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Lesson

GMC: Genes, Mutations and Cancer – Group Concept Map Development

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Abstract

It has been shown that active learning strategies used in the classroom can increase student learning and retention of information. We generated an active learning exercise that can be used in the classroom to explore the relationship between genes, mutations, cancer, and cancer therapeutics. The learning objectives for this exercise include defining and understanding the functional relationships between genes that regulate cell division, major types of mutations, and the onset of cancer. The active learning exercise begins with a take home quiz to define terms related to the information covered during the lecture portion of the class. Students are then divided into groups to generate a concept map that displays the interrelationships between these terms. Each group is then instructed to exchange their concept maps with another group, evaluate the map for accuracy, and identify targets for inhibiting or activating drug therapies. The lesson plan was implemented in undergraduate biology courses at two public universities. Survey data indicate that students perceived the activity helped increase their knowledge and understanding of the learning objectives.

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Supporting Materials: S1. Genes, Mutations and Cancer - Pre-class assignment; S2. Genes, Mutations and Cancer - Pre-class assignment answer key; S3. Genes, Mutations and Cancer - Example assessment questions; and S4. Genes, Mutations and Cancer - Example assessment questions answer key.

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Learning Goal(s)

- Evaluate the connection between cell division and cancer.
- Compare roles of tumor suppressors and oncogenes in the development of cancer.

Learning Objective(s)

Students will be able to:

- describe the roles of oncogenes, proto-oncogenes, and tumor suppressors in cancer progression.
- determine the relationships between the types of mutations that can regulate cell division or contribute to cancer formation.
- identify potential cancer treatment strategies that could target the gene mutations including oncogenes and non-functional tumor suppressor genes.

INTRODUCTION

Active learning has been shown to be an effective approach for increasing student learning in undergraduate coursework across many disciplines (1). Furthermore, student-centered approaches including active learning reduce the achievement gap for first generation college students and students from underrepresented minority groups (2,3). Given that expanding the STEM workforce is crucial for continued scientific progress (4,5,6), there is a growing emphasis on implementing active learning at undergraduate institutions with high enrollment of these student groups. Developing, assessing, and making available active learning exercises for important components of the biology curriculum is one way to facilitate more widespread incorporation of these approaches.

Relationships between genes, mutations, and cancer are the core concepts addressed by the active learning exercise we describe. Cancer is of relevance to all populations of students, but misconceptions about the association between genes and cancer remain prevalent (7). Given this, our goal was to develop an activity that engaged students in the concepts

underlying the genetic mechanisms that lead to cancer. The exercise aims to have students explore how different types of genetic mutations can lead to cancer depending on the types of genes involved. The underlying concept is that cancer largely results from dominant gain-of-function mutations for oncogenes and recessive loss-of-function mutations for tumor suppressors (8,9). This exploration also highlights the role of somatic mutations and a multistep mutation model of cancer progression (10). There are several published active learning strategies and case studies that explore the relationship of proto-oncogenes and tumor suppressor genes in the genetics of cancer inheritance (11-14). Additionally, some address how tumorigenesis is due to progressive accumulation of mutations in these genes that control cell cycle (14,15). Some of these challenge students with the task of identifying potential drug targets (16) or classifying genes associated with cancer progression (17). The active learning strategy described here is unique in that it addresses the role of proto-oncogenes and tumor suppressor genes in the prevention of cancer using a group generated concept map to promote student understanding of how mutations in these genes may contribute to cancer generation while simultaneously highlighting the role of drug therapeutics in targeting proteins to combat cancer progression.

Concept mapping was used because it is amenable to group collaboration and requires students to create a visual representation of their understanding of connections within complex systems (18). There are variations on the approach, but, in general, concepts maps include the following stages: 1) *brainstorming* - selecting the most important terms or concepts; 2) *organization* - ordering of terms or concepts; 3) *layout* - construction the map of concepts; and 4) *linking* - connecting the concepts with arrows and verbs describing the nature of the relationships (19). Thus, the approach involves students making connections between concepts and is well suited to developing an understanding of the connections between genes, functional consequences of mutations, and cancer. Concept maps lead to significant gains in student learning in a variety of contexts (20-22). Furthermore, the concept maps created by students offer another mechanism to assess the progression of student understanding of complex topics (23).

Intended Audience

The target audience for this active learning exercise are students in a Biology course for biology majors. The lesson was designed for smaller classrooms up to 50 students, but can be adapted for larger classrooms and upper division biology courses.

This lesson was implemented at two separate public institutions, and in two different courses. In both courses, students were majors in the biological sciences. The first course was an introductory biology course and the second was a sophomore level cell biology course; both courses are required for students majoring in biology.

Required Learning Time

This active learning exercise can be completed in one lesson period and lasts about an hour. This does not include time to introduce the topic or for a quiz to review relevant terms and definitions.

Prerequisite Student Knowledge

Before beginning the mapping activity, students should understand a variety of topics addressed in introductory biology courses including: 1) the structure and function of DNA, 2) roles of individual genes in generating functional proteins (including the processes of transcription and translation), 3) effects of mutations in genes on protein function, 4) steps of the cell cycle, 5) major checkpoints of cell division, and 6) links between mutations and cancer.

Prerequisite Teacher Knowledge

Prior to implementation of this active learning exercise, teachers should be comfortable with all of the pre-requisite student knowledge. In addition, instructors should have a firm grasp of the role of oncogenes and tumor suppressor genes in cancer progression. Teachers must also be familiar with the use of a concept map in the classroom to either guide students on how to create one or to provide handouts explaining the process. Teachers should also be prepared to help students use their maps to design drug therapies to combat cancer progression.

SCIENTIFIC TEACHING THEMES

Active Learning

The lesson plan implemented here is inherently an active learning exercise by design. Students utilize active learning throughout each portion of the exercise and we have detailed this in relation to whether the activities take place outside of the classroom or during class time. The exercise uses the active learning strategies of group discussion and concept mapping to help students make connections between related terms that describe cell division regulation. The exercise also challenges students to use higher order cognitive skills to evaluate and build upon a concept map generated by another group. Students also use metacognition by reflecting on the learning process.

Pre-class activities:

Instructors will assign relevant reading from textbooks and provide resources such as online media from publishers or openly available online videos to supplement the initial instruction of the related course material. After content introduction using didactic lectures, worksheets, group work, or a combination of the above based on instructor style and preference, students will complete a take-home quiz to be done individually. This take-home quiz contains a list of terms and matching definitions where students need to identify the associated term (Supporting File S1: Genes, Mutations and Cancer - Pre-class assignment and Supporting File S2: Genes, Mutations and Cancer -Pre-class assignment answer key). This quiz serves as a pre-assessment to evaluate whether students have gained the foundational knowledge and includes a list of terms that students will use to complete their concept maps.

In class activities:

During the first class meeting after covering the associated content and assignment of the take home quiz, instructors will first lead a group discussion of the terms and definitions covered on that assignment to ensure student familiarity with the relevant terms. Students then work in groups of 4-6 to generate a concept map using the terms on the take home quiz. After group concept maps are completed, students exchange

concept maps with another group, evaluate its connections, and edit as they see fit. Finally, students are tasked to design potential therapies on the exchanged map using inhibiting and activating drugs.

After completion of the active learning activities during class, students will write down any concepts from the lesson that they do not fully understand and submit it as a 'ticket-out-the-door'. This process not only helps students reflect upon the information, but also allows the instructor to identify any topics that may need to be addressed before any additional assessments are given.

Assessment

Instructors have the option of evaluating student knowledge entering into the activity by using the take-home quiz as an assessment. There is also an informal assessment of student knowledge during the class discussion of the relevant terms and definitions. Students are involved in self-assessment throughout the in-class activity when creating concept maps, evaluating a map from another group, applying drug therapies, and writing the ticket-out-the-door. Summative assessments can include multiple choice, fill in the blank, or short answer questions on quizzes or exams; we have provided a variety of assessment questions as examples (Supporting File S3: Genes, Mutations and Cancer - Example assessment questions and Supporting File S4: Genes, Mutations and Cancer - Example assessment questions answer key). We recommend including assessment questions based on a scaffold of the concept map to evaluate content knowledge and critical thinking aligned with the learning outcomes.

Inclusive Teaching

Our concept map activity promotes inclusion because the concept map is completed as a group project and includes many opportunities for exchange of ideas. Students are exposed to diverse ideas and opinions during initial generation of the concept map. Furthermore, students also view another group's approach after the concept map exchange.

LESSON PLAN

Prior to Class

Prior to introducing the role of mutations in the progression of cancer, instructors should assign the relevant materials for students to prepare themselves for class. This can include reading from the textbook and any related online work provided by the publisher or associated online videos (listed in Table 1). After students have read and viewed associated media, instructors should introduce roles of mutations in cancer progression. Cell cycle checkpoints, proto-oncogenes, and tumor suppressor genes should all be introduced in the context of cancer progression. These lessons could be in the form of a traditional didactic lecture, videos, readings, or any other relevant media.

Take home quiz:

After the general content introduction, instructors should assign the take home quiz that contains terms and definitions used to generate the concept map at the next class meeting (Supporting File S1: Genes, Mutations and Cancer - Pre-class assignment and Supporting File S2: Genes, Mutations and Cancer - Pre-class assignment answer key).

During Class

Class discussion of take home quiz

When the class reconvenes, instructors should lead a group discussion of the take home quiz. The quiz contains terms used in the concept maps; therefore, it is critical that students verify and correct all definitions before beginning their maps. This discussion should take about 10 minutes.

Group development of concept maps

Instructors can discuss how to develop a concept map with their students and show an instructional video (listed in Table 1). Students are divided into small groups of 4-6 students, these groups can be self-selected or instructors can use random number generators to assign groups to increase inclusivity and diversity within each student group. Groups can either use whiteboards in the classroom or easel pads with the terms written on sticky notes. Both of these methods allow students to revise their concept map layout because terms can be moved. Instructors should give groups 10-15 minutes to create their concept maps. During this time, the instructor should observe and interact with each group to answer questions and ensure that they are making progress. Examples of student generated concepts maps are provided (Figure 1A and 1B), and an example completed concept map for instructor use is shown (Figure 1C).

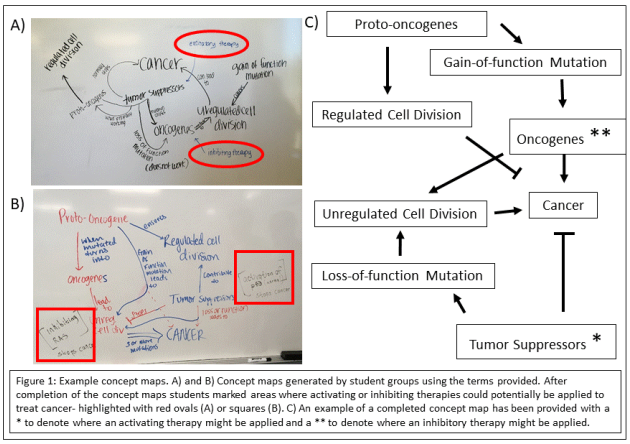

Figure 1: Example concept maps. A) and B) Concept maps generated by student groups using the terms provided. After completion of the concept maps students marked areas where activating or inhibiting therapies could potentially be applied to treat cancer- highlighted with red ovals (A) or squares (B). C) An example of a completed concept map has been provided with a * to denote where an activating therapy might be applied and a ** to denote where an inhibitory therapy might be applied.

Figure 1. Example concept maps.

Group exchanging of concept maps

Instructors should have students view other concept maps in the same room for a few minutes and make note of similarities and differences before progressing to the next step. After students have completed their concept maps, instructors will facilitate exchanging maps between groups; this may simply be moving students clockwise around the room - if they are using whiteboards - or exchanging easel pads. Students should be given 2-3 minutes to assess their exchanged concept map and make any needed revisions.

Students are then given 5-10 minutes to design and annotate potential drug therapies on the exchanged map. Specifically, students should annotate one activating drug (increases activity of a protein target) and one inhibitory drug (decreases activity of a protein target). Students are instructed to use their knowledge of how altered protein function would be able to be used as a drug therapy to inhibit cancer progression.

To achieve this, they are instructed to identify an area on the concept map that could serve as a target for these two types of therapies, examples of student applications of where on the concept map they would apply an activating or inhibitory drug therapy are outlined (Figure 1A and 1B). Additionally, in the completed concept map provided, areas for applying an activating or inhibitory therapy have been denoted with a * or **, respectively (Figure 1C).

This part of the activity is designed to promote critical analysis of interactions in the concept map and an example of how rational drug design begins.

Ticket-out-the-door

After completion of all concept map activities, students are instructed to complete a "ticket-out-the-door" assignment. A "ticket out the door" is a formative assessment that asks students to write one to two sentences rating their understanding of the learning objectives and asking any questions that remain. A student response to the ticket out the door might be: 1) I am confused by how the term proto-oncogene is related to oncogene or 2) I understand how an activating therapy might be applied to a tumor suppressor, but would this work on the DNA or on the protein?

Recommended Timeline:

A recommended timeline is provided in Table 1. Below is a list of materials for teaching this lesson:

- Background reading (associated textbook for the course)
- In class lecture (prepared by individual instructors)
- Pre-class assignment (Supporting File S1: Genes, Mutations and Cancer)
- Pre-class assignment answer key (Supporting File S2: Genes, Mutations and Cancer)
- Example assessment questions (Supporting File S3: Genes, Mutations and Cancer)
- Example assessment questions answer key (Supporting File S4: Genes Mutations and Cancer)

TEACHING DISCUSSION

Student Reactions to the Lesson

Both of the instructors who have implemented this concept map activity monitored student enthusiasm and engagement within the classroom. We found students to be engaged in the activity, using their knowledge and reasoning skills to generate a concept map and apply drug therapies.

To determine the student reactions to the lesson, we administered a survey at the end of the class session. This survey was performed in 3 class sessions, two Cell Biology sections (n=33 students) and one Introductory Biology section (n=39 students). Survey questions were given on a Likert scale with answers being rated on a scale of 1-5, 1 being strongly disagree and 5 being strongly agree. Students were asked to rate their experiences with parts of the active learning exercise including the effectiveness of the take home quiz, group discussion of the take home quiz, group generation of a concept map and application of drug therapies to the concept maps. Student reaction was overwhelmingly positive with >75% of students selecting "Agree" or "Strongly agree" to the survey question "The take home quiz helped me understand the material better", and > 70% of students selecting "Agree" or "Strongly agree" to the statement "Group work to develop a concept map helped me apply my knowledge to the material learned" (Figure 2 left and center panel). The range of responses to the question "Applying drug therapies to my concept map helped me to evaluation my understanding of the big picture" was more varied, ranging from with 88% responding Agree or Strongly agree in the Cell Biology class and 55% from Introductory Biology. (Figure 2 right panel). In total, both from instructor observation and the attitudinal data from students, this concept map activity shows high levels of student engagement and enthusiasm for learning the content.

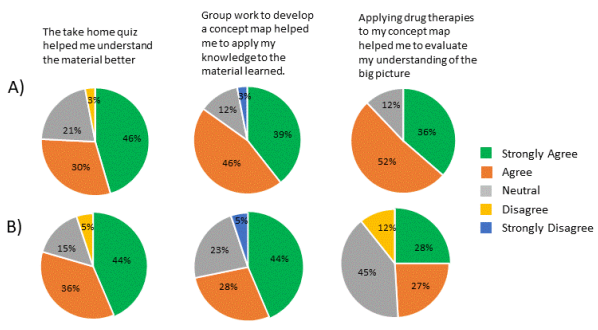

Figure 2: Attitudinal data from students in A) an sophomore level Cell Biology course (n=33) or B) an Introductory Biology course (n=39). Student responses are depicted below each question about the effectiveness of the active learning strategies implemented in the classroom.

Figure 2. Student Attitudinal data towards active learning lesson.

Possible improvements or adaptations

The concept map exercise was used initially in an introductory biology class and a sophomore level cell biology course. We believe that student group concept mapping is practical to implement in a smaller classroom and could be scaled up to a large classroom as long as enough instructors and/or TAs are available to answer questions. Based on our experience implementing this activity in the classroom, we provide some potential adaptations. If time permits, the take home quiz could be completed in class as a group exercise prior to generation of the concept map, promoting enhanced group work and discussion of terms and definitions. In additional upper division courses such as Cancer Biology, the activity could be modified by omitting the term list to perform formative assessment of student's identification of key terms during the concept mapping, and increasing the complexity with the addition of more terms, mutations, and drug targets.

Mapping can also be completed on virtual canvases in programs such as Google Drawing; this free software allows multiple students to collaborate on a single concept map from multiple computers and devices simultaneously or sequentially. Google Drawing also allows students to import images, save multiple versions, exchange with multiple groups, and export and submit their maps in multiple formats for grading.

SUPPORTING MATERIALS

- S1. Genes, Mutations and Cancer - Pre-class assignment. Includes the individual take home quiz that contains the terms and definitions that will be used to generate the concept map.
- S2. Genes, Mutations and Cancer - Pre-class assignment answer key.
- S3. Genes, Mutations and Cancer - Example assessment questions. Includes a variety of assessment questions that instructors can use for summative assessments.
- S4. Genes, Mutations and Cancer - Example assessment questions answer key

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Table 1. GMC: Genes, Mutations and Cancer - Group Concept Map Development teaching timeline

Activity	Description	Time	Notes
Prior to Class			
Assign associated reading or online videos	Instructors can assign pre-reading from the associated pages in the textbook being used for the course. Instructors can also assign videos from the associated text book or those provided here to introduce the topic.	NA	• Tumor Suppressor Genes: https://www.khanacademy.org/test-prep/mcat/biomolecules/gene-control/v/tumor-suppressors • Oncogenes: https://www.khanacademy.org/test-prep/mcat/biomolecules/gene-control/v/oncogenes
Content Introduction	Instructors can cover the content necessary in a traditional didactic lecture, using group work, and/or videos in a flipped classroom.	1-2 class meetings	
Assign take home quiz	Take home worksheet (Supporting File S1. Genes, Mutations and Cancer - Pre-class assignment).	NA	
During Class			
Class discussion of take home worksheet	Instructors lead a discussion on the terms and definitions covered in the worksheet	~10 minutes	
Discussion or video of how to create a concept map	Instructors lecture on how to integrate terms into a concept map and/or show the associated video.	5-10 minutes	How to create a concept map: https://m.youtube.com/watch?v=sZJj6DwCqSU
Group development of concept map	Instructors break the class into groups of 4-6 and assign the groups to develop a concept map using the terms provided in the take home worksheet	10-15 minutes	
Group swapping of concept maps	Instructors prompt students to swap concept maps, evaluate understanding, and apply drug therapies to the maps.	5-10 minutes	
Assign ticket-out-the-door	Instructor assigns students to finish an exercise describing any information they are not yet comfortable with after the active learning exercise.	~5 minutes	