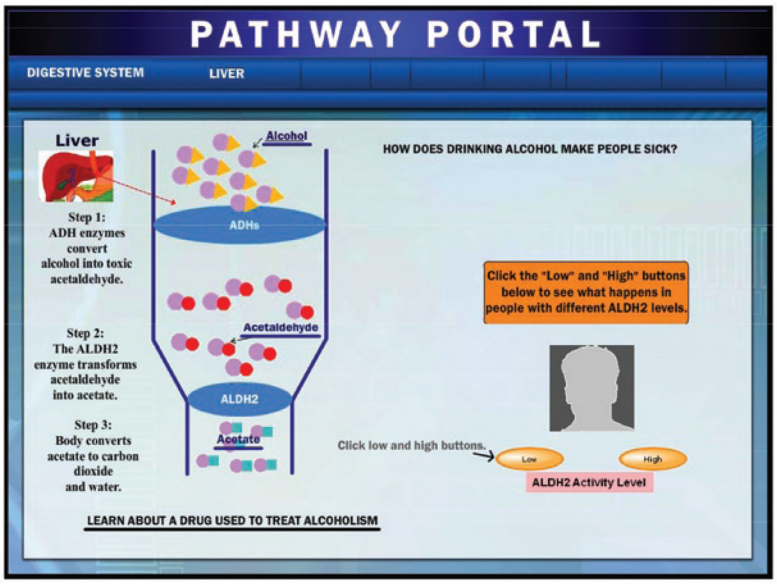

Figure 1.

The Pathway Portal illustrates the metabolism of alcohol in the liver. Clicking on the “Low” and “High” buttons reveals the effect on alcohol metabolism of low vs. high aldehyde dehydrogenase 2 (ALDH2) enzyme activity. ADH, alcohol dehydrogenase.

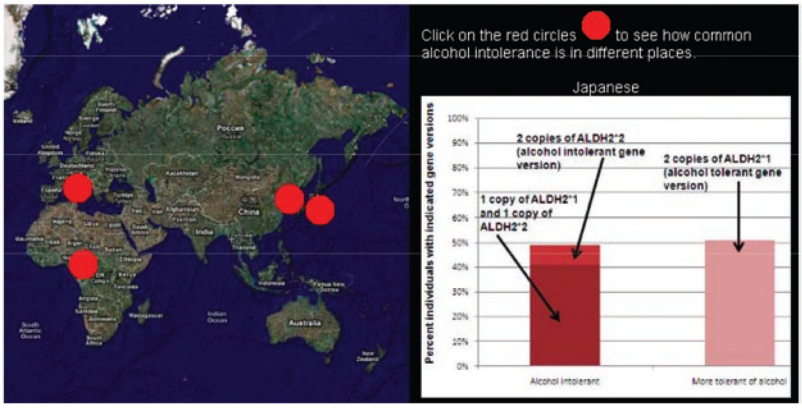

Figure 2.

Gene World: clicking on a red circle displays the prevalence of aldehyde dehydrogenase 2 (*ALDH2*) genotypes in the population located in that region. Users quickly observe the different frequencies of *ALDH2* genotypes in various populations.