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Article

Experimenting with Spirituality: Analyzing *The God Gene* in a Nonmajors Laboratory Course

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References linking genes to complex human traits, such as personality type or disease susceptibility, abound in the news media and popular culture. In his book *The God Gene: How Faith is Hardwired into Our Genes*, Dean Hamer argues that a variation in the *VMAT2* gene plays a role in one's openness to spiritual experiences. In a nonmajors class, we read and discussed *The God Gene* and conducted on a small scale an extension of the study it describes. Students used polymerase chain reaction to replicate a portion of their *VMAT2* genes, and they analyzed three polymorphic sites in the sequence of these products. Associations between particular *VMAT2* alleles and scores on a personality test were assessed by *t* test. The course, of which this project was a major part, stimulated student learning; scores on a test covering basic genetic concepts, causation/correlation, and laboratory methodology improved after completion of the course. In a survey, students reported the laboratory project aided their learning, especially in the areas of statistics and the linking of genes to behaviors. They reported high levels of engagement with the project, citing in particular its personal nature as motivating their interest.

INTRODUCTION

Rapidly expanding knowledge about the human genome has increased the urgency of students' appreciation of the roles that genes and the environment play in determining human characteristics. The popular press frequently discusses the influence of genes on diseases, such as cancer, or personality traits, such as risk taking or sexual orientation. In response to this barrage of information, students might take a variety of positions—at one extreme, they become adherents of genetic determinism; at the other extreme, they reject any role of genetics in human behavior as incompatible with free will. Some might simply be confused as to what is known about the roles of nature and nurture in human characteristics. Although details of their models vary, prominent scholars in the field see an interplay between heredity and environment, rather than a dichotomy (e.g., Collins *et al*., 2001; Cherney *et al*., 2004). Teaching students a more nuanced understanding of the interaction of genetics and environment and how the role of each is assessed should help them become more informed consumers of the "gene of the week" information that surrounds them.

Dean Hamer's book, *The God Gene: How Faith is Hardwired into Our Genes*, details a recent example of a purported link between a particular gene and human behavior (Hamer, 2004). The book was covered heavily by the popular press, including an article in *Time* magazine featured on the magazine's cover (Kluger *et al*., 2004). In his book, Hamer contends that one's predisposition toward spirituality is influenced by genetic factors. More controversially, he proposes that the *VMAT2* gene is one of many potential genes that impinge on spirituality. Hamer identifies one particular variation, a change from an A to a C, present in 28% of the alleles in his data set, as a marker for the more "spiritual" version of this gene. This work has not been published in a scientific journal.

VMAT2 encodes a transporter protein that imports several monoamine neurotransmitters into vesicles in the brain (reviewed in Zheng *et al*., 2006). Thus, an alteration in the transporter could potentially affect the levels of multiple types of neurotransmitters, resulting in altered brain function. Changes in this monoamine transporter's sequence or expression have been associated with substance abuse and Parkinson's disease (Lin *et al*., 2005; Schwab *et al*., 2005; Glatt *et al*., 2006; Yamamoto *et al*., 2006).

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I decided to use Hamer's book as a focal point for an interdisciplinary nonmajors class in genetics and biotechnology. Because biotechnology has an impact on so many other fields of study, this area seemed appropriate for interdisciplinary focus while allowing significant scientific content. In addition to its high profile, *The God Gene* was likely to provoke discussion because it touches on an area of personal interest for many of the students and had substantial gray areas—the work had not been subjected to rigorous peer review, Hamer's observed correlation of a particular *VMAT2* allele with spirituality had not been reproduced in another population, and, as Hamer notes, *VMAT2* is at best a small player in influencing spirituality. The book lends itself to a discussion of basic concepts underlying data interpretation, such as the distinction between correlation and causation and the role of statistical analysis, as well as such genetics essentials as homozygosity and heterozygosity, the relationship of genotype and phenotype, and mutation.

In addition to discussions about the book and the underlying science, we extended Hamer's project by examining *VMAT2* variations in the laboratory. Each of the students isolated genomic DNA from his or her cheek cells, amplified a region of the *VMAT2* gene, and determined his or her genotype at three polymorphic sites. We also completed the Temperament and Character Inventory (TCI) (Cloninger *et al*., 1993, 1994), a personality test that Hamer used to gauge spirituality. The self-transcendence portion of the score was used as a spirituality index. The class performed a simple statistical analysis on the class data set to look for correlations between *VMAT2* genotype and spirituality phenotype. Even though significant results were not expected given the small size of our class, this provided an opportunity for the students to see how results could be assessed. Students extended the research question by looking for associations between *VMAT2* genotype and another phenotype of their choosing.

Our structured inquiry laboratory project offered an opportunity for active learning (see Colburn, 2000 for a description of different types of inquiry laboratories). Although the problem and procedures are provided, this lab presents a research-like experience in that the outcome is truly unknown. It responds to Hamer's statements in *The God Gene* that replication of his results in different populations is necessary to test the validity of his findings and that it is likely that many genetic variations contribute to differences in spirituality. Although our study may not directly replicate Hamer's (it is not clear which A/C polymorphism he examined), students enter into this dialogue by testing whether they too see an association between *VMAT2* variation and spirituality. Furthermore, because of the unsettled nature of the question being investigated, the larger meaning of any findings is open for debate. Inquiry labs are recommended as a strategy to increase scientific literacy in all students as they stimulate construction of knowledge and recognition of science as a process (Project 2061, 1989; National Research Council, 1999; Handelsman *et al*., 2004). Among the many strengths of active-learning methods in general are their ability to motivate by offering the sheer pleasure of solving a puzzle (Svinicki, 1998) and to increase students' self-efficacy (Wilke, 2003). Self-efficacy, or a student's belief in his ability to succeed at a particular task, is one predictor of achievement (Pajares, 1996). Because nonmajor students can come to science courses with little faith in their ability to perform tasks involving science, increasing self-efficacy is a key consideration in preparing students who may learn all their future science informally, outside of science courses.

Nonmajor students may also believe science is uninteresting or boring. Openness toward learning science is a crucial building block in preparing students to independently tackle the myriad and unpredictable science-related issues arising in their lives—a central goal of a nonmajors course. In meeting this need, it is helpful that the God Gene project is context-based. In context-based approaches, rather than beginning with scientific principles and applying them to a question, students begin with a question (typically with social, here with personal, implications), then learn the science needed to answer the question. In a systematic review Bennett *et al*. (2007) found that context-based approaches result in improved attitudes toward science. In the case of this project, relevancy of the contextual question to the students is high; students would not only be the investigators, but also serve as the subjects of this investigation. The combination of active student involvement in the development of their own understanding, clear relevance of the question to the students' own experience, and the interdisciplinary nature of the question are components of the "lived curriculum" Hurd (1998) describes as promoting scientific literacy.

There were several goals for this project. First, as a result of the project students should master some basic scientific content, in this case about what genes are and do, and have an increased understanding of some approaches to studying genes. Second, I wanted students to become more informed and critical consumers of scientific studies as reported in the media. Our in-depth analysis of a particular news story could provide a model for such critical thinking. Because Hamer's work involves concepts that are widely accepted (genes play a role in complex traits) and controversial (the *VMAT2* gene contributes to spirituality) students have the opportunity to both master ideas and to draw their own conclusions. This goal builds on the first, as mastery of the underlying scientific concepts would enable students to draw more meaningful and considered personal conclusions. Finally, as many nonmajors have trepidation about learning science or find science boring or irrelevant, I wanted to intellectually and actively engage students in a scientific problem. Once students see that they can successfully think about and be interested in science, there is one less barrier to learning more about science when it affects their later lives. It was hoped that the personal and active nature of this investigation would literally bring home concepts that might otherwise fail to engage students.

NATURE OF THE COURSE

The course was part of an interdisciplinary honors program at a small liberal arts university in southern California. In the program, a dozen students take several courses together during their years at the university, starting in their sophomore year. Students are chosen for the program based on strong academic performance, interest in interdisciplinary study, and ability to work well within a diverse group of students. The program's course offerings are generally

unique for each cohort of students; courses are seldom repeated. Most of the students in the sophomore-level biotechnology course were not focusing on science in their studies; only one of the 12 students in the class was planning a major in the sciences and another was planning an interdisciplinary major that included several biology courses. Only the latter student had taken our introductory biology course for majors. The course was taught in May term, a 3.5-wk term, with class meetings 4 hours a day, 4 days a week. The amount of time spent in lab, discussion, lecture, and group activities varied as needed from day to day. None of the lab activities took longer than a standard 3-h lab period, so they could easily be adapted to a more typical semester or quarter term schedule.

STRUCTURE OF THE PROJECT

Setting the Foundation for the Project

The God Gene project was preceded by laboratories in which students viewed cheek cells stained with methylene blue and isolated DNA from wheat germ. Viewing their stained cells allowed students to become familiar with the cellular location of the DNA they would isolate in the God Gene lab. The wheat germ DNA isolation allowed them to see isolated DNA in bulk and reminded students that living things besides humans also contain DNA. An opportunity for practice with micropipettors before beginning the God Gene lab would have been useful, but we did not do this because of the compressed 1-mo nature of this class.

After the first day of class, before the project was introduced, students completed the TCI. The TCI uses a series of true/false questions to examine the following personality traits: novelty seeking, harm avoidance, reward dependence, persistence, self-directedness, cooperativeness, and self-transcendence. Hamer used the self-transcendence scale of the TCI as a measure of spirituality. The test does not focus on a belief in a higher being or religious practice, but rather the ability to be immersed in the moment, identification of oneself as a part of the universe as a whole, and one's degree of openness to the unexplained. The self-transcendence score has three subscores: ST1, creative self-forgetfulness versus self-consciousness; ST2, transpersonal identification; and ST3, spiritual acceptance versus rational materialism. The ST1 subscale probes a person's tendency to "lose oneself" in an experience. The ST2 facet measures how strongly one feels connected to nature and the universe, including the physical environment and people. Finally, the ST3 "mysticism" subscale assesses the subject's acceptance of things that cannot be rationally explained, such as miracles or a "sixth sense" (Cloninger *et al*., 1994).

The TCI is available for purchase from its developer, C. Robert Cloninger, at Washington University Medical School (http://psychobiology.wustl.edu/TCI/whatIsTCI.htm). Alternatively, a few of the questions relating to self-transcendence and instructions as to how they are scored were reprinted in *Time* magazine (Kluger *et al*., 2004) and are available online at http://www.time.com/time/covers/1101041025/quiz.html. The full-length test (version 9), with 240 T/F questions, was used in our class. We used the paper "starter set," although more expensive computerized versions that include scoring software are available. With the exception of a few questions that are used for validating that the test taker is answering sincerely, each of the 240 questions is linked to a particular personality trait scale. In each case, 0 or 1 point is added to the relevant scale, depending on the answer that is given. The manual that comes with the test describes which questions apply to each scale and whether the true or false answer is awarded the point. I used this key to construct a self-scoring Excel (Microsoft, Redmond, WA) spreadsheet, which I made available to students on the course website. When students entered their answers into the spreadsheet, formulas linked to each question's cell would add a point (or a 0) to the appropriate scale. However, students or the instructor could readily score the tests by hand, particularly if only a subset of the questions is of interest due to focus on a particular scale. For example, the self-transcendence score is drawn from 33 questions, the majority of which must be answered "true" for a point to be awarded. It would be fairly simple to scan these for these answers manually. Alternatively, the computerized scoring system could be purchased.

The nature of the TCI, beyond that it was a personality test, was not discussed with the students before they took it, and although students were immediately aware of their numeric scores, they were not told what each score meant until a later time. To maintain maximum flexibility in assessing the data, it is best if the students submit their entire set of responses to the instructor. In our course, two students submitted only the scores for each section, and for these students information about subscores was lost.

After the first day of class the students were also asked to take a precourse assessment. This assessment was composed of a series of questions, some true/false, some multiple choice, and some with Likert scales (1–5 scales). The questions probed both understanding of scientific concepts and student beliefs. The same questions were again asked at the end of the course, with additional questions regarding the students' opinions about various aspects of the God Gene project. This posttest is available in the Supplemental Material. All students were given the option to decline use of their pre- and posttest data in this publication; none declined. One student was not available for the posttest, so the corresponding pretest was excluded from the analysis.

The Laboratory Sessions

Handouts used by the students for each laboratory session may be found in the Supplemental Material. Below is an overview of the steps, composition of reagents, and technical details of note. A timeline of the laboratory project is shown in Figure 1.

First Laboratory Session—DNA Isolation and Polymerase Chain Reaction (PCR). Students isolated DNA from their cells by using a standard protocol. A saline wash (0.9% NaCl), followed by centrifugation in a clinical centrifuge, was used to collect cells from the mouth. Cells were lysed by resuspension in an alkaline slurry of Chelex 100 resin (10% in 50 mM Tris-NaOH, pH 11), followed by heating to ~95°C for 10 min. Chelex 100 resin (Sigma-Aldrich, St. Louis, MO) increases efficacy of PCR, perhaps by binding metal ions that would serve as cofactors for DNA degradation (Walsh *et al*., 1991). Chelex and cell debris were cleared from the sample by a brief centrifugation in a microcentrifuge.

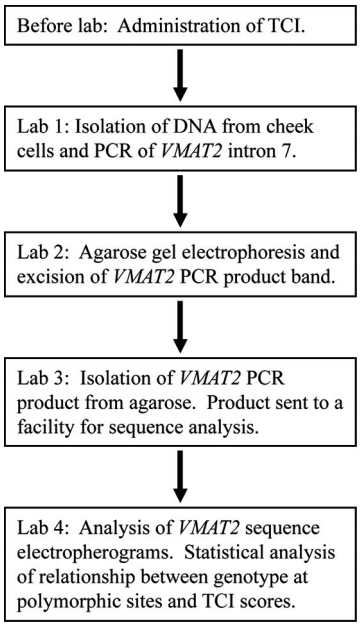

Figure 1. Flowchart of the God Gene project laboratory periods.

We were not able to identify conclusively the A/C polymorphism studied by Hamer from the description in his book. Hamer states that the A/C variation he followed was typically associated with several other polymorphisms; thereit was used as a general indicator for this set of changes. Thus, even though one would imagine that a relevant change should affect the coding or expression of the protein, it is unclear whether the "indicator" A/C polymorphism discussed in *The God Gene* is in a regulatory region, an exon, or an intron. Inspection of publicly available data on polymorphic sites in *VMAT2* (Edwards, 2001; Database of Single Nucleotide Polymorphisms, 2006) revealed 16 A/C polymorphisms, all of which were in noncoding regions. Of the polymorphisms that had frequency data, only two, one in intron 7 and one in intron 12, had a similar frequency to that given by Hamer. When the composition of Hamer's sample was factored in (mostly European ancestry), an A/C transversion at position 71 of intron 7 was the best match (29% frequency of the C allele vs. 28% in Hamer's sample; Edwards, 2001). Furthermore, there were two other nearby polymorphic sites that varied at considerable frequency (Table 1), so these could also be examined in our study. Thus, primers were designed to amplify this region. The sequence of the expected 341-base pair product is shown in Figure 2.

Table 1. *VMAT2* single nucleotide polymorphisms (SNP) studies in the God Gene project[a]

Intron base no.	Variation	Frequency of minor allele
52	C or T	0.074
54	T or C	0.309
71	A or C	0.292

[a] SNPs in the*VMAT2* intron 7 sequence as given in National Center for Biotecnology Information SNP database (dbSNP, 2006) and by UCSF Pharmacogenetics of Membrane Transporters (PMT) Project (Edwards, 2001). Variations are listed with the more common base first. Frequency data taken from the UCSF PMT project, a study of 450 ethnically diverse individuals.

```
   cccaaagcct tattggaaca aagtagagag agaaacacaa gagtcaaata
   gatggttcta gtacagggag agggcatgtg tcccaggggt ggtgtcccca
   ctttctctcc ctgcagtggg ccccccttc gggagtgtgc tctatgagtt
   tgtggggaag acggctccgt tcctggtgct ggccgccctg gtactcttgg
   atggag gtga gtgagtccac gtgggcgcca tgccatgacc ttggcatcgt
45 gctggcaCgC gcttgggcca cacctgCttt ctgaagaggg gcttgtcttt
95 tttatttta ttttttagct attcagctct ttgtgctcca g
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Figure 2. *VMAT2* PCR product sequence. Primer target site sequences are shown in bold and doubly underlined. *VMAT2* (also known as *SLC18A2)* sequence taken from human chromosome 10 sequence (GenBank accession no. NT_030059). The sequence of intron 7 is boxed and italicized. The numbering of intron 7 bases is shown on the left. C's at positions 52, 54, and 71 in this intron are at polymorphic sites and are shown in bold capitals.

PuRe Taq Ready-To-Go PCR beads (Amersham Biosciences, Piscataway, NJ) were used to amplify DNA around the seventh intron of *VMAT2* from each student's sample. Students used 5 μl of their cell lysate and 20 μl of the 250 nM primer mix solution for each reaction. The primer sequences were 5′-CCCAAAGCCTTATTGGAACA-3′ and 5′-CTGGAGCACAAAGAGCTGAA-3′.

Second Laboratory Session—Identification and Isolation of* VMAT2 *PCR Product. As much as possible of each 25 μl reaction was loaded onto a preparative agarose gel and electrophoresed. The results from one agarose gel are shown in Figure 3. Every student successfully obtained PCR product. Students excised the lower, more intense band (closest to the expected size of 341 base pairs) with a razor blade and stored it in a microcentrifuge tube in the refrigerator until the next lab period.

Third Laboratory Session—Purification and Sequencing of* VMAT2 *PCR Product. A QIAquick Gel Extraction kit (QIAGEN, Valencia, CA) was used to extract the DNA from the gel slice as per manufacturer's instructions. DNA was sent to California State University, Northridge, for sequencing via dye termination reactions. One of the primers used in PCR, 5′-CCCAAAGCCTTATTGGAACA-3′, was also used for sequencing.

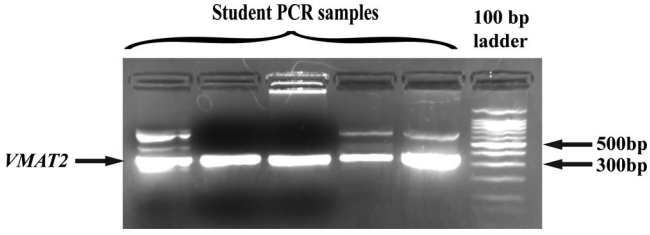


Figure 3. Agarose gel electrophoresis of *VMAT2* PCR products. The expected product was 341 base pairs. The band indicated by the arrow labeled *"VMAT2"* was excised for sequence analysis. Variations in tracking dye bands between lanes are due to use of loading buffers with differing compositions.

Each student obtained readable sequence data. One student's data were useable in conjunction with the known sequence, but were of poor quality, probably because of low yield of PCR product. Quality and reliability of the sequence data could probably be improved further by using a sequencing primer closer to the variant region. Two examples of the data from the variant region of intron 7 are shown in Figure 4.

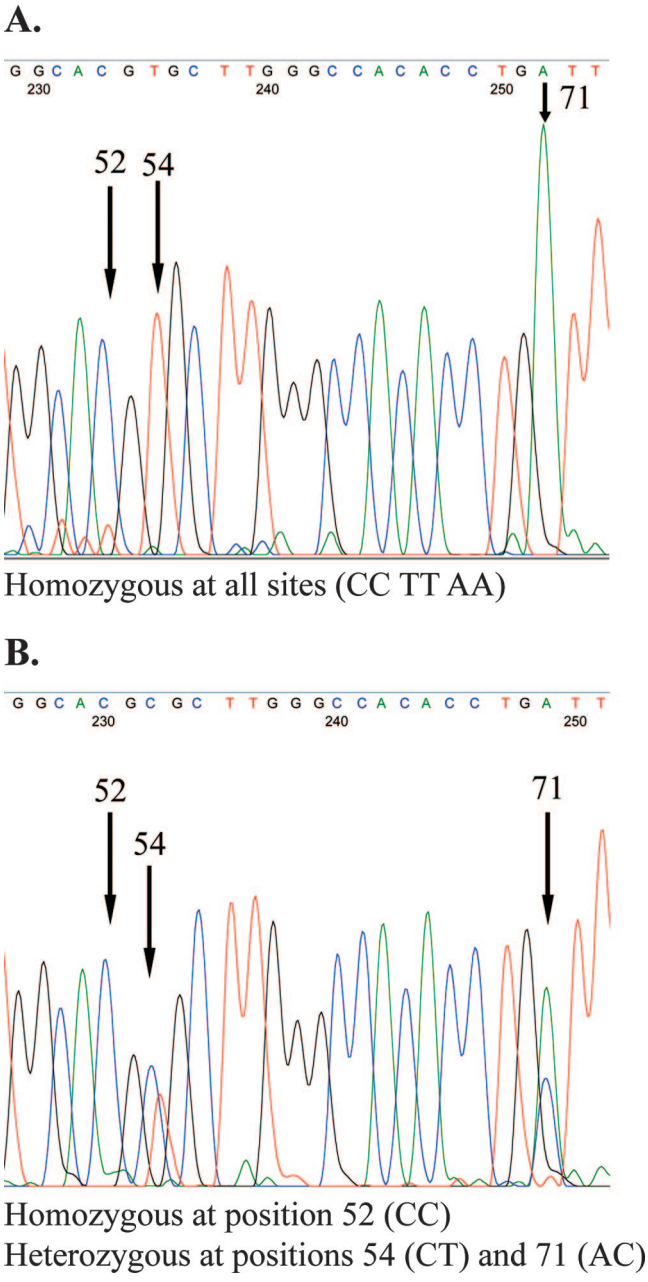


Figure 4. Samples of student sequence data. Excerpts from electropherograms of the *VMAT2* intron 7 sequence are shown for two students in the class. Polymorphic sites (bases 52, 54, and 71) are marked by labeled arrows over the peaks. The derived genotype for the student is given under each electropherogram. (A) Single peaks at positions 52, 54, and 71 indicate this student is homozygous at all three polymorphic sites. (B) Overlapping peaks corresponding to bases 54 and 71 indicate this student is heterozygous at these sites.

Fourth Laboratory Session—Analysis of Sequence and TCI Data. Students used the program Editview (Applied Biosystems, Foster City, CA) to view the sequence electropherograms of their *VMAT2* PCR product. A text search for an adjacent invariant sequence (GGGCCA) simplified the process of finding the relevant region of the sequence. Examples of data such as that shown in Figure 4 were provided so students could see the difference in appearance of homo- and heterozygotes in the electropherograms. Students recorded their genotypes at each of three sites, positions 52, 54, and 71 in intron 7.

Because of time constraints, the genotypes were also read in advance by the instructor and compiled into a table with the TCI scores of each student. This table was posted on the course website so it was available to the students immediately after they had read their own electropherograms. The immediate posting allowed statistical analysis of the results during the same lab period, but this could easily be deferred to a separate lab period in a longer course.

The genotype and TCI score data are shown in Table 2. Even within this small group there was a range of TCI scores and genotypes. For example, self-transcendence scores varied from 4 to 29 of 33 possible points, and at least two individuals had a variation for each of the three sites analyzed. All possible genotypes were seen at sites 54 and 71. Two students submitted only the scores for the major areas of the TCI and so subscores such as ST1, ST2, and ST3 were not available for these individuals. Another student did not turn in any TCI scores.

A *t* test (two sample assuming unequal variances) was used to test the significance of any association between the presence of a "C" at position 71 and the degree of self-transcendence as measured by the total ST score on the TCI. Microsoft Excel was used to arrange the data and perform the *t* test (note that performing the *t* test requires loading the optional Analysis Toolpak functions). As did Hamer, we sorted the individual genotypes into two groups, those containing at least one allele with a C at position 71 (CC or AC individuals) and those with the AA genotype. Students typically needed some minor assistance in sorting the data. The *t* test compares the mean self-transcendence score in each group and assesses the probability that the difference in means is due to random chance. The output from the *t* test is shown in Table 3.

Our data did not show a statistically significant difference in mean self-transcendence between the individuals with the "C" allele, which may correspond to Hamer's "spiritual C," and those with the AA genotype (one-tailed $p = 0.19$, well above the cut-off of 0.05). The average self-transcendence score for the C- group was 18.5 of 33 possible points versus 12.5 for the AA group. In spite of the lack of significance, that the average C- group score was higher than the AA group score caught students' attention and provided an opportunity to discuss the limited power of statistical testing in small samples—that it is possible that actual differences exist, but this cannot be verified without increasing the sample size.

To cement their understanding of the *t* test, students were then asked to look at associations between any *VMAT2* genotype and any other variable of their choosing, for example scores on a different section of the TCI. Students were also asked to provide ideas about what factors might limit our ability to find significant associations in our data set. Students identified sample size and possible homogeneity of the population (e.g., all college students) as pitfalls in our analysis. *The God Gene* discusses the idea that chance associations can occur if enough sites or traits are examined. Because we focused on a few sites in one gene, we did not emphasize this additional complication, but *The God Gene* could be used to explore this idea as well, if desired.

To enable a larger data set to be created and increase the chance of statistically significant results, I have created an online spreadsheet containing the TCI and genotype data from this project. I hope to provide an opportunity for future students to participate in a larger scientific community. Other instructors may add data from their courses if they wish, or use the posted data in addition to that collected in their own courses. The spreadsheet may be accessed via http://bulldog2.redlands.edu/fac/silveira/vmat2/vmat2.html. Students (and their guardians, if students are minors) should provide informed consent before their data are shared, and any institutional policies (e.g., Institutional Review Board [IRB] approval) regarding sharing of student data should be followed before data are submitted.

Related Learning Experiences

Students used paper models to investigate the structure of DNA and model the processes of DNA replication, transcription, and translation. Similar models are commercially available from Delta Education (http://www.delta-education.com/productdetail.aspx?Collection = Y&prodID = 2159&menuID = 111). Animations depicting PCR and DNA sequencing were also shown (Dolan DNA Learning Center, 2007a). We modeled the effects of different types of mutated alleles on the outcome of a biochemical pathway by making peanut butter and jelly sandwiches in a pair of assembly lines, altering some workers so that they failed to do their job (recessive) or did their job differently (dominant). To gain some background information on signaling in the nervous system, in addition to what is described in Hamer's book, students played the "Lost Synapse" game at http://www.nobelprize.org. This game, no longer available, asked students to label a synapse and assemble a text about synapse function. To learn more about the distinction between correlation and causation, students read and discussed a news report about a study correlating tooth brushing with slenderness (Reuters, 2005).

We read all 11 chapters of *The God Gene* in the course, generally tackling one or two chapters at a time over the course of 3 wk. We discussed the book in class; some sample discussion questions are given in the Supplemental Material. The book could conceivably be used differently in different courses; it is not necessary to read the entire book to have an understanding of the project. The first six chapters, which at 118 pages make up about half of the book, describe Hamer's study most directly. The first chapter overviews the book, outlines the idea that there may be a genetic component to spirituality, and describes some caveats about the study and its findings. These caveats raise important issues, such as the very limited contribution that any one gene, including *VMAT2*, would have to the complex trait of spirituality, and

Table 2. Student TCI scores and genotypes[a]

	TCI scores							Self-transcendence subscores			Genotypes		
Individual	NS	HA	RD	P	S	C	ST	ST1	ST2	ST3	52	54	71
1	19	21	22	8	34	35	10	7	3	0	cc	tt	aa
2	23	7	12	7	33	40	8	2	1	5	cc	tt	aa
3	16	17	19	5	40	33	7				cc	ct	ac
4	17	25	13	8	25	23	11	7	0	4	cc	tt	aa
5											ct	tt	aa
6	17	30	12	5	22	36	12	4	1	7	ct	ct	ac
7	18	3	12	7	41	35	8	1	4	3	cc	tt	aa
8	21	28	18	2	14	24	14	8	2	4	cc	tt	aa
9	15	4	10	8	38	39	28	8	7	13	ct	ct	ac
10	30	18	21	4	40	30	4	2	0	2	cc	tt	aa
11	24	11	14	7	36	32	27	7	8	12	cc	cc	cc
12	20	6	16	8	33	36	29	8	9	12	cc	tt	aa
13	30	10	19	7	32	38	18				cc	tt	aa
Maximum section score	40	35	24	8	44	42	33	11	9	13			

[a] Scores on the TCI subscales (Cloninger *et al.*, 1994) are listed for students in the course and for the instructor (individuals 1–13). Scores for individual 5 were not submitted. TCI scales are as follows: NS, novelty seeking; HA, harm avoidance; RD, reward dependence; P, persistence; S, self-directedness; C, cooperativeness; and ST, self-transcendence. ST scores were broken down into subscores: ST1, creative self-forgetfulness versus self-consciousness; ST2, transpersonal identification; and ST3, spiritual acceptance versus rational materialism. Individuals 3 and 13 did not report subscores. The number of possible points for each scale and subscale is shown in the last row. The higher the score the more a person displayed the named trait—novelty seeking, creative self-forgetfulness, and so on. Genotypes for each individual at three positions in intron 7 of *VMAT2* (bases 52, 54, and 71) are shown in the last three columns.

that the study does not address the validity of any particular belief. The second chapter describes self-transcendence and the TCI, whereas the third discusses previous twin studies that suggest that there is a significant genetic component to spirituality. The fourth chapter, which is the core of the study, describes the identification of a particular *VMAT2* variation and its correlation with the TCI's self-transcendence scale. This chapter could be used alone if students were provided with some necessary background information, such as a description of the TCI. The next three chapters address neurobiology—how psychoactive chemicals can alter spiritual experiences, how monoamine neurotransmitters work, VMAT2's role in neurotransmitter function, and what parts of the brain may contribute to spiritual experiences. Other chapters describe possible selective pressures for spirituality, religious practices and memes, a DNA signature indicating the relatedness of one group of people also defined in religious terms (the Jewish Cohanim), and the enduring idea of a Deity.

In addition to reading and discussing the book itself, students also read the *Time* magazine article (Kluger *et al*., 2004) and reviews of *The God Gene* to see some additional perspectives on the book (for example, Zimmer, 2004, who suggested changing the title to "A Gene That Accounts for Less Than One Percent of the Variance Found in Scores on Psychological Questionnaires Designed to Measure a Factor Called Self-Transcendence, Which Can Signify Everything from Belonging to the Green Party to Believing in ESP, According to One Unpublished, Unreplicated Study"). We also read the chapter "How Life Works" from Ursula Goodenough's *Sacred Depths of Nature* (Goodenough, 1998) that discusses whether one demeans or enhances the beauty of nature by studying it in a reductionist manner; Goodenough argues for the latter.

If the project were to be used in a majors-level course, several opportunities for more advanced reading are available. In his book, Hamer includes a list of suggested reading keyed to each chapter, which includes articles from the primary literature. For example, students might read Kirk *et al*. (1999), which describes a twin study that attributes ~40% of human spirituality as assessed by the TCI to genetic factors (this article and other twin study articles are available at http://genepi.qimr.edu.au/staff/?staffusername = nickM). For more detailed information about *VMAT2*, students might read Wang *et al*. (1997) or Takahashi *et al*. (1997), both of which describe the phenotype of *VMAT2* knockout mice. Both papers detail similar observations; the Wang paper, published second of the two, has more extensive background information that might be helpful to students. Lin *et al*. (2005) is an example of a published study linking *VMAT2* single-nucleotide polymorphisms (SNPs) to a complex trait, describing the effects of variations in the *VMAT2* promoter on alcoholism. However, many of the analyses described in this paper would be challenging for instructors and students without a background in human genetics. Burman *et al*. (2004) describe the effects of rare SNPs in the *VMAT2* coding sequence on the biochemical and pharmacological characteristics of the encoded transporter. For published studies analogous to the one described in *The God Gene*, of particular interest may be papers linking personality test scores on novelty seeking and harm avoidance scales to variations in the dopamine D4 receptor and serotonin transporter genes, respectively (Benjamin *et al*., 1996; Ebstein *et al*., 1996; Lesch *et al*., 1996). These studies garnered significant media attention—the serotonin transporter gene was referred to as the "Woody Allen gene" in *U.S. News and World Report* (1996). Hamer is an author on two of these papers. Herbst *et al.* (2000) describe an attempt to replicate these studies in which an association was not seen, as well as factor analysis to examine the validity of the TCI scales. The article also cites other papers examining the harm avoidance and novelty-seeking studies, some of which do replicate the original results. Although the conclusions from the factor analysis are clearly stated in the article (they find that several TCI scales are composed of subscales that do not seem to be measuring the same underlying factor), the methodology and data interpretation involved in factor analysis will likely not be clear to those readers not already familiar with this method. For a more psychology-oriented course, the TCI manual cites many other references in which the TCI is used and its validity tested.

In our course, three activities helped students to explore other areas of human genetics. At the end of the course, each student wrote a paper describing the contribution of genetics to a complex trait of their choosing. This assignment was intended to generalize the idea of genes influencing complex abilities or behaviors and to encourage students to read about studies that had been peer-reviewed. A second assignment was to analyze some pedigrees of families with mutations in *BRCA1.* This enabled students to learn about Mendelian inheritance and also to see an example where an allelic difference has been clearly demonstrated to have an effect on human phenotype. This addresses one of the challenges of the project—that because in the case of *VMAT2* and spirituality there are not sufficient data to support a conclusive link, students could conclude that it is impossible to link variations at a locus to a particular human trait. In another activity that addressed this point, students examined several single-gene traits, e.g., tongue rolling and phenylthiocarbamide tasting, in the members of class.

Table 3. Output from *t* test examining association of the self-transcendence TCI score and the presence of at least one C at position 71[a]

	Genotype AA	Genotype C-
Mean ST TCI score	12.75	18.5
Variance	60.79	112.33
Observations	8	4
Hypothesized mean difference	0	
df	5	
t statistic	−0.96	
p (T<=t) one-tailed	0.19	
t Critical one-tailed	2.01	
p (T<=t) two-tailed	0.38	
t Critical two-tailed	2.57	

[a] Data were generated with Microsoft Excel, *t* test: two-sample assuming unequal variance.

Ethical Considerations

Whenever one asks students to examine their own DNA it is important to consider the impact, immediate or eventual, of any information that one may uncover. I did not find published reports linking variation at the sites we examined to any phenotype. Because we are looking at changes in an intron sequence, it is unlikely that there will be future discoveries linking these particular alterations to disorders of the brain. A common variation in intron 7 (site 54) was studied for an association with schizophrenia, and no such association was observed (Kunugi *et al*., 2001).

It was possible that students would not want their particular genotypic or personality data to be identified when given to the other members of the class. Thus, all data were released to the class with the names of the students removed. In practice, students often identified themselves on the data tables when discussing the experiment with other students. If students' data are to be shared outside the course, such as on a publicly available website, IRB approval is likely to be required. After obtaining approval for our course, students were given the option to opt out of public use of their data, such as in this publication; none chose to opt out.

Finally, it is important to emphasize, as Hamer does, that the project is not seeking to investigate whether any particular spiritual belief is valid. Rather, Hamer's book and this project explore whether there is a genetic component underlying some of the variation in people's receptiveness to spiritual belief and whether *VMAT2* in particular contributes to that variation. Students in this course had a variety of spiritual beliefs and practices, and none expressed discomfort regarding the project's focus. Ability to opt out or in to the exercise could be considered by the instructor, perhaps with a substitution of a project involving similar manipulations, such as determining the allele(s) present at the PV92 locus (Dolan DNA Learning Center, 2007b).

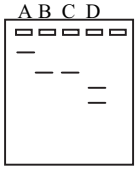
ASSESSMENT OF PROJECT EFFECTIVENESS

Structure of the Assessment Instrument

To assess student learning and attitude shifts as a result of the course, a pre- and posttest (see Supplemental Material) were given. Because the God Gene project was not the only course activity, a series of questions asking the student to evaluate this project's impact on their understanding was

Table 4. Sample questions from pre- and posttests

Question	Correct pretest answers (n = 11)	Correct posttest answers) (n = 11)	Change (post − pretest)
Selections from question 5 (true/false)			
If a 100% correlation is seen between factors A and B, then A must cause B or B must cause A. (F)	6	8	2
Genes encode proteins. (T)	9	9	0
Most of the "jobs" in a cell are carried out by DNA. (F)	9	11	2
Genes are made of protein. (F)	7	6	−1
The order of bases holds information as to genetic traits. (T)	10	11	1
Sample size strongly affects the credibility of genetic studies. (T)	8	11	3
Some genetic traits are due to a single gene. (T)	11	9	−2
It is not yet possible to determine the exact sequence of DNA isolated from humans. (F)	3	6	3
Some traits are due to multiple genes. (T)	11	11	0
DNA can be replicated in a test tube to produce large amounts of specific regions. (T)	9	11	2
The position of a mutation in a sequence affects its severity. (T)	10	11	1
DNA can be isolated from cells by using detergents and salts. (T)	5	9	4
Selections from question 6 (true/false).			
People often refer to *BRCA1* as "the breast cancer gene." This shorthand means:			
If one has the *BRCA1* gene, one is more likely to get breast cancer. (F)	2	7	5
Some versions of *BRCA1* make it more likely that one gets breast cancer. (T)	10	10	0
Selections from question 8 (true/false)			
a. The band marked A is bigger than the band marked B. (T)	3	8	5
d. It is not possible for the two forms of DNA in lane D to be isolated from one another. (F)	5	10	5
e. Someone remembers that the DNA in lanes A and B are related in that one was derived from the other by PCR. She can't remember which was the starting DNA and which was the PCR product. It is more plausible that the DNA in lane A was derived via PCR from the DNA in lane B than vice versa. (F)	6	7	1



added to the posttest. These questions, which may be found as questions 9–11 on the posttest, were the sole difference between the pre- and posttest questions. Question 9 is composed of a series of questions in which the students were asked to use a Likert scale to quantify their learning or attitude shifts as a result of the project. These questions were designed to probe whether students attributed learning or change in opinion in a given area to this particular project, as opposed to the other course activities. Questions 10 and 11 were open-ended questions asking students to comment on the most and least interesting/effective parts of the project.

Assessment of Understanding of Scientific Concepts

To measure the impact of the course on learning scientific concepts, students answered questions in a few basic subject areas. Representative questions and scores are shown in Table 4. About half the questions assessed understanding of genetics. Some dealt with the roles of and relationship between genes and proteins and how mutations in genes would affect the encoded proteins (parts of question 5). Others probed the students' understanding of the relationship between genes and traits (question 6 and parts of question 5). Questions about methodology asked about such subjects as agarose gels, twin studies, DNA isolation, and statistical analysis (question 8 and parts of question 5). Questions about concepts influencing data quality and interpretation dealt with correlation versus causation, imperfect correlation, and sample size (questions 4, 7, and parts of question 5).

When the pre- and posttest scores of each student were compared for these "content" questions, the mean test score rose from 24.5 (74% correct) to 28.5 (86% correct) out of 33 possible points. All but two students of the 11 students improved, and those two whose scores declined had modest 1 or 2 point decreases in score. A paired *t* test showed that the increase was statistically significant (one-tailed $p = 0.002$), even though the sample size was small. If the questions were divided into the three areas described above, gains in the mean score were seen in each area (Table 5).

The strongest performance was in understanding of correlation/sample size issues (91% correct in posttest) followed closely by the genetics questions (88% correct in posttest). The greatest gains were made in the methodology area, where students had the lowest initial scores and hence the most "room for improvement" (scores rising 19 percentage points from 62% on the pretest to 81% on the posttest). For example, two of the three questions that had the biggest upward shift in correct answers (five additional students answering correctly in the posttest vs. the pretest) dealt with interpreting an agarose gel (sections a and d of question 8).

The third question with the largest degree of improvement addressed the misconception that "disease genes" such as *BRCA1* or *CFTR*1 have no normal functions and are not found in people without the disease (or with normal risk for the disease). Students were asked to interpret the reference to *BRCA1* as a "breast cancer gene." Initially, only two students correctly labeled the statement "If one has the *BCRA1* gene, one is more likely to get breast cancer" as false. On the posttest, seven students answered this correctly, and nearly all (10 of 11) maintained the correct answer "true" to "Some versions of *BRCA1* make it more likely that one gets breast cancer." These questions directly address a course goal—that students realize the genes have different versions (alleles) and that these versions of the gene are responsible for the variation in phenotype. This is a more sophisticated understanding of genetics than simply the understanding that genes can influence susceptibility to disease.

Two questions showed a decline in correct answers from the pretest to the posttest. In both cases, one can make reasonable conjectures as to how the focus of the project led to the misunderstanding. The number of students answering "true" to the section of question 5 that states "some genetic traits are due to a single gene" declined from 11 to nine. The course's emphasis on complex traits may have contributed to this confusion. Indeed, all 11 students correctly answered "true" to the question "some traits are due to multiple genes."

In the second case, the number of students answering "false" to the statement "genes are made of proteins" declined from seven to six (question 5). This was also one of three questions with only six students answering correctly on the posttest, the lowest score seen for a posttest question. Interestingly, nine students were able to answer a similar T/F question "genes encode proteins" correctly with a "true" response. It may be that after the course students were better aware that there was a relationship between genes and proteins, hence having a tendency to answer "true" to statements connecting the two, but several had an imperfect understanding of the nature of that relationship.

Assessment of Alterations in Student Opinions

The posttest revealed that students' opinions shifted as a result of the course. When asked to rate the statement "I personally believe genes play a role in complex traits such as intelligence and/or behavior" on a Likert scale (1 = strongly disagree, 5 = strongly agree) there was no significant change

Table 5. Summary of student scores on content questions[a]

Question type	Pretest mean % correct (correct/total points)	Posttest mean % correct (correct/total points)	Paired *t* test p value
All content questions	74 (24.5/33)	86 (28.5/33)	0.002
Genetics	81 (13/16)	88 (14.1/16)	0.03
Methodology	62 (6.8/11)	81 (8.9/11)	0.004
Data quality/interpretation	79 (4.7/6)	91 (5.5/6)	0.006

[a] n = 11.

in the mean score from pretest to posttest ($p = 0.06$ in a paired t test). However, the pattern of the scores did change in that they converged much more tightly around the mean of 3.5 after the course, with the SD dropping from 1.3 to 0.7 ($p = 0.02$ in an F-test). Thus, after the course, students more uniformly embraced a modest agreement with the statement. In survey questions that were present only on the posttest (Table 6) students disagreed with the statement "The VMAT2 project convinced me that genes do not play a role in behavior." They disagreed slightly with the statements "I think it is harder to analyze a DNA sequence than I thought it would be before I took this course" and "I think it is harder to link DNA variations to a complex trait than I thought it would be before I took this course," showing that while the course did not radically alter their ideas, they now believed that it was somewhat easier to do these analyses than they had imagined previously.

Student Attitude toward the Project and Evaluation of Its Role in Their Learning

Students were enthusiastic about the project and believed that it helped their understanding. In the posttest students were asked to use a Likert scale to describe their level of agreement with several statements about the project (described as the VMAT2 project in the test question). The results of this survey are shown in Table 6. The strongest agreement was with the statements "The VMAT2 project helped me to understand the use of statistics in biology," and "The VMAT2 project increased my interest in genetics." Each of these statements was rated at or above 4 on the 1–5 scale (5 = strongly agree). Thus the project met its goal in engaging students in a scientific problem. Other statements earning high levels of agreement were "The VMAT2 project helped me to critically evaluate science as reported by the press," and "The VMAT2 project helped me to evaluate the role of genetics in behavior." Again here students believed that the project helped them to meet course goals: to gain a more nuanced appreciation for the role of genetics and use that understanding to think critically about new information that comes to them via the media. Students more moderately agreed that the project helped them understand genetic concepts such as the relationship between genes and proteins or gene variation and phenotypic variation.

Table 6. Student responses to God Gene project survey[a]

Statement	Mean Likert score ± SD
The VMAT2 project helped me to understand the use of statistics in biology	4.33 ± 0.62
The VMAT2 project helped me to evaluate the role of genetics in behavior	4.00 ± 1.00
The VMAT2 project helped me to critically evaluate science as reported by the press	4.08 ± 1.04
The VMAT2 project convinced me that genes do not play a role in behavior	1.92 ± 0.76
The VMAT2 project helped me to understand how variations in DNA sequence can alter phenotype	3.58 ± 1.32
The VMAT2 project helped me to understand the relationship between genes and proteins	3.67 ± 1.18
The VMAT2 project increased my interest in genetics	4.33 ± 0.75
I think it is harder to analyze a DNA sequence than I thought it would be before I took this course	2.75 ± 1.48
I think it is harder to link DNA variations to a complex trait than I thought it would be before I took this course	2.67 ± 1.25

[a] At the end of the course, students (n = 11) were asked to respond to each statement using a Likert scale (1 = strongly disagree, 5 = strongly agree). The God Gene project was referred to as the VMAT2 project in the survey.

Students were also asked to comment on effective or interesting aspects of the project as well as those that failed to be effective or interesting. The most frequently cited interesting aspect of the project was the personal nature of the project (7 of 11 students). Some of the comments in this area were as follows:

> "It was so helpful to have the personal involvement with this project. It helped me to inspect this esoteric notion of behavioral genetics . . . the entire notion of 'nature' controlling something of me – is just cool."

> "Having our 'scores' made us pay attention to the nature of the work and research involved."

> "Seeing a graph of my genetic makeup was pretty awesome."

These data support that the project did indeed meet the goal of being relevant and engaging to the students.

About one-third of the students commented about finding it interesting to think about the influence of genes on complex traits, particularly that the project made this more "real" to them or made the issues clearer (4 of 11):

> "That one could link an allele to a behavior didn't really resonate with me before this."

> "I have always grappled with the nature versus nurture argument, and the scientific vantage point helped to clarify some issues I had with the debate. I've always been dubious of the suggestion of causal relationships between DNA and complex traits; the findings of our VMAT2 experiments have helped me substantiate my questioning of their legitimacy and also proven [*sic*] that compelling evidence in support of those relationships exists."

Students also appreciated the opportunity to do "real science:"

> "It was fascinating to work with all the high-tech equipment."

> "I liked talking about exactly what is going on in the lab . . . I learned tons."

> "[The most interesting/effective aspect was] that we could replicate—albeit unscientifically and statistically suspect—the project Hamer outlined in his book."

Other strengths mentioned were having fun speculating as to what classmate matched which scores/genotypes, and looking at a connection between religion and science.

The most frequently cited uninteresting/ineffective part of the project was the book *The God Gene* (cited by four students). The reasons for the dissatisfaction varied. One student did not like the writing style and another struggled with reading in general, but two more took issue with what they saw as the lack of conclusive evidence for *VMAT2* variation playing a role in spirituality:

> "*The God Gene* was really frustrating to me simply because it never really reached a concrete conclusion . . . "

> "The place he isolated didn't seem to me to be the real cause of it all."

These answers suggested that these students were dissatisfied with the evidence presented in the book, as opposed to feeling that the book did not enhance the course. Buttressing the idea that the ambiguity in Hamer's data was a frustration that could actually enrich the course, another student stated that discussing the validity of Hamer's data was the most interesting part of the course.

Another aspect of the project that about one-quarter of the students cited as problematic concerned the length or pacing of the project. Two students commented that it was difficult to keep ideas straight through a long project or through lab protocols with many steps, and another noted that it would have been nicer to have more time to look at the sequence data but that the short nature of the term precluded this. These issues are inherent in a project-based lab and were exacerbated by the 1-mo term. The need to integrate all of the information, and in the case of a shortened term, to do so quickly, can be both a useful challenge and a source of frustration for students.

Other issues cited were dislike of using computers (two students), struggling to understand and interpret gels and PCR, finding the lack of a previous science background challenging, and finding having previous science background made for repetition (one student each). One student did not have any negative comments and most had only one comment rather than the two the question requested.

Impact of the Choice of SNP on Project Goals

Initially, I was concerned that the lack of certainty as to identity of the authentic "God Gene SNP" would affect the students' interest in the project or prove confusing. However, as shown above, students responded to the project with enthusiasm and did not raise the SNP issue on the survey. In our many interactions, students never commented to me about the use of this SNP, whereas they did express other points of confusion or frustration. Given that the ambiguity in the SNP's identity did not alter student engagement, it does not alter the pedagogical goals of the project. Students must master the same content to understand the project and formulate conclusions as to the validity of any association between genetic and phenotypic variation, regardless of whether we are extending Hamer's work by direct replication in a new population or by looking at a (potentially) different SNP in the same gene.

Scientifically, either use of the "real" SNP or an alternate SNP is defensible; both are authentic explorations of an unresolved and interesting question. Regardless of the SNP being examined, the question is the same—is this particular variation in the DNA correlated with the variation that is seen in the personality test scores? Hamer's preliminary work provides a motivation for focusing on *VMAT2* variations, but it is not proscriptive; he notes that the variation he sees could at best explain only a small fraction (<1%) of the variation in spirituality. Along with exploring the effects of other genes on spirituality, an understanding of the changes, or set of changes, in *VMAT2* that contribute to spirituality would be a valuable addition to Hamer's work. Working toward answering this question provides students with a genuine research experience.

Because the change is in an intron, any observed significant correlation would presumably reflect other associated changes in the gene's coding or regulatory sequences. This consideration presumably also affects Hamer's work, as the known A/C transversions all fall in introns or the 3′ untranslated region (Edwards, 2001; dbSNP, 2006), except for three in the promoter region, none of which have similar frequencies to Hamer's SNP (Lin *et al*., 2005). There is substantial linkage disequilibrium among the SNPs in this gene (Lin *et al*., 2005), so it is likely that one polymorphism is coinherited with other changes to form a haplotype. In his book Hamer explains that he examined a single SNP as a means to test an associated set of changes in *VMAT2*. As noted previously, the indirect nature of potential correlations between genotype and phenotype is actually an advantage in our case. By studying a change in an intron, students will not learn of alterations they may have in *VMAT2* that would affect the structure or expression of this gene, insulating them from any future findings that such alterations are deleterious.

It was an advantage that the polymorphism we studied had other nearby SNPs that students could include in their analysis. To make the project interesting for the students, it is critical that they see genetic variation. Having three relatively common sources of variation increased the complexity of the genotypic patterns students saw, so that even in our small sample of 13 we saw five distinct genotypes. Based on their behavior in the lab and their survey comments, students seemed to enjoy seeing the many different "types"—both genotypic and phenotypic—present in the class. For example, in the survey students commented that it was fun or interesting to see the results of other students, to test different alleles for association with various traits, and to see that two of the students in the class carried the more rare variation at position 52.

CONCLUSION

The God Gene project should prove adaptable to other types of courses and institutional settings. Although my focus was the nonmajor student, the science behind *The God Gene* is sufficiently complex that it would be informative to biology majors as well. Indeed, the project has been used in an upper-level genetics course for biology majors (P. Connerly, Indiana University East, personal communication). Although significant resources are required, the project is not

prohibitively costly and does not use equipment beyond that normally available in laboratories equipped for molecular biology. The major expenses are the sequencing reactions, the PCR beads, and the kit for extracting the band from agarose, some of which could be substituted with more inexpensive alternatives. The experiments and discussions could fit within the time constraints of typical lab periods. Finally, the laboratory experiments proved technically feasible, even for students inexperienced in molecular biology. Each student was able to isolate DNA from his or her cells, amplify a portion of the *VMAT2* gene, and obtain readable sequence information. The robust nature of the labs should make the project easily transferable to other settings.

This project provided an opportunity for students to explore biology in an interdisciplinary and personal context. The project met its goals of informing students about genetics, enabling them to be more critical consumers of media, and stimulating their interest in science. After the project and other course activities were completed, students were better able to answer questions about genetics concepts and data interpretation and reported that they strongly believed the project assisted them in evaluating science as reported by the popular press. Students were very engaged in the project, enjoying its personal nature, the opportunity to do DNA-based laboratory work, and the exploration of the interplay between genetics and the environment in determining complex traits. Students strongly agreed that the God Gene project increased their interest in genetics. It is hoped students' increased knowledge and interest stimulates an active, critical, and confident engagement with science as it touches their daily lives.

AUTHOR NOTE

This paper notes that none of the sites examined in the God Gene project had been linked to any deleterious phenotype. In particular, *VMAT2* polymorphisms including site 54 (rs363420) had been investigated for an association with schizophrenia in a Japanese population and no such association was seen (Kunugi *et al.*, 2001). After this manuscript was submitted, two reports that investigated correlation between *VMAT2* variations and schizophrenia became available. In Talkowski *et al.* (epub ahead of print, Nov. 27, 2007, Hum. Mol. Genet.) a series of genes involved in dopamine synthesis or function were investigated, including *VMAT2*. Three polymorphisms in *VMAT2* (rs363393, rs363338, and rs363227) were correlated with schizophrenia in two populations; none of these were those SNPs studied in the God Gene project. Site 71 (rs363343) was found to have an association of borderline significance ($p = 0.046$) in a U.S. population, but this effect was not replicated in a Bulgarian population ($p = 0.782$), nor when the two populations were considered jointly. Sites 52 and 54 were not investigated in this report. In Gutierrez *et al.* (2007, Am. J. Med. Genet. Part B *144B*, 502–507), both sites 54 and 71 were examined (referred to as C2666T and A2683C of *SVMT*) for association with severe bipolar disorder and schizophrenia. This report finds a correlation of borderline significance ($p = 0.051$) with schizophrenia at site 54 in a case-control study in a Spanish population. Both sites 54 and 71 contribute to three-site haplotypes (together with the SNP rs363272, A745G in intron 14, which was not studied in the God Gene project) that are significantly correlated with increased risk or protection against schizophrenia and bipolar disorder. The relationship of the individual sites and risk is complex as both the common alleles and the rare alleles at sites 54 and 71 appear in various combinations in both haplotypes associated with risk and those correlated with protection against these disorders. For example, the haplotype correlated with the highest risk (fourfold above typical levels, which are cited as a 1% lifetime morbid risk in the Talkowski *et al.* paper) is that with the two common alleles at the 54 and 71 sites and a G at A745G, but another haplotype associated with elevated risk contains the minority allele for each of the 54 and 71 sites. Similarly, each allele is present in apparently protective haplotypes that were not seen in patients but were observed in controls. As all of the SNPs named in these three-site haplotypes, including positions 54 and 71, are present in introns, it is unlikely that they are directly causal of any of the phenotypes seen. Furthermore, the variations are extremely common, much more so than is schizophrenia. According to Edwards (2001), the frequency of the "rare" allele at site 54 is 0.309, and dbSNP (2006) reports heterozygosity at site 71 as 0.495. Thus more than a third of individuals will have the minor allele at one or both of these positions. Overall, information about the sequence at these individual sites has limited, if any, predictive value for any particular person's schizophrenia risk.

These new findings illuminate a difficulty in the study of human genetics in the educational setting that must be grappled with by the instructors of such courses. In any study of human genotypes, even those restricted to noncoding regions, information may be revealed that may later be associated with a phenotype different than that being studied. For example, the Alu insertion/deletion polymorphism in an intron of the tissue plasminogen activator gene that is studied in many laboratory courses (see http://www.accessexcellence.org/AE/AEPC/DNA/detection.html for a description of this lab) has been linked to heart disease, as well as other phenotypes (see, for example, van der Bom *et al.,* 1997, Circulation *95*, 2623–2627). While the study of noncoding regions, such as those studied in the God Gene project, generally will not reveal information that could show that a student carries an allele that causes a disease, it is always possible that a neutral variation could be linked to a variation that alters phenotype. Instructors should consider the possibility of association with other phenotypes when analyzing genotypes of students at any locus and incorporate it into their proposals to their Institutional Review Board. In the implementation of the God Gene project, instructors could ask their students to study a single site, as this is less likely to be informative of risk than a set of sites, and could choose a site that currently shows no association with phenotype (e.g., rs363387, studied in Gutierrez *et al.* or one of several sites examined by Talkowski *et al.*). The study could be done blinded so that students would not know their particular genotype or TCI score. Alternatively, students could examine a different locus that has not currently been linked to any deleterious phenotypes (e.g., PV92; Dolan Learning Center 2007b), but discuss this study in the context of *The God Gene* book, or they could test variations at the alternative locus for association with scores on any of the scales of the TCI.

Given the rapid increase in genetic testing as well as the possibility of purchasing information about one's own genome outside of a medical context (for example, www.23andme.com offers customers analysis of 600,000 SNPs in their genomes), our students will likely become aware of at least some portion of their genomic sequence in their lifetime. Thus, labs helping students to evaluate the implications of knowing their own genomic information, while carrying inherent risk, are also of great relevance.

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