Teacher Resource for:

Smoking is associated with mosaic loss of chromosome Y

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GENERAL USE OF *Science* in the Classroom

**Student Learning Goals:**

“One fundamental goal for K-12 science education is a scientifically literate person who can understand the nature of scientific knowledge.”

The U.S. National Academy of Sciences defines science as: “Any new finding requires independent testing before it is accepted as scientific knowledge; a scientist is therefore required to honestly and openly report results so that they can readily be repeated, challenged, and built upon by other scientists. Proceeding in this way over centuries, the community effort that we call science has developed an increasingly accurate understanding of how the world works. To do so, it has had to reject all dogmatic claims based on authority, insisting instead that there be reproducible evidence for any scientific claim.”

An important student learning goal, central to any understanding of “the nature of scientific knowledge,” is to give each student an appreciation of how science is done.

This includes knowing why:

- Scientists must be independent thinkers, who are free to dissent from what the majority believes.
- Science can deal only with issues for which testable evidence can be obtained.
- All scientific understandings are built on previous work.
- It is to be expected that one scientist’s conclusions will sometimes contradict the conclusions of other scientists.
- Science is a never-ending venture, as the results from one study always lead to more questions to investigate.

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Using This Resource

Learning Lens:

The Learning Lens tool can be found on the right sidebar of each resource and is the source of annotations. Click on the headings to highlight portions of the text of the corresponding research article. A subsequent click on the highlighted text will produce a text box containing more information about that particular piece of text. Below is an example of the Glossary function of the Learning Lens.

An example of the resource with the Glossary, Previous Work, Author’s Experiments, News and Policy Links, and References and Notes tools turned on. The Glossary tool is in use.
Learning Notes:

Learning Notes accompany each figure and are designed to help students deconstruct the methods and data analysis contained within each figure.

Fig. 1. Spatial distribution of head scales. (A) Head scales in most snakes (here, a corn snake) are polygons (two upper panels) with stereotyped spatial distribution (two lower panels); left (yellow) and right (red) scale edges overlap when reflected across the sagittal plane (blue). (B) Polygonal head scales in crocodiles have a largely random spatial distribution without symmetrical correspondence between left and right. (C) Head scales from different individuals have different distributions of scales' sizes and localizations (blue and red edges from top and bottom crocodiles, respectively).

The authors took 120 color pictures of each animal to create detailed, three-dimensional models of reptile heads. Watch this video in which the authors further explain their modeling methods:

http://www.sciencemag.org/content/suppl/2012/11/29/science.1226265.DC1/1...
References:

The Reference section of each resource is annotated with a short statement about how or why each reference relates to the current research study.
Thought Questions

Thought Questions are located above the Learning Lens in the right sidebar of each resource. These questions were written to be universal and applicable to any primary research paper. Thought questions do not have a single answer, or a correct answer for that matter, and can be used to stimulate discussion among students.
Suggestions for Classroom Use:

In addition to the thought questions discussed above, other resources are provided for use in the classroom. These can be found toward the end of the teacher guides associated with each specific article and include:

1. Discussion questions specific to the article, related to the standards, and/or associated with the figures.

2. Activities tied to the articles.

Some ways to use the *Science* in the Classroom articles:

1. Assign to student groups to read and discuss during class.

2. Assign small sections of the article to student groups to read and discuss during class, with the expectation that they will present or use jigsaw to teach the entire class what is in their part of the article.

3. Assign to individual students to complete during class or as homework.

4. Assign reading as an extra credit project.

Some ideas for interactive student engagement after reading the article:

1. Students write answers to discussion questions (for example, those linked to the standards or those linked to the diagrams).

2. Go over the abstract, as well as information about the purpose and structure of an abstract, and have students write their own abstracts for the articles in language that could be understood by their peers.

3. Have students edit the article, or parts of the article, to a simpler reading level.

4. Have students, alone or in small groups, use the annotated list of references to explain how the scientists who wrote this article built on the published work of at least one independent group of scientists in making their discoveries. In the process, did they produce data that supports the findings of the earlier publication that they have cited in the text? In what way does this article support the statement that scientific knowledge is built up as a “community effort”? 
5. Use the article and discussion questions linked to the standards and the diagrams for a teacher-led classroom discussion. The discussion can focus on the nature of science and scientific research, as well as on the science in the article itself.

6. Have students give a classroom presentation about the article, parts of the article, or their answers to discussion questions.
ARTICLE-SPECIFIC MATERIALS

Connections to the nature of science from the article

- Can environmental factors increase the risk of disease?

The importance of this scientific research

- Learning about factors that contribute to cancer informs improved approaches for treating cancer; learning about how chromosomal aberrations can occur during life may elucidate the etiology of diseases not yet understood; learning how chromosomal aberrations can occur during life and may be affected by smoking and other factors may elucidate processes involved in cell division and aging; learning about the effects of smoking may contribute to the ability to design less damaging cigarettes.
Connect to Learning Standards:

AP Biology Standards:  

Essential Knowledge 2.C.2: Organisms respond to changes in their external environments.

1. Which factors in the external environment did Dumanski et al. (2015) analyze for an association with the degree of mosaic LOY?

Essential Knowledge 3.C.1: Changes in genotype can result in changes in phenotype.

2. What are phenotypic changes the authors predict are associated with a higher degree of mosaic LOY?

3. How might mosaic LOY increase the risk of developing cancer?

http://www.nap.edu/read/13165/chapter/7#42

Practice 1: Asking questions

4. Which experimental questions did Dumanski et al. (2015) seek to answer with the research reported in this paper?

Practice 3: Planning and carrying out investigations

5. Were the male samples used in these experiments collected specifically for this research? What are the advantages and disadvantages of using samples collected in this way?
6. What are the advantages and disadvantages of analyzing data from three independent datasets?

Practice 4: Analyzing and interpreting data

7. Which types of statistical analyses were used to determine whether there were significant differences between the groups compared?

8. How were the data displayed to enable the reader to understand what types of difference existed between groups?

Practice 7: Engaging in argument from evidence

9. Note that, when discussing the results reported in Figure 1, Dumanski et al. (2015) says, “We found a strong association between smoking and LOY status in the three independent cohorts.” How does saying there was “a strong association” differ from saying that smoking causes LOY.

10. What do Dumanski et al. (2015) conclude about whether the high degree of mosaic LOY associated with smoking is a “neutral passenger mutation” or a factor that is likely to increase the risk of cancer and mortality?

11. Do you think the data reported support that conclusion?
Summary of the Article for the Teacher:

It is recommended that this not be used by students in place of reading the article.

General Overview:

The genetics of some diseases (e.g., cystic fibrosis, Huntington disease) is pretty clear cut: A person is born with a disruption, or mutation, in a critical gene that causes the disease. The genetics of many common diseases, however, are more complicated. In most cases, diseases like cancer, inflammatory bowel disease, or hypertension cannot be explained by mutations in a single gene. Recent work has suggested that, instead of mutations in a single gene, people may be born with variants in many genes that may increase the risk of developing some of these diseases. Although exciting findings have identified such variants that contribute to disease risk, our current understanding of them still does not fully explain how these diseases develop. As a piece to this puzzle, there is increasing evidence that changes that occur in a person’s DNA during life may impact disease risk. Such changes are often referred to as acquired changes because they occur after cells and tissues are already established. Because each established cell may be affected differently, a mosaic pattern may result in which some cells have the change and some cells do not. In addition, there is increasing evidence that environmental factors also impact disease risk. Here, the authors report that the cells in men who smoke lose their Y chromosome significantly more than cells in men who do not smoke. This loss of the Y chromosome has been associated previously with the development of cancers.

Topics Covered:

- chromosomes
- cancer development
- DNA genotyping
- tumor immunosurveillance
- tumor suppressors
- X-chromosome inactivation

Methods used in the Research:

- analysis of median logR ratio (LRR) of SNP array data collected from markers on the Y chromosome (mLRR-Y)
- ANOVA
- Kolmogorov-Smirnov test
Conclusions:

- Smoking was significantly associated with the degree of mosaic LOY in the three datasets analyzed. This suggested that smoking increases the risk of mosaic LOY.

- The risk of having a high degree of mosaic LOY was 2.4 to 4.3 times greater in current smokers than in nonsmokers in these datasets.

- The number of packyears smoked was significantly greater in those with a high degree of mosaic LOY than in those without. This suggested that smoking more may increase an individual's risk of LOY.

- There was no significant difference in the degree of mosaic LOY between the never-smokers and the previously regular smokers. Dumanski et al. (2015) hypothesized that this lack of difference could be because the previously regular smokers who had had a high degree of mosaic LOY had already died or the degree of mosaic LOY returned to more normal levels after smoking cessation.

- The degree of mosaic LOY was different in the different cell types analyzed. This suggested that the degree of LOY was having an effect on the survivability of cells and wasn't sure occurring randomly because of widespread chromosomal damage.

Areas of Further Study:

- Determine whether smoking causes mosaic LOY versus just being associated with mosaic LOY

- If evidence supporting a causal relationship is identified, elucidate the mechanism of how smoking causes mosaic LOY

- Research how mosaic LOY might contribute to the risk of cancer and mortality.
Resources for Interactive Engagement:

Discussion Questions

1. What other factors might contribute to the fact that males have a higher incidence and mortality from most non-sex-specific cancers?

2. Why do you think Dumanski et al. (2015) only studied samples from men?

3. Why do you think Dumanski et al. (2015) decided to measure the degree of mosaic LOY using their mLRR-Y method instead of using the whole-genome NGS method they use to validate the mLRR-Y method in 100 samples?

4. Why do you think it is important for Dumanski et al. (2015) to use a multivariable model to adjust for the above-mentioned potential confounders?