Gaining a Deeper and More Integrated Understanding: Linking Mendelian Genetics with Molecular Genetics Using Web-Based Bioinformatics Tools

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Biography

Isabelle Barrette-Ng graduated from Queen's University in 1998 with a BSc (Hons.) in Biochemistry. She received a MSc in Bioinformatics/Biochemistry from the University of Montreal in 2001 and completed her PhD studies in Biochemistry at the University of Alberta in 2003. Isabelle has been an Instructor at the University of Calgary since 2006, where she teaches large courses in genetics and biochemistry, primarily at the second-year undergraduate level. Her interests include the development and integration of inquiry-based learning approaches in large undergraduate courses.

Don MacMillan has been the Liaison Librarian for Biological Sciences, Math, Physics and Astronomy at the University of Calgary Library since 2003. He provides program-integrated information literacy instruction and advanced reference and training services to students and faculty in those disciplines and carries out research on student learning, information literacy and the incorporation of tools and technology in information literacy instruction. Prior to his present position, Don was EMBA/MBA librarian at the Haskayne School of Business, University of Calgary and held several positions at the Calgary Public Library. Don received his Bachelor of Science and MLS degrees from Dalhousie University, Halifax, Nova Scotia.

David Hansen received his Ph.D. in Genetics from the University of Alberta in 1999 studying sex determination in *C. elegans*. He then was a post-doctoral fellow in the Department of Genetics at the Washington University School of Medicine. During his post-doctoral studies, he studied the genetic control of proliferation in the *C. elegans* germ line. He joined the faculty of the University of Calgary in the Department of Biological Sciences as an Assistant Professor in 2004, where he continues his research on *C. elegans* germline proliferation. He teaches developmental biology and genetics to undergraduate students, including Mendelian genetics in the second-year Introduction to Genetics course.

Introduction

In most universities and colleges, the traditional model of teaching introductory genetics begins with a description of classical Mendelian genetics, which is followed by a somewhat abrupt transition to modern topics of molecular genetics. Bioinformatics, if covered at all in an introductory course, is usually presented as an add-on topic towards the end of the course. We re-evaluated this traditional model and asked whether the teaching of traditional Mendelian and molecular genetics topics could be improved by integrating the use of bioinformatics tools into the existing curriculum. To address this question, we implemented a month-long, inquiry-based, experiential learning laboratory exercise. In this exercise, students investigated classic Mendelian and molecular genetics aspects of a genetically inheritable disease using basic bioinformatics science tools, such as PubMed, OMIM, and BLAST, as well as more practical and applied tools such as the Google Patents search engine. Our experience in implementing this inquiry-based experiential learning approach in a large (greater than 500 students) second-year undergraduate introductory genetics course for biology majors revealed a number of challenges and opportunities. A particularly important element in the success of our experiment in a large enrolment class was a comprehensive plan to use the university library's resources and expertise. This enabled us to develop an interactive, hands-on workshop to expose students to bioinformatics tools, which was reinforced throughout the classroom lecture component of the introductory genetics course. This exercise led to a high level of student satisfaction and an improved integrated introduction to classical and molecular genetics.

Student Outline

It has been our experience that many students have difficulty relating concepts from both classic Mendelian and molecular genetics. As a result, many students only have a superficial understanding of these concepts, and have difficulty retaining or applying this information to novel situations. Our goal in developing this laboratory exercise was to use interactive, on-line bioinformatics tools to relate concepts from classical Mendelian genetics to concepts from molecular genetics through an inquiry-based learning exercise, which takes advantage of freely available interactive bioinformatics tools.

The month-long exercise consisted of four main stages. In the first stage, students were presented with a list of 80 genetically heritable diseases and were asked to select, in groups of two, a disease of interest. The actual list of diseases used for our class in the fall of 2007 is presented in Appendix One. Our primary purpose in presenting students with a fairly broad list of diseases was to increase the chance that each pair of students would be able to select a topic of some personal interest. It was interesting to observe that students did select a wide range of diseases, and for a variety of reasons.

In the second stage, students were asked to perform searches of peer-reviewed scientific publications using the PubMed database and gene-based therapies using the Google Patents database to uncover the breadth of basic information and gene-based applications related to their chosen disease. A key aspect of this portion of the exercise was the implementation of interactive training sessions conducted by a team of librarians and graduate teaching assistants to familiarize students with the databases and tools. Students were guided in the development of efficient search techniques

and then challenged to apply these techniques to uncover information related to their specific topic. Specifically, students were asked to select two review articles and a patent. The exercise was structured to encourage students to use the basic genetics concepts they had recently learned through the lecture and laboratory components of the course to allow them to develop a basic understanding of their chosen disease.

In the third stage, students were asked to employ an array of bioinformatics tools to discover the molecular basis of the heritable disease chosen for study. As in the second stage, interactive training sessions were conducted by a combination of librarians and teaching assistants to show students how to effectively use these tools to investigate their specific diseases. Students were shown how to use the Online Mendelian Inheritance in Man (OMIM) database and the Basic Local Alignment and Search Tool (BLAST), two commonly used tools for the study of genes, gene sequences and diseases in genetics and biochemistry. By using OMIM, students have access to a rich source of information on various aspects of their chosen disease, such as inheritance patterns and common types of mutations observed. BLAST allows students to try and find homologues of genes responsible for their chosen disease in various organisms and to provide a basis for understanding differences in function between related proteins. Students responded to the training sessions very positively and most students appeared confident in the use of these tools on their own following the initial training.

The final component of the exercise asked that each pair of students organize and present the results of their research to the other students in their laboratory section, as well as to a graduate teaching assistant. Each pair of students prepared a poster in which they presented (1) basic background information on their chosen disease, (2) the classical Mendelian pattern of inheritance (e.g., autosomal or sex-linked), (3) molecular information on the genetic basis of the disease and (4) practical, gene-based therapies described in the patent literature. Students were given 10 minutes to present their findings and to answer questions from other students in their regular laboratory sections (each containing 24 students). For many students, this was their first opportunity to present formal, scientific data. Most students rose to the challenge and demonstrated a high degree of enthusiasm and professionalism in presenting their findings to their peers.

Notes for Instructors

One of the major challenges that we faced in implementing an inquiry-based exercise in a large class of over 500 students was to organize the exercise in a way that maximized the inquiry experience of each student without placing excessive demands on the limited time and resources of a small team of graduate teaching assistants, librarians and instructors. Several design elements of the exercise were specifically chosen to meet this significant challenge.

First, the exercise was integrated into four of the regularly scheduled, weekly laboratory sections of the introductory, second-year genetics course. By scheduling the exercise near the end of the course, the students already had been taught the basic concepts of Mendelian inheritance and molecular genetics learned earlier in the course, and they were able to apply this understanding to a specific disease. The relatively small groups of students in laboratory sections (approximately 24 students in each of 21 laboratory sections) facilitated the interactive nature of the computer-based sessions during weeks two and three by providing opportunities for one-on-one interactions with teaching assistants and librarians, as well as peer-to-peer learning opportunities. It was particularly effective to use the final laboratory session for student presentations and discussion. Rather than

viewing this last session as just one last hoop to jump through, most students viewed the final presentation of their results as a meaningful learning experience. Through this part of the exercise, students had to organize and present their work in a way that demanded a deeper level of understanding than normally required in a typical exam or laboratory report. Most students were genuinely engaged by this exercise and took pride in competing for preparing the best presentations. Additionally, students listening to the presentations were very engaged, asking many thoughtful questions.

A second key design element was to encourage a student-driven inquiry-based learning experience. The students enjoyed making the initial choice of their research topic from a broad list based on personal interests. In addition, it was particularly important to provide an open and flexible learning environment during the library and bioinformatics sessions to encourage student-initiated inquiry-based learning. Sessions were geared towards explaining the technical aspects of software tools, and students were required to apply their basic understanding of classical Mendelian and molecular genetics to effectively use these tools to find the information necessary for their presentations. The combination of librarians and graduate teaching assistants leading small groups in a somewhat unstructured setting was particularly effective for guiding students through the technical and conceptual aspects of this inquiry-based discovery process.

The third important design element essential for the success of the exercise was the use of a combined poster/oral presentation as a final evaluation tool. One of the most difficult challenges facing this project was to devise a way to evaluate how students performed in the inquiry-based exercises. Since the combined poster/oral presentation was designed to be the culmination of the student-initiated inquiry-based learning process, the overall performance of the students in this exercise was evaluated by marking the quality of the poster/oral presentations for each pair of students. To deal with the large number of students typical of core undergraduate biology courses, we prepared a detailed marking rubric that provided specific guidance to the graduate teaching assistants regarding the grading of the final student presentations (Appendix Two).

The marking rubric was carefully designed to emphasize the importance of creativity and inquiry, as opposed to a non-selective listing of information. Students were informed well in advance of their presentations that they would be marked for their creativity and the quality of their presentation, as well as for the scientific accuracy and completeness of information. As a result, students needed to master basic concepts and apply them in a meaningful way to prepare a successful presentation. To prepare their final presentation, each pair of students synthesized their abstract knowledge and applied it towards explaining a specific disease. This was the first opportunity for most of the students to present scientific information in a formal setting, and it proved to be a challenging but rewarding experience for most of them. The high quality of most of the presentations attests to the success of this method of evaluation, as well as the success of the project as a whole.

List of Websites

OMIM: http://www.ncbi.nlm.nih.gov/sites/entrez?db=omim

BLAST: http://blast.ncbi.nlm.nih.gov/Blast.cgi

Google Patents: http://www.google.com/patents

Literature Cited

Hamosh, A., A.F. Scott, J.S. Amberger, C.A. Bocchini, and V.A. McKusick. 2005. Online Mendelian Inheritance in Man (OMIM), a knowledgebase of human genes and genetic disorders. Nucleic Acids Research, 33:D514-D517.

Altschul, S.F., T.L. Madden, A.A. Schäffer, J. Zhang, Z. Zhang, W. Miller, and D.J. Lipman. 1997. Gapped BLAST and PSI-BLAST: a new generation of protein database search programs. Nucleic Acids Research, 25:3389-3402.

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Appendix A

Adrenoleukodystrophy
Alzheimer disease
Amyotrophic lateral sclerosis
Anemia, sickle cell
Alpha-1-antitrypsin deficiency
Angelman syndrome
Achondroplasia
Alport syndrome
Adrenal hyperplasia, congenital
Autoimmune polyglandular syndrome
Ataxia telangiectasia
Atherosclerosis
Breast and ovarian cancer
Best disease
Burkitt lymphoma
Colon cancer
Crohn's disease
Cockayne syndrome
Charcot–Marie–Tooth syndrome
Deafness
Diabetes, type 1
DiGeorge syndrome
Duchenne muscular dystrophy
Diastrophic dysplasia
Ellis-van Creveld syndrome
Epilepsy
Essential tremor
Familial Mediterranean fever
Fragile X syndrome
Friedreich's ataxia
Fibrodysplasia ossificans progressiva
Gaucher disease
Glaucoma
Gyrate atrophy of the choroid and retina
Glucose galactose malabsorption
Harvey Ras oncogene
Hemophilia A
Huntington disease
Hereditary hemochromatosis
Leukemia, chronic myeloid
Lung carcinoma, small cell
Lesch-Nyhan syndrome
Long QT syndrome

Malignant melanoma
Marfan syndrome
Myotonic dystrophy
Male pattern baldness
Menkes syndrome
Maple syrup urine disease
Multiple endocrine neoplasia
Obesity
Immunodeficiency with hyper-IgM
Neurofibromatosis
Niemann–Pick disease
Narcolepsy
The p53 tumor suppressor protein
Paroxysmal nocturnal hemoglobinuria
Pancreatic cancer
Polycystic kidney disease
Porphyria
Prader-Willi syndrome
Prostate cancer
Pendred syndrome
Parkinson disease
Phenylketonuria
Retinoblastoma
Refsum disease
Rett syndrome
Severe combined immunodeficiency
SRY: Sex determination
Spinal muscular atrophy
Spinocerebellar ataxia
Thalassemia
Tangier disease
Tay-Sachs disease
Tuberous sclerosis
Von Hippel-Lindau syndrome
Wilson's disease
Williams syndrome
Waardenburg syndrome
Werner syndrome
Zellweger syndrome

Appendix B

MARKING RUBRIC FOR POSTERS AND POSTER PRESENTATIONS

Name:_____
Topic:_____

Content (5 marks):

Give 1 mark if that aspect is well done, 0.5 marks for evidence of effort, and 0 for no effort.

_____ clearly state chosen genetically-inheritable disease
_____ information presented is clear and coherent, demonstrating good understanding and knowledge
_____ appropriate amount of background information is presented
_____ findings from OMIM and BLAST are clearly explained
_____ references are properly cited on poster

Presentation (7 marks):

Give 1 mark if that aspect is well done, 0.5 marks for evidence of effort, and 0 for no effort.

_____ demonstrate good speaking skills (tone, volume, pace, avoiding "ums", "you know", etc.)
_____ logical and confident delivery of material
_____ presentation is well-organized
_____ presenters make eye contact, engage the audience and are euthusiastic
_____ poster is clear and can be easily read
_____ poster is appealing, interesting and inviting
_____ equal participation of group members

Answering questions (2 marks):

2 marks will be given if all questions are answered thoroughly
1 mark will be given if the questions are only partially answered
0 marks will be given if the questions are not answered satisfactorily

Asking questions to others (2 marks):

2 marks will be given if 2 thoughtful questions are asked
1 mark will be given if only 1 thoughtful question is asked or if the questions are not thoughtful
0 marks will be given if no questions are asked

Deduct 1 mark for every minute that the talk goes over 10 minutes or for every minute that is missing to reach a minimum of 5 minutes.

Poster and presentation mark = _____/16; Comments: