**Instructor Guide: Calculating Lifetime Cancer Risk Resulting from DNA Replication**

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**Relevance and goals for the module**

Student interest in cancer as a topic of study and discussion is high, as most students can closely identify with the impact of cancer on an individual and their loved ones. DNA replication and repair is a topic essential to understanding reproduction and is foundational to students' understanding of gene expression. This module seeks to address two distinct learning goals, one that is content-based and one that is develops quantitative competency in freshman biology students.

*Learning Goals for "Calculating Lifetime Cancer Risk Resulting from DNA Replication"*

1. To give students context for the importance of high fidelity DNA repair by capitalizing on their inherent interest in cancer and curiosity as to what causes cancer.
2. To develop students' science process skills by teaching experimental design as well as developing skills in scientific notation, relationships between two variables in a scatter plot, and correlation between variables.

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| ***Content Learning Objectives*** | ***Quantitative Learning Objectives*** | ***Process of Science Learning Objectives*** | ***Formative Assessment Ideas*** | ***Summative Assessment Ideas*** |
| 1) Explain the role of stem cells in the development and maintenance of tissues.  2) Assess the effect mutations in the replication machinery would have on DNA replication.  3) Relate how errors in DNA replication could affect lifetime cancer risk. | 1) Express numbers in scientific notation and percentage.  2) Evaluate a Pearson correlation coefficient (r) to identify relationships between variables.  3) Illustrate correlation between variables by generating scatterplots. | 1) Utilize experimental design to propose a scientific question relating one variable to another, generate a hypothesis, and formulate a method to test the hypothesis. | 1) Use the embedded questions in the PowerPoint presentation.  2) Have students/teams present answers to questions in each handout, and share/discuss their reflections. | 1. Multiple- choice questions are provided.  2. Present a scatterplot on an exam and ask students to interpret the plot. |

**Background for instructor**

This case study uses data from: Tomasetti, C. & Vogelstein, B. Variation in cancer risk among tissues can be explained by the number of stem cell divisions. *Science* **347**, 78–81 (2015).

The article presented in this case study found that the lifetime risk of cancers of many different types is strongly correlated with the total number of divisions of normal stem cells. The results presented suggests that as much as 66% of the variation in cancer risk among tissues may be attributable to random mutations arising during DNA replication in normal, noncancerous stem cells.

In this module, students are asked to generate a scientific question that relates DNA replication to cancer risk, propose a hypothesis to answer their question, and suggest one way to test their hypothesis.

The data in this study spanned over five orders of magnitude, and logarithmic transformation of the data was employed. Competency in describing or performing logarithmic transformations is not prerequisite for this module, however. A second student handout is included for your use, should you desire to teach your students more about logarithmic transformations.

In this module, students are asked to generate scatterplots that illustrate correlation values of +1, 0 and -1. When r = +1, the variables are perfectly linearly correlated in the same direction. When one variable increases, the other increases. When r = -1, the variables are perfectly linearly correlated in the opposite direction. When one variable increases, the other decreases. When r = 0, no correlation between the two variables.

The greater the absolute value of r, the stronger the linear relationship between the two variables. Students are also asked generate a statement that interprets the meaning of sample correlation values, indicating both the strength and the direction of the correlation. In this module, correlation is measured by a Pearson correlation coefficient.

The conclusion of this case study asks students to interpret the correlation statements made by this paper, generate written statements that interpret the stated correlation value between lifetime cancer risk and the number of stem cell divisions, and apply their knowledge of DNA replication and repair to justify the authors' findings. Their statements should reflect statistical literacy as well as application of content and science process skills.

More Detail

*Authors’ Published Abstract:* "Some tissue types give rise to human cancers millions of times more often than other tissue types. Although this has been recognized for more than a century, it has never been explained. Here, we show that the lifetime risk of cancers of many different types is strongly correlated (0.81) with the total number of divisions of the normal self-renewing cells maintaining that tissue’s homeostasis. These results suggest that only a third of the variation in cancer risk among tissues is attributable to environmental factors or inherited predispositions. The majority is due to “bad luck,” that is, random mutations arising during DNA replication in normal, noncancerous stem cells. This is important not only for understanding the disease but also for designing strategies to limit the mortality it causes."

**Prerequisite knowledge for students**

Before studying this topic, students should already be able to:

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| 1. Describe the structure of DNA and the evidence that it is the genetic material. 2. Describe the process of replication and the process by which DNA repair occurs. 3. Organize the components of the DNA replication machinery by task completed and order in which each occurs. 4. Perform basic math skills including multiplication and manipulation of exponents. |

**Scenarios for use of this activity include:**

1. Utilize the PowerPoint presentation of the case study to facilitate class discussion and students' completion of the provided student handout A.
2. Ask students to read the original article published by Tomasetti and Vogelstein as homework. Have students work in teams to complete student handout A and/or handout B using the article as a reference.

**Sample assessment questions**

1. Every fall, business at the Icee Sno-Cone stand slows as the weather changes and temperatures drop. An analysis of sales shows that the number of sno-cones sold on any given day is directly proportional to the temperature that day. If you generated a scatterplot and a Pearson’s r coefficient was calculated to measure the relationship described, what variables would be plotted on the x- and y-axis?

1. daily temperature and total dollars in sales per day
2. *daily temperature and number of sno-cones sold per day*
3. months of the year and average temperature each month
4. number of sno-cones sold per day and the average price per sno-cone

2. Every fall, business at the Icee Sno-Cone stand slows as the weather changes and temperatures drop. An analysis of sales shows that the number of sno-cones sold is directly proportional to the decrease in temperatures. If you generated a scatterplot and a Pearson’s r coefficient was calculated to measure the relationship between the variables, to what value would r be closest?

1. *r = +1*
2. r = 0
3. r = -1
4. r cannot be approximated from the given information

3. Pizza is served in the school cafeteria 4 out of 5 times each week. Pepperoni pizza is served 50% of the time that pizza is served. What are the chances that Emily can buy a pepperoni pizza on a given day of the week?

1. 80%
2. 50%
3. *40%*
4. 30%

**References**

1. Tomasetti, C. & Vogelstein, B. Variation in cancer risk among tissues can be explained by the number of stem cell divisions. *Science* **347**, 78–81 (2015); <http://science.sciencemag.org/content/347/6217/78.full>
2. OpenStax CNX; https://cnx.org/contents/esgfrPlv@3/Accessory-Organs-in-Digestion-
3. HHMI Biointeractive; <https://www.hhmi.org/biointeractive/data-points>
4. Khan Academy; https://www.khanacademy.org
5. Math Bench Biology Modules; <http://mathbench.umd.edu/modules/misc_scaling/page07.htm>