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# A low-cost, in silico nutritional genomics course-based undergraduate research experience applicable to multiple disciplines

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## Abstract

This article describes the development and assessment of a Nutritional Genomics course, designed to be held in a regular classroom during normal class periods, with few extra costs to the students or the department. The course was run as an upper-level undergraduate and lower-level graduate student course. Student taking the course spent 11 weeks learning and then 4 weeks using various in silico methods to independently characterize genes of interest in the field. During the last 4 weeks of the course, students combined their methods to test a hypothesis they generated about a gene they have not yet studied and completed a final report in the form of a journal article. Two students have published or are in the process of publishing work from their final project. Validated surveys of genetic knowledge given at least 6 months following the course indicated a very high level of genetic knowledge retainment, and favorable attitudes toward genetics testing and medical use of genetics. Finally, self-perceived critical thinking skills were high, and students indicated that they perceived these skills to be gained by their participation in the course. Materials and syllabus provided in the manuscript makes this CURE easily transferrable to other disciplines.

## KEYWORDS

cost-effective, CURE, genetics, single nucleotide polymorphism, web conference

## 1 | INTRODUCTION

While traditional laboratory courses are designed for students to learn standard techniques in a field and replicate known discoveries, course-based undergraduate research experiences (CUREs) are designed to let students design authentic, hands-on research questions, and to make new discoveries in that field within a college course. Multiple assessments of CUREs over traditional laboratory courses have shown that CUREs provide increased content knowledge, increased technical skills, and increased persistence in science, among other outcomes (reviewed by Reference 1.

In addition, increased science self-efficacy is seen for students taking CUREs, possibly because they see themselves as independently addressing a problem, tackling setbacks, and ultimately achieving results.<sup>1,2</sup> While there are calls for more CUREs to be developed,<sup>3</sup> professors cite lack of time to develop a CURE, lack of money for research projects, and lack of laboratory research space to run the CURE. However, recent studies have found that computer-based empirical research projects done by undergraduates can produce similar, if not higher gains in satisfaction and sense of achievement with the course, when compared to bench-based laboratories.<sup>4</sup>

Knowledge about genes, genomics, and phenotypes has expanded at a rapid pace, but undergraduate genetics courses are often taught the same way as they have been for years, with basic knowledge attainment about genes and inheritance provided in a lecture format and with little-to-no hands-on activities. This has likely resulted in a knowledge-gap in genetics/genomics trained professionals. For example, a recent study found that only 10% of didactic programs in dietetics had any specialized training for their students in nutritional genomics or genetics.<sup>5</sup> An earlier review reported that in a systematic analysis of studies, the majority of employed dietitians had little to no confidence in nutrigenomics knowledge, and less than half of the directors of dietetics programs felt confident in their own nutrigenomics/nutrigenetics knowledge.<sup>6</sup> This lack of knowledge and confidence in genomics is not limited to dietetics programs—medical educators are also finding that training in clinical genetics for the medical workforce is limited.<sup>7</sup>

This article describes the development and assessment of learning gains for a Nutritional Genomics CURE, designed to be held in a regular classroom during normal class periods, and with no extra costs to the students or the department. Students in the CURE use *in silico* to test independent hypotheses. While the focus for the course being described was nutrition, the topic, and content could be changed very broadly still using the same approach that will be described.

## 2 | METHODS

### 2.1 | Course description and structure

The course was designed as a 50 min, 3-day per week (Monday–Wednesday–Friday) schedule for juniors, seniors, and graduate students with no genetics course prerequisite, and no departmental restriction. Mondays were reserved for a brief lecture and some discussion, Wednesdays for *in silico* activities, and Fridays for guest speakers. The course could easily be changed to a Tuesday/Thursday schedule, omitting the guest speakers. An ebook, available through our library was used for required readings.<sup>8</sup> Topic-specific journal articles supplemented the required readings. Table S1 shows the syllabus from 2018, during the third year of the course and was typical for previous semesters. *In silico* lab activities are described below. Outside speakers volunteered their time to come to class either in-person, or via web-based conferences (either Zoom or WebEx). In 2017, the education director from 23andMe<sup>®</sup> came to the class from San Francisco in time for the “personalized genetics” section,

and even gave out free ancestry test kits to all students in the course.

Students were graded based on attendance in class, a weekly reflection piece, and lab reports due at the end of each block. Students were told to pick a single gene for each block of activities and analyze that gene with each of the newly introduced tools. For the final report, students were told to pick another gene (not to have been used by them in any of the previous blocks) and perform at least three different analyses on the gene or genetic region, which would be designed to test a hypothesis based on the gene or phenotype of interest. Four weeks of the course were dedicated to the independent project. The professor made herself available in class each of these days but students were not required to come to class and could do nearly all of their experiments on their own time.

#### 2.1.1 | *In silico* lab activities

All websites used in the *in silico* activities methods are listed in Table S2. The activities are described in the supplemental methods. Each week one or more of the *in silico* activities were demonstrated, and then students tried them on a gene of interest. For the hypothesis-based individual experiments, students picked a new gene or phenotype of interest, developed a hypothesis about this gene and/or phenotype and then tested and investigated the hypothesis using at least four of the techniques they had learned during the course.

#### 2.1.2 | Participants

The course has been run since 2015 as a small CURE with both graduate and undergraduate students. In 2015, there were five undergraduates and four graduate students. In 2016, there were two graduate students and two undergraduates. In 2017, there were five undergraduates and three graduate students, and in 2018, there were nine undergraduates enrolled, but no graduate students. The course was not run in the Fall of 2019 but plans to run the class in the Fall of 2020 are in place. Total students enrolled were 20 undergraduates and 9 graduate students for a total of 29 students over 4 years.

#### 2.1.3 | Human subjects

The course surveys were reviewed and approved by the Institutional Review Board at Virginia Tech. This study is

part of a larger study on gains in critical thinking skills throughout departmental courses.

### 2.1.4 | Postcourse survey

In the spring of 2019, all previous students were emailed with a link to a Qualtrics<sup>®</sup> survey using the course email lists. Students had completed the Nutritional Genomics course at least 6 months prior, or as long as 4 years and 6 months prior to taking the survey. A total of 12 students returned the survey (40% response rate, four graduate students, and eight undergraduate students). The survey was developed by combining questions from two separate published surveys on genetics knowledge, and genetic testing, which have been used in other studies.<sup>9–12</sup> In addition, questions about skills learned in the course were asked using a Likert scale.

## 3 | RESULTS

### 3.1 | Course outcomes

For three of the 4 years, the course utilized a “Student Centered Active Learning Environment with Upside-down Pedagogies (SCALE-UP) classroom (Figure 1a) where students worked at computer workstations with bookmarked webpages. During the fourth year of the course when the SCALE-UP room was not available, the course was run in a regular, small (~20 desk) classroom. Like others who have published on the subject,<sup>13</sup> the problem-based nature of the course, rather than the technology per se was needed. Thus, even in the regular

classroom, students used their own laptops to do the in silico work. Using the traditional classroom made it harder for the instructor to walk around and help individual students, or for students to help each other, but otherwise the course ran similarly.

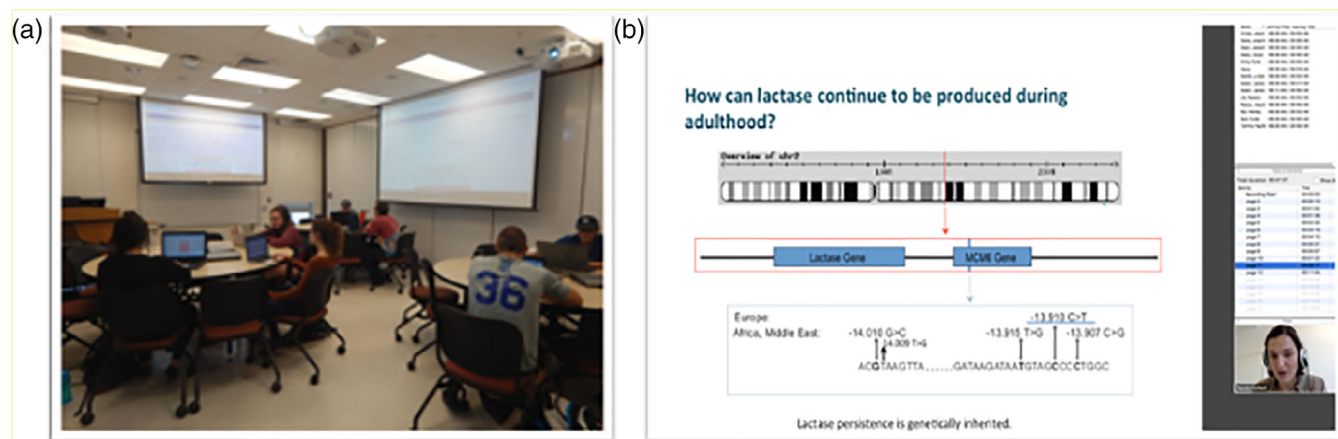
Unique to many CUREs, this course used web conferencing to bring experts from around the world to the class. Scientists were contacted by email, and most readily agreed to do a web conference for no additional compensation. A screen capture showing a web conference by Dr. Pascal Gerbault, University of Westminster, UK, is shown in Figure 1b. The professor sent thank you notes following each guest speaker's presentation. Students commented (in their annual student course assessments):

The weekly guest lectures were awesome - I learned so much from these professional researchers in diverse fields and, importantly, I gained new perspective on some very relevant issues by listening to their talks.

... valuable information from professionals in our fields.

The guest speakers were very interesting and really added to the course material. I would absolutely recommend this class to any student.

Of the 29 students enrolled in the course over the last 3 years, most biological science disciplines were represented including animal science, food science, nutrition, neuroscience, biomedical engineering, biology, and biochemistry. Gender ratio was skewed toward females (66%), which is not representative of the university



**FIGURE 1** Student activities and conferences. (a) Scale-up classroom showing round tables and students using computers with multiple projection screens in the room. The professor's podium can be seen in the left corner. (b) Screen capture of a Friday web conferences showing Pascal Gerbault (University of Westminster, UK) talking about evolution of SNPs in the lactase gene (LCT) [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

gender ratios. Each student chose a different gene or phenotype of interest to research for their final project. Examples of some of the figures generated by students for their final project are shown in Figure 2.

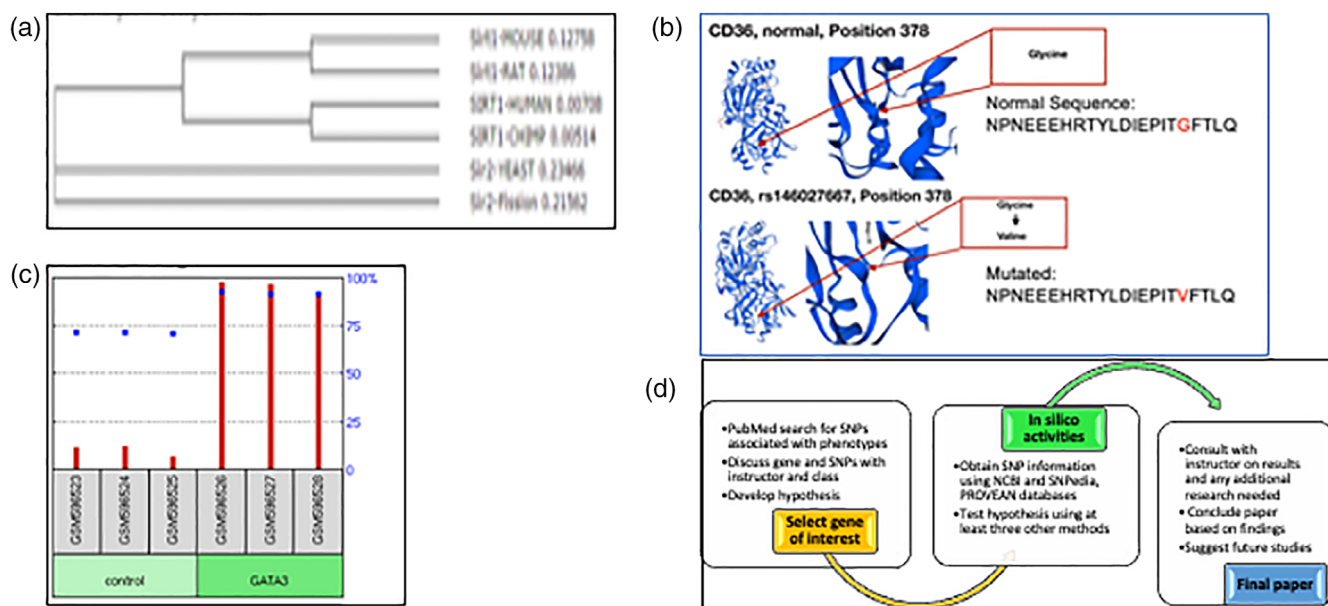
One student has published an article based on work done in the course.<sup>14</sup> Of note, he was a graduate student in the author's laboratory, but the project was a separate analysis from his thesis project. Another student submitted an article based on work he did in the class on the gluconolactone (*GULO*) gene. The student contacted the professor after graduation and asked to work with her remotely on the project while he took a year off from academics. He has since been accepted to graduate school and is working in the genetics/genomics field. While that article was rejected, we have plans to resubmit to another journal after additional edits.

### 3.2 | Survey results

Only 40% of students returned the survey. All course years were represented except for 2016 when there were the lowest number of students in the course, and none of them returned the survey. Five of 12 students (41.6%)

indicated that they had taken another genetics course in addition to Nutritional Genomics. Three of 12 students (25%) indicated that they had taken a personalized genetics test—of note, only one of these respondents was from the 2017 course when 23andMe<sup>®</sup> representatives had given a free ancestry kit to each student. Four of 12 students (33.3%) indicated that either they or someone in their family had a genetic disease.

In the part of the survey on genetics knowledge, which was a true/false quiz, 15 of the 17 questions were answered correctly by 91% or more of the students giving an overall score of 92.6% (Table 1). The survey also measured student's understanding of genetic issues (medical and social) in society, although this was not a main focus on the course. This part of the survey was retained in our study, as it is part of the original validated survey materials.<sup>9–11</sup> The Nutritional Genomics students scored low (overall score 54.5%) (Table 2). This result was somewhat expected because most of these topics were not directly discussed in class, except during the section on genetic engineering. The next part of the genetics survey measured attitudes toward genetics research and testing. In this survey students who took the Nutritional Genomics course generally scored high (strongly agree and



**FIGURE 2** Student-generated data. Examples of student data generated using online databases and analysis sites. (a) Phylogenetic tree for the sirutin 1 (SIRT1) gene using Clustal. This data was generated to test the hypothesis that SNPs in Sirt that affect conserved phosphorylation or acetylation domains would be more detrimental than those that were either not conserved not within secondary modification. (b) Protein 3D structures of cluster of differentiation (CD36) gene, generated using Swiss-Model. The student was testing the hypothesis that 371 previously uncharacterized SNPs in CD36 could be grouped by Severity using 3D modeling to predict structure–function relationships. (c) Gene expression profiles for GATA binding protein 3 (GATA3) using GEO expression database from NCBI. This student was testing the hypothesis that transcription regulation of MAO-A gene could mediate differences in motivation, through a Variable Nucleotide Tandem repeat (VNTR) located in the promoter, which variably a GATA binding motif. (d) Schematic showing how the student develops an independent project that results in a final article [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

**TABLE 1** Results of genetic knowledge survey

Genetics knowledge survey	Percent with correct answer
The onset of certain diseases is due to genes, environment and lifestyle.	91.60%
A gene is a disease.	100%
One can see a gene with the naked eye.	100%
Healthy parents can have a child with a hereditary disease.	100%
The carrier of a disease gene may be completely healthy.	100%
All serious diseases are hereditary.	100%
The genotype is not susceptible to human intervention.	100%
The genes of humans and other animals can be modified using genetic engineering.	100%
Genes control hereditary characteristics.	100%
The child of a disease gene carrier is always also a carrier of the same disease gene.	100%
A gene is made of DNA.	91.60%
Genes are inside cells.	91.60%
A gene is a cell.	91.60%
A gene is a part of a chromosome.	100%
Genes are bigger than chromosomes.	100%
Different body parts include different genes.	66.60%
It has been estimated that a person has about 40,000 genes.	41.60%
<b>Overall score</b>	<b>92.6%</b>

Note: The percent of students who answered correctly were reported ( $N = 12$ ).

agree) on those statements grouped as favorable or positive toward genetic testing and research for medical genetics (range 4.25–4.83), while they scored lower (neutral, disagree, strongly disagree) on the statements grouped as reserved or negative (Table 3).

In the final part of the survey, students were asked to reflect on their overall course experience, as related to skills and knowledge gains. Generally, self-perceived critical thinking skills and research/data analysis were high using a reverse-wording survey question scheme. Students scored high for the statements supporting attributable gains (range 4.17–4.83), and lower for the statements which did not support those skills (range 1.08–2.67). Interestingly, students indicated that they have or would use the skills in future courses or their career ( $4.42 \pm 1$ )

**TABLE 2** Self-perceived knowledge in medical genetics and ethics

Medical genetics and ethics	Percent with self-perceived sufficient knowledge
<i>Medical uses of genetics</i>	
The possibility of early detection of certain disorders using DNA-testing	66.60%
The significance of DNA-testing for my relatives	75%
The significance of DNA-testing for my offspring	83.30%
The possibility to use genetic knowledge to prevent or treat a disorder	41.60%
The possibilities and risks of gene therapy	41.60%
Your rights to refuse DNA-testing	75%
<i>Social consequences of genetic testing</i>	
The consequences of DNA-testing for my daily life	66.60%
The consequences of DNA-testing for my work	41.60%
The consequences of DNA-testing for taking out insurance	33.30%
Your own possibilities to apply for a DNA-test	41.60%
The rights of third parties to inquire about the results of a DNA-test	33.30%
<i>Medical average score</i>	<i>64%</i>
<i>Social average score</i>	<i>43%</i>
<i>Overall average</i>	<i>54.5%</i>

Note: Students ( $N = 12$ ) were asked to rate themselves as having “sufficient knowledge,” “some but not enough knowledge,” and “no knowledge.” Percent with self-perceived sufficient knowledge is calculated. The categorical listing is based on the report by Haga and colleagues<sup>9</sup>.

but did not necessarily think they learned more in this course than in other college courses ( $3.83 \pm 1.11$ ; Table 4).

## 4 | DISCUSSION

CUREs serve as ways for educators to expose more students to authentic research experiences over the course of a semester. This study describes the implementation and assessment of a CURE that uses in silico tools for a low-to-no cost research project. In addition, and somewhat unique to other CUREs described in the literature and on CUREnet (<https://serc.carleton.edu/curenet/>)



**TABLE 3** Attitudes toward genetic research and testing

Statement	Score
<i>Favorable attitudes</i>	
I think the development of DNA research is hopeful for the treatment of diseases	4.83 ± 0.39
I think that DNA/genetics research represents positive medical progress	4.83 ± 0.80
I approve of using DNA-testing for early detection of diseases	4.58 ± 0.67
I would want to know whether my disease is hereditary	4.75 ± 0.62
I would inform my children about the results of a DNA-test for a specific disease	4.42 ± 0.51
I would inform my parents about the results of a DNA-test for a specific disease	4.25 ± 0.97
I would inform my siblings about the results of a DNA-test for a specific disease	4.42 ± 0.90
<i>Negative or reserved attitudes</i>	
I worry about the consequences of DNA-testing for being able to take out insurance	3.58 ± 0.90
A DNA test will change one's future	3.67 ± 0.89
As long as a disease cannot be treated, I do not want a DNA test	2.17 ± 1.40
If I had a DNA test done, my family need not know about the result	2.92 ± 1.00
I do not want a DNA-test to tell me that I am at risk for a certain disease	2.58 ± 1.16
I worry about the consequences of DNA-testing for the chances of finding a job	2.33 ± 0.98
The idea of a DNA test frightens me	2.17 ± 0.94
I actively seek information about genes, genetics, and genetic testing	3.75 ± 1.14

*Note:* Items were answered by students ( $N = 12$ ) using a 5-point Likert scale with 1 = strongly disagree and 5 = strongly agree. The average score ± standard deviation is shown. The statements were divided into positive attitudes and negative attitudes, according to Haga and colleagues<sup>9</sup>.

index.html), the actual research takes place in the last 4 weeks of the course as an iterative project, occurring after the students have learned and used multiple in silico databases and web sites for analysis of other genes. Thus, this CURE both trains the student in the basics of in silico research using projects that they can help each other on, and then finishes with an independent project based on those activities. The Nutritional Genomics CURE could easily be converted to one on bacterial resistance genes, or cancer biology, or tree ecology, based on availability of genome databases to students to utilize.

This course was also offered to both graduate students and undergraduates. While originally the thought was that the graduate students could mentor the undergraduates, this was not the case. Most graduate students came in with similar levels of genomics knowledge, especially with the tools, and in some cases, undergraduates mentored the graduate students.

In developing this course, the goals were (a) to create a course where students could learn genetics in a topic area they were interested in, hopefully sparking interest in genetics and genomics and (b) to create lasting genetics competence and understanding, that could be used in their careers. In the last goal, I was hoping to instill a confidence in using our public databases to understand genetics, genes, and phenotypes, in people who were not going into careers as genetic counselors. This is crucial to society in general. As scientists continue to increase what is known about genotype–phenotype interactions, including personalized genetics, pharmacogenetics, and nutritional/lifestyle genetics, more health professionals, in addition to genetic counselors, need to feel comfortable in digging through the genetic databases and literature to understand the functional consequences of genetic variants.

Student artifacts indicated that each student gained knowledge on how to use the databases and web-analysis servers to tackle a hypothesis-based question. Over the course of four semesters teaching Nutritional Genomics, none of the students have chosen the same gene or phenotype to study. For example, students have chosen to analyze interleukin 6 gene and tumorigenesis, the melanocortin-1-receptor and melanoma, the insulin promoter factor 1 gene and diabetes, Patatin-like phospholipase domain-containing protein 3 (PNPLA3) and nonalcoholic fatty liver disease, and the Glutamate Ionotropic Receptor NMDA Type Subunit 2B gene and Alzheimer's Disease. All of the genes were unique, and most ones that the professor did not know about, making the final articles interesting for the professor to read as well. Each article contained at least three (and usually more) original data figures, generated by the student, and for the most part, not present in published literature. The students tested their hypotheses using the results from these data, and then used the literature to support or refute their findings. During the last 4 weeks of the course, students worked independently outside of class but also had open class time to get help from the instructor. In some cases, the students needed refreshers on some of the tools, while in other cases, students needed help in deciding which tools would best test their hypothesis. Most of the time the students were not able to fully test their hypothesis without considering some “wet lab” activities that were included in their final article

**TABLE 4** Student responses on course experience

Please rate the following questions, based on your experience in the nutritional genomics course	Average $\pm$ standard deviation
<i>Critical thinking/problem solving skills</i>	
<i>Supports attributes</i>	
This course required you to use critical thinking skills to understand the content	4.75 $\pm$ 0.62
In this course, you gained critical thinking skills	4.50 $\pm$ 0.67
Your instructor taught you how to distinguish assumptions, inferences, and implications from facts	4.17 $\pm$ 0.94
Your instructor encouraged critical thinking skills in the learning process	4.83 $\pm$ 0.58
<i>Does not support attributes</i>	
As there were no exams in the course, you did not need to memorize the content in order to be successful	2.67 $\pm$ 1.44
In this course, you could memorize material without really understanding the content	1.67 $\pm$ 0.89
<i>Research/data analysis skills</i>	
<i>Supports attributes</i>	
Your instructor provided you with skills or methods to evaluate course materials	4.67 $\pm$ 0.65
Your instructor taught you how to ask questions that scientists routinely ask	4.33 $\pm$ 0.78
This course taught you to think more logically	4.42 $\pm$ 0.90
Because of this course, you are better able read and correctly interpret complex data in a scientific article	4.50 $\pm$ 1.17
You gained skills in evaluating, observing, problem-solving and interpreting data.	4.58 $\pm$ 0.90
<i>Does not support attributes</i>	
In this course, all data was interpreted for you	0.92 $\pm$ 1.00
In this course, you were provided with all questions and just had to answer them	1.08 $\pm$ 0.90
Your instructor provided you with all of the content you needed to be successful in the course. You did not need to investigate, interpret or problem solve to complete assignments	2.75 $\pm$ 1.29
<i>Course utility</i>	
You learned more in this course than other courses you took during college	3.83 $\pm$ 1.11
You can (or have) use(d) the skills learned in this course in future courses or your career.	4.42 $\pm$ 1.00

*Note:* Questions are grouped for content area for this table, but the questions were asked in a random order for the survey. A Likert scale of 1 = strongly disagree to 5 = strongly agree was used. The questions were grouped into critical thinking/problem solving skills, and research/data analysis skills, and course utility, as well as further subdivided into positive attributes and negative attributes (reverse wording for validity) by the authors who designed the survey (Jallinoja & Aro, 1999)<sup>11</sup>. *N* = 12 student respondents.

conclusion/discussion. One student put the following comment at the end of the postcourse survey:

Wonderful, wonderful class. I never enjoyed (or really understood) the applications of genetics. The instructor allowed us to explore our questions in self-discovery.

Thus, the first goal of student's genetics/genomics learning in an area of their interest, was achieved. In addition, two students submitted their work from this course for publication. One of these was rejected and is being prepared for submission to another journal. The second student did extensive additional analyses as part of his thesis project, and this article was accepted.<sup>14</sup> These article submissions and the one acceptance to date

indicate that students are contributing to general science knowledge about genomics.

Validated, previously published survey instruments were used to gauge student learning outcomes. The scores for "Genetics Knowledge" for students who had previously taken the course at least 6 months prior to taking the survey was higher (92.6% answered correctly, with a range of 82–100% correct) than those reported by two other groups who used these survey questions. In a previously published article using this survey, the percent correct ranged from 18%–88% with an overall average score of 63.5%.<sup>11</sup> However, this study was conducted more than 10 years ago, when many older adults would not have been exposed to genetics in school. The other study by Haga and colleagues was more recent, but still, the correct percentages ranged from 25 to 99% with an

average of 83.6%.<sup>9</sup> Two of the questions scored lower on our survey results as well as on the published results. One of these asks if humans have an estimated 40,000 genes. Students who had taken Nutritional Genomics only got this question correct (false) about 41% of the time. This question is actually not worded well (in being a true/false question but asking about an estimate) but was kept in the survey to make sure nothing about the validity of the survey was compromised by removing it. Thus, in our survey, the number was changed to 40,000 to account for this, and to attempt to make the question clearly false. According to the latest data (build 38p12<sup>15</sup>) humans have 20,454 protein coding genes<sup>15</sup> with 23,940 noncoding genes, and 15,204 pseudogenes. The current total number of genes in humans, counting all of these is 59,598.<sup>15</sup>

In considering current ethical, social and medical genetics issues, such as a person's understanding of the significance of DNA testing for relatives or children (medical issue), or the consequences of DNA testing on insurance coverage (social issue), students who had taken the Nutritional Genomics course scored their overall self-perceived understanding higher (54.4% in this study, compared to 17% in Haga and colleagues and 9% in Morren and colleagues).<sup>9,12</sup> However, our student's scores still indicated that this was not an area that they had strong self-perceived knowledge. In considering the syllabus, only 1 week was spent on clinical genetic testing or personalized genetics, and 1 week on genetically modified foods (another social issue). The topic issues were focused on the science of clinical or personal genetic testing, or making genetically modified foods, rather than medical or social ethics of these topics. Another person running the course could easily change the focus to address this area.

The last area of the genetics survey covered genetic testing in general, with students either agreeing or disagreeing with the statement on a Likert scale. These results suggest that students who took the Nutritional Genomics course had an overall more favorable attitude toward genetic testing and medical genetics research, as the statements that were more favorable toward genetic testing received scores in the "agree- to- strongly agree" range, while statements that were more unfavorable to reserved toward genetic testing were scored "neutral-to-strongly disagree" by students who took the Nutritional Genomics course. The results were similar to what Haga and colleagues found using the same survey instrument.<sup>9</sup>

The last survey taken by students was seeking to understand their course experience. This survey was developed by the professor based in part on a validated assessment of critical thinking skills.<sup>16</sup> Students scored the statements based on a sliding 0-5-point Likert scale,

with higher scores indicating agreement with the given statement. Generally, students scored their self-perceived critical thinking skills gains as high (e.g.,  $4.50 \pm 0.67/5$  points for the statement "In this course you gained critical thinking skills, and conversely low for the statement "in this course all data was interpreted for you— $0.92 \pm 1.0$ , with many students choosing 0 on the slider rather than 1 = strongly disagree).

Several confounders exist for these data. First, all data, and especially that for the critical thinking skills/problem solving skills were self-reported. However, students who took nutritional genomics have received very high scores on their final articles, which could be used as artifacts to examine these skills in more detail. Second, compared to others who have used the genetics knowledge and attitudes surveys,<sup>9,11,12</sup> we have very low numbers. The 12 students who did respond (of 29 taking the course over the last 3 years), represent nearly half of those contacts (41.3%) and except for one section, represent all levels and sections taught.

## 5 | CONCLUSION

In conclusion, a genomics-based CURE was developed that was (a) cost-effective; and (b) could be used in standard classrooms, overcoming some of the barriers to a CURE. Students who took the Nutritional Genomics CURE retained high levels of general genetics and genomics knowledge, compared to other studies of the public, with high self-perceived critical thinking skills. These students also produced independent, new data which was, in two cases, published or in review for publication. For the professor teaching this course, each semester was unique and the material and assignment grading never became boring. All materials and exercises were provided to make this course easily transferrable to other disciplines.

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## CONFLICT OF INTEREST

The author has no conflict of interest to report.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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## Supplemental Methods

### *In silico* Lab Activities

Taste phenotype activity: This was one of the wet labs that was done in a regular classroom on campus. Materials were paid for by the professor (~\$20). Students took a survey of taste preferences prior to coming to class (available upon request), and then using liquids (grapefruit-unsweetened; tonic water, lemon juice, salt water) students rated the sweetness, saltiness, sourness and bitterness of the liquids (online survey available upon request). They then indicated their ability to taste based on using genetics taste strips for thiourea, PTC, and sodium benzoate (Fisher Scientific, Pittsburgh, PA). Their data were added to the online survey. All of the data were deidentified by the professor and then shared for student analysis of class statistics.

Make your own pedigree activity: Students were encouraged to contact their family and have them rate taste preferences for the liquids prior to the start of class. Alternatively, they could choose another phenotype to analyze. Family data was input to the “My Family Health Portrait” database) to generate a pedigree. Students were shown how to predict genotypes based on phenotypes, and used the e!Ensembl phenotype viewer (Hunt et al., 2018) to hypothesize which genes and which variants might be responsible for the phenotypes in their family members.

Make your own DNA activity: This was the second wet lab, done in a regular classroom. Materials were paid for by the professor (~\$20). Students were asked not to eat or drink for at least one hour prior to lab. Students placed ~ 1 ml of spit into the cup (cups were transparent shot glasses- Dollar Tree, Chesapeake, VA). The students were instructed to scrape their cheeks as they were spitting to get even more cells off. Each reagent was then added, in sequence, to the cup followed

by stirring everything with a toothpick-- a drop of dishsoap (Dawn™, Procter & Gamble, Cincinnati, OH), was used, a dash of meat tenderizer (Kroger brand, Cincinnati, OH), a sprinkle of salt (Kroger brand, Cincinnati, OH) and a drop of diluted food coloring (Blue, Kroger brand, Cincinnati, OH). Ice cold 91% isopropyl alcohol (Kroger brand, Cincinnati, OH) was added to double the volume of the solution, pouring so that the alcohol slipped under the DNA solution. The students then watched while DNA strands formed between the layers and could use their toothpicks to stab the DNA and put it into a microcentrifuge tube (USA Scientific, Inc. SealRite® tubes, Ocala, FL). Most students took their DNA samples with them.

Exploring SNPs activity: For this activity, the professor used results from her personalized 23andMe® genetics test, but any genotype set could be pulled either from online genetics educators resources (such as those on the 23andMe® education website) or by creating a genotype using SNPedia. An example genotype type is shown in **Supplemental Figure 1A** for the taste receptor TAS2R38. Students were directed to the SNP database “SNPedia” to start to analyze the SNPs (Cariaso & Lennon, 2012). For their lab report, students were asked to consult the Online Mendelian Inheritance in Man database (Amberger, Bocchini, Scott, & Hamosh, 2019), and PubMed, both of which are housed under the domain of the National Center for Biotechnology Information (NCBI) (National Center for Biotechnology Information (U.S.), 2013).

Phylogeny and phylogenetic tree building activity: The Howard Hughes Medical Institute (HHMI) Interactive website on phylogeny was assigned prior to the lab. Students were told to use the lactase gene (LCT), although any gene with orthologs could be used for this exercise. FASTA (“FAST-ALL (Pearson & Lipman, 1988)) formatted sequences for the LCT protein from humans,

and other animals were obtained using the NCBI homologue database. NCBI also provides a multiple sequence alignment tool as well as a BLAST (Basic Local Alignment Search Tool) tool for the human sequence. BLAST provided more results for orthologs than the homologue database allowing students to add additional sequences for their phylogenetic analysis. Phylogenetic trees were made using the Clustal Omega multiple sequence alignment tool.

X-chromosome gene mapping activity: For this activity, several previous activities were combined into one lab for an iterative experience. Students use the glucose-6-phosphate dehydrogenase gene (G6PD) in which SNPs in the protein coding region (missense mutations) can lead to the inability to eat fava beans and the condition “favism.” However, these variants can also lead to resistance to malaria (Luzzatto & Arese, 2018). Students made phylogenetic trees from the variants in G6PD (this time using both SNPedia and the NCBI SNP database). Students also inserted the SNP variations into the FASTA sequence to create the variant protein sequence. Finally, students considered population frequencies for the SNPs using the NCBI and SNPedia databases.

Polymorphisms and protein function activity: During this activity, students used a gene of interest (either G6PD or TAS2R38, for example) and using the FASTA sequence of the protein, created variant sequences based on human SNPs that affect the protein coding region. They then learned to use three different web-based programs to predict whether the variant was deleterious. First, they used the I-TASSER server, which requires an individual registration, but is free for academic professors and students (Yang et al., 2015). I-TASSER provides several different protein function

and structure predictions, as well as 3-D models of the protein. The students then used the Swiss-model to make 3D structures (Waterhouse et al., 2018), which allowed one to zoom into the region of interest and see in more detail how the substituted amino acid might affect the structure. Finally, the students used PROVEAN, in which many different variants can be put in at once and predictions about function are provided in the output (Choi & Chan, 2015). Links were also provided for online sites that would predict protein secondary changes (such as acetylation or phosphorylation) and whether these could be gained or lost with the SNP variant.

Pseudogene analysis activity: For the pseudogene lab, the students were given an unknown sequence formatted in a FASTA sequence format (also available as a supplemental file “pseudogene analysis.docx) (**Supplemental Figure 1B, C**) and told to use BLAST using “other” databases (not just human and mouse, which are default selections) and the “highly similar sequences” selection. Several sequences come up with the word “pseudogene” in the title. Students were then instructed to grab the FASTA sequence for at least two different pseudogenes and use the EXPASY translate tool to translate the mRNA to protein. When they do this, they find numerous stop codons or gaps within the pseudogene sequence, which demonstrates that pseudogenes look like protein coding sequences but do not make full-sized proteins, compared to true protein-coding genomic DNAs and mRNAs.

Genome-wide association study activity: In this activity, students are given four Genome-wide Associate Study (GWAS) database sites (**Supplemental Table 2**) to explore with a single phenotype (in the case of this course, Vitamin D serum concentration). Each database has slightly



different searches and slightly different database components. Students pick at least one GWAS study and then identify one or more of the SNPs, investigating that SNP further using PubMed, SNP databases, and other techniques.

Promoter analysis and transcriptomics activity: For this activity the students are asked to look for Vitamin D receptor (VDR) binding sites in promoter and then use transcriptomics studies to identify genes that show transcriptional response to Vitamin D levels. To do this, students were given an article which identified the preferred VDR binding site (Carlberg & Campbell, 2013) and were asked to have this DNA sequence determined and available prior to coming to class. They were then asked to use one or more of the genes listed in the paper as containing VDR sites and retrieve the promoter sequence using the Eukaryote Promoter Database site (Dreos, Ambrosini, Groux, Cavin Perier, & Bucher, 2017). The retrieved sequence is put into the PROMO search engine (Messeguer et al., 2002), which identifies putative sites within the promoter region. They will find a VDR/RXR homodimer site within at least one these promoters. Students then used the Gene Expression Omnibus (GEO) database with either the search term “Vitamin D” or searched for one of their genes (i.e. the calcium receptor, TRPV6), or both together. The database provides normalized expression levels which can be averaged across individual samples to get an average expression for the gene of interest in a certain condition (and tissue).

Clinical genetic testing activity: In this activity, students use the Genetic Testing Registry, which is part of NCBI (Rubinstein et al., 2013), to investigate genetic tests currently used to test for newborn errors of metabolism. Since much of the newborn testing is actually done non-

genetically, they are asked to compare and contrast cost, time, accuracy, etc. between a non-genetic and a genetic test.

Genetically modified foods activity: This activity involved discussion of papers by groups of students, with each group making a presentation back to the class. Students were asked anonymous questions on their comfort-level with genetic modification of plants and animals (including humans), and class-based results were discussed.

**Supplemental Table 1:** Class Syllabus showing lectures, activities, and invited speakers for 2018 Nutritional Genomics course. The lab activities are described in more detail in the methods.

MONDAY (lecture)	WEDNESDAY (activity)	FRIDAY (speaker)
<b>INTRO TO GENETICS/GENOMICS</b>		
Intro to the course	Genetics of taste activity	Dr. Martin Kohlmeier, UNC Chapel Hill, Zoom Conference
Basic genetics	Make your own pedigree	None
Personalized genetics	Make your own DNA Exploring SNPs	Dr. Greg Lennon, SNPedia/Prometheus, Zoom Conference
<b>NUTRITIONAL GENOMICS-COMPLEX INTERACTIONS</b>		
Complex inheritance	Phylogeny activity	none
Gender differences	X-chromosome mapping	Dr. Peihui Jiang, Monell Chemical Sense Center, Zoom Conference
Nutrient-SNP interactions	Polymorphisms and protein function	None
Pseudogenes	Genomic annotation of pseudogenes	None
<b>NUTRIENT GENE INTERACTIONS</b>		
Genomic-wide association studies	Using GWAS databases	Tour Biocomplexity Institute, in person
Transcriptomics	Promoter SNPs Activity	None
Epigenetics and Imprinting	MTHFR promoter methylation activity	Dr. David Xie, Biocomplexity Institute, in person
<b>PERSONALIZED NUTRITION</b>		
Genetic Testing	Genetic test database- which is best?	Dr. Tahnee Causey, Assistant Director, VCU Genetic Counseling Program, Zoom Conference
Genetically modified foods	None	Dr. Eric Hallerman, Virginia Tech, in person
<b>INDEPENDENT ANALYSIS</b>		
Four weeks of individual analysis of a gene or genetic region of interest as final project.		

**Supplemental Table 2:** List of websites used in *in silico* activities. The websites are listed in the order mentioned in the text.

Website Name	Purpose	Website address
My Family Health Portrait	Pedigree generation	<a href="https://phgkb.cdc.gov/FHH/html/index.html">https://phgkb.cdc.gov/FHH/html/index.html</a>
E!Ensembl Phenotype viewer	Links phenotype to genotype	<a href="http://www.ensembl.org/info/genome/variation/phenotype/phenotype_annotation.html">http://www.ensembl.org/info/genome/variation/phenotype/phenotype_annotation.html</a>
23andMe® education site	Genetic resources and sample genetic profiles	<a href="https://education.23andme.com/">https://education.23andme.com/</a>
SNPedia	Wiki of SNP genotypes	<a href="https://www.snpedia.com/index.php/SNPedia">https://www.snpedia.com/index.php/SNPedia</a>
Online Mendelian Inheritance in Man	Genetic inheritance with genotypes and phenotypes	<a href="https://www.ncbi.nlm.nih.gov/omim">https://www.ncbi.nlm.nih.gov/omim</a>
PubMed	Database of published journal articles	<a href="https://www.ncbi.nlm.nih.gov/pubmed/?term=">https://www.ncbi.nlm.nih.gov/pubmed/?term=</a>
National Center for Biotechnology information	database warehouse with many genomic/genetic links	<a href="https://www.ncbi.nlm.nih.gov/">https://www.ncbi.nlm.nih.gov/</a>
HHMI Interactive website on phylogeny	Genetics/genomics videos	<a href="https://www.biointeractive.org/classroom-resources/creating-phylogenetic-trees-dna-sequences">https://www.biointeractive.org/classroom-resources/creating-phylogenetic-trees-dna-sequences</a>
NCBI homologene database	Gene sequence comparison between different species	<a href="https://www.ncbi.nlm.nih.gov/homologene/">https://www.ncbi.nlm.nih.gov/homologene/</a>
Clustal Omega	Multiple sequence alignment tool	<a href="https://www.ebi.ac.uk/Tools/msa/clustalo/">https://www.ebi.ac.uk/Tools/msa/clustalo/</a>
NCBI SNP database	Government curated SNP database	<a href="https://www.ncbi.nlm.nih.gov/snp/?term=">https://www.ncbi.nlm.nih.gov/snp/?term=</a>
I-TASSER server	Protein 3D structural analysis	<a href="https://zhanglab.ccmb.med.umich.edu/I-TASSER/">https://zhanglab.ccmb.med.umich.edu/I-TASSER/</a>
Swiss-model	Protein 3D structural analysis	<a href="https://swissmodel.expasy.org/">https://swissmodel.expasy.org/</a>
PROVEAN	Protein variant effect analysis	<a href="http://provean.jcvi.org/index.php">http://provean.jcvi.org/index.php</a>
PAIL	Protein acetylation prediction	<a href="http://bdmpail.biocuckoo.org/prediction.php">http://bdmpail.biocuckoo.org/prediction.php</a>
NETPhos	Protein phosphorylation prediction	<a href="http://www.cbs.dtu.dk/services/NetPhos/">http://www.cbs.dtu.dk/services/NetPhos/</a>
BLAST	Comparison of two or more sequences	<a href="https://blast.ncbi.nlm.nih.gov.ezproxy.lib.vt.edu/Blast.cgi">https://blast.ncbi.nlm.nih.gov.ezproxy.lib.vt.edu/Blast.cgi</a>
ExPASY	Tool to translate mRNA sequences to protein	<a href="https://web.expasy.org/translate/">https://web.expasy.org/translate/</a>
Pseudofam	Pseudogene database	<a href="http://pseudofam.pseudogene.org/">http://pseudofam.pseudogene.org/</a>
NHGRI-EBI GWAS catalog	GWAS studies database	<a href="http://www.ebi.ac.uk/gwas/">http://www.ebi.ac.uk/gwas/</a>
dbGAP	NCBI GWAS database	<a href="http://www.ncbi.nlm.nih.gov/gap">http://www.ncbi.nlm.nih.gov/gap</a>

GWAS Central	GWAS database	<a href="https://www.gwascentral.org/index">https://www.gwascentral.org/index</a>
GWAS database	GWAS studies database	<a href="http://gwas.biosciencedbc.jp/cgi-bin/gwasdb/gwas_top.cgi">http://gwas.biosciencedbc.jp/cgi-bin/gwasdb/gwas_top.cgi</a>
Eukaryote promoter database	Promoter sequences from a variety of species	<a href="https://epd.epfl.ch//index.php">https://epd.epfl.ch//index.php</a>
PROMO	Promoter transcription factor binding site search engine	<a href="http://alggen.lsi.upc.es/cgi-bin/promo_v3/promo/promoinit.cgi?dirDB=TF_8.3">http://alggen.lsi.upc.es/cgi-bin/promo_v3/promo/promoinit.cgi?dirDB=TF_8.3</a>
GEO database	Database of transcriptomic data	<a href="https://www.ncbi.nlm.nih.gov/geoprofiles">https://www.ncbi.nlm.nih.gov/geoprofiles</a>
Genetic Testing Registry	Database of clinical genetic tests	<a href="https://www.ncbi.nlm.nih.gov/gtr/all/?term=">https://www.ncbi.nlm.nih.gov/gtr/all/?term=</a>



	Variants	Genotype
39	C or T	T/T
6	A or G	A/A
3	G or T	G/G
8	C or G	C/C

Alignments						
Taxonomy						
Download Manage Columns Show 100						
GenBank Graphics Database of results						
Description	Max Score	Total Score	Query Cover	E value	Per. Ident	Accession
member 2 (TAS2R38) .eff6	1010	1010	100%	0.0	81.60%	XM_010330046.1
member 2 (TAS2R38) .eff6	1710	3000	99%	0.0	88.01%	XM_020600079.1
1 member 2 (TAS2R38) .eff6	1020	2000	99%	0.0	85.02%	XM_020600079.1
1 member 2 (TAS2R38) .eff6	1020	2000	99%	0.0	85.02%	XM_020600079.1
1 member 2 (TAS2R38) .eff6	1010	2027	99%	0.0	86.74%	XM_020600079.1
1 member 2 (TAS2R38) .eff6	1010	2000	99%	0.0	85.00%	XM_020600079.1
1 member 2 (TAS2R38) .eff6	1007	2000	99%	0.0	85.07%	XM_020600079.1
1 member 2 (TAS2R38) .eff6	1000	2000	99%	0.0	85.11%	XM_020600079.1
1 member 2 (TAS2R38) .eff6	1480	2000	99%	0.0	85.00%	XM_020600079.1
1 member 2 (TAS2R38) .eff6	1480	2070	99%	0.0	85.04%	XM_020600079.1
1 member 2 (TAS2R38) .eff6	1480	2000	99%	0.0	84.73%	XM_020600079.1
1 member 2 (TAS2R38) .eff6	1480	2071	99%	0.0	85.48%	XM_020600079.1

B.

>TEST\_001

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ATGGGACCCCGGGCCAGGGAGGTCTGCTCCCTGATTATTCTGCTGCAGGTCTGGCTGAG
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GAGTATGAAATGAAGGTGTTGGGCTACAACCTCATGCAGGCCATGCGCTTCGCAGTGGAG
GAGATCAACAATCACAGCAGCCTGCTGCCCGGGGTGCTGCTGGGCTACGAGATGGTGGAA
ACCTGCTADGTCAACAACGTCCAGCCCGTGTCTACTTCTGGCACAGAAGGACTACTCC
CTGCCCCATCCAGGAGGATTACAGCCACTATGTGCCCGCATGGTGGCTGTATTGGCCCC
AACAACTGGGAGTCCACCGTAACGGTGGCCTCTTCTCTCTTCCACAGATCACCTACAGC
GCCATCAGTGACGAGGTGCGCGACAAAGGGCGCTTCCCGGCCGTCTGCGCACCGTGGCC
GGCGCCGATCACAGATCGAGGCCCTGGTGCAGCTGATGCTGCTCTACTGCAACTGGATC
GTGCTGCTGGTGAGCGGGGACGACTATGGCCGCTACAACGCCAGCTGCTCAACGACCG
CTGGCCCGCGCCACATCTGCATCGCTTCCAGGAGACGCTGCCCGTGGCGCGGCCAGC
CAGGCGGTGACGCGGTGGGAGCGCCAGCGCTGGAGACCATCGTGGACAAGCTGCAGC
AGCTCGGCGCGCGTTGTGGTCTGCTGTGCCAGACCTGGTCTGCACAACTCTTCCGC
GAGGTGCTCCGCCAGAACTCACGGGCGCCGTGTGGATCGCTCCGAGTCTGGGCCATC
GACCCCAACAACGCCCAAGCGCTGCACGGCTCTGCGCGGCACCTGCTCCGTGGTCTAC
CCTGGCAGCTGCTTAAGGAAATCTGGAAGGTCAACTTCAACCTCTGGGCCACAGATC
TTTTTGACAAGCAAGGGGACCTGCCCATGGGCTGGAGATCATCCAGTGGCAATGGGG
CTGAGCCAGAACTTCCGGAGCATCGCTCTCTACTGCCCGGACTATGGCAGCTGAGGGCC
ACCGGCAACGTCTCTGGCACACCGGCAACAACACGATCCCTGTGTCCATGTGTTCAG
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GCCCTGCTGTCTGTCTGGGCTTCTCAGCACCCCTGGCCATCTGGTCACTCTTTGGAGG
TACTCCACACGCGCGGTTGGTTCGGCGCGGGCCATGTACTTCTGATGCTGATGCCGCTG
CTGGGATGGTCCCCATGTACGTGGGCGAGGCCATGGTTTCAATGCTCTGCCGCCAG
ACCTTCTTCAAGCTGTCTTCAACATCTGCATCTCTGTATGCCGTGCACTCTTTCATC
GTCTGCATCTTCAAAATGGCCAGGCACCTCCCGGTGCTACTACTGGGTCCGCTACCAT
GGGCCCTGTGTCTTTGTGGGTCTTTCAGGCTGCTCAAGGTGGCATTGTGGTGGGCAAC
GTGCTGGCCATGACCGCCAGCCCCACCGCCCGCCCGGACCCCGACGACCCCAAGGTCA
GTTCTCTCTGCAACTACCCCAAGGCGCTGCTGTTCAACACGAGCCTGGACCTGCTTCTG
TCCGTGGAGGGCTTCAGCTTCACTACATGGGCAAGGAGCTGCCACCAACTACAACGAG
GCCAAGTTCATCACTTCTGCATGACCTTCTACTTCACTTCTCCGTCTCCCTCTGCACC
TTCATGCTGTCTACGAGGGGGTCTGGTCAACCATCTGGACCTCTTGGTCAAGGTGCTC
AACCTGGGCATCAGCCTCAGCTACTTGGCCCCAAGTGCTACATGGTCTCTTCTTCCCA
GAGCGCAACACGCGCGTCTACTTCAAGCAGCATGATTCAGGGCTACACCAAGCGGAAGGAC

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1: Samples of professor's materials used for course. A. The human taste receptor, TAS2R38 genotype profile used for TAS2R38 genotype represents a single person's complex genotype that could be analyzed for predicted phenotype. (B.) Pseudogenes for the pseudogene module. This file is available in supplemental data. (C.) Results of a BLAST using the file in B.