

Teacher Notes for “Cell Differentiation and Epigenetics”¹

In this analysis and discussion activity, students answer minds-on questions as they learn about the differentiation of specialized cell types, including the role of changes in epigenetic control of gene expression during cell differentiation. Students also learn about environmental influences on epigenetic control of gene expression and the need for cell division and differentiation even in a fully grown adult.

This activity is intended to follow “Mitosis – How a Single Cell Developed into the Trillions of Cells in a Human Body” (http://serendipstudio.org/sci_edu/waldron/#mitosis). In this mitosis activity, students learn about genes and how mitosis ensures that each cell gets a complete set of chromosomes with a complete set of genes.²

Learning Goals³

In accord with the Next Generation Science Standards⁴:

- Students will gain understanding of the Disciplinary Core Idea LS1.B: Growth and Development of Organisms.
 - “In multicellular organisms individual cells grow and then divide via a process called mitosis, thereby allowing the organism to grow. The organism begins as a single cell (fertilized egg) that divides successively to produce many cells, with each parent cell passing identical genetic material (two variants of each chromosome pair) to both daughter cells. Cellular division and differentiation produce and maintain a complex organism, composed of systems of tissues and organs that work together to meet the needs of the whole organism.”
- Students will engage in the Scientific Practice:
 - Constructing Explanations. “Apply scientific ideas, principles, and/or evidence to provide an explanation of phenomena...”
- This activity provides the opportunity to discuss the Crosscutting Concept:
 - Cause and effect: Mechanism and explanation. Students “suggest cause and effect relationships to explain and predict behaviors in complex natural and designed systems”.
- This activity helps to prepare students for the Performance Expectation, HS-LS1-4:
 - “Use a model to illustrate the role of cellular division (mitosis) and differentiation in producing and maintaining complex organisms.”

Instructional Suggestions and Background Biology

To maximize student participation and learning, I suggest that you have your students work individually, in pairs, or in small groups to answer each group of related questions. Then, after each group of questions, have a class discussion of student answers to probe their thinking and

¹ By Dr. Ingrid Waldron, Department of Biology, University of Pennsylvania, © 2017. These Teacher Notes and the related Student Handout are available at <http://serendipstudio.org/exchange/bioactivities/epigenetics>.

² In preparation for this activity, you might also want to use the hands-on activity, "From Gene to Protein – Transcription and Translation" (http://serendipstudio.org/sci_edu/waldron/#trans) or the analysis and discussion activity, "From Gene to Protein via Transcription and Translation" (<http://serendipstudio.org/exchange/bioactivities/trans>).

³ The best way to meet these Learning Goals will be to have your students first complete the recommended mitosis activity and then complete this activity on cell differentiation and epigenetics.

⁴ Quotations from <http://www.nextgenscience.org/sites/default/files/HS%20LS%20topics%20combined%206.13.13.pdf>

guide them to a sound understanding of the concepts and information before moving on to the next group of questions.

If you use the Word version of the Student Handout to make changes for your students, please check the PDF version to make sure that the figures and formatting in the Word version are displaying correctly on your computer.

A key is available upon request to Ingrid Waldron (iwaldron@sas.upenn.edu). The following paragraphs provide additional instructional suggestions and background information – some for inclusion in your class discussions and some to provide you with relevant background that may be useful for your understanding and/or for responding to student questions.

In discussing question 1, you might want to mention the different levels of organization shown in the figure, i.e. cells, tissues and organs.

For simplicity, the Student Handout does not mention the multiple genes that code for different types of hemoglobin or keratin proteins.

Levels of gene expression vary along a continuum, but for simplicity the Student Handout refers to genes as being turned on or off. On page 2, the second and third figures show an oval representing the proteins that bind to DNA to begin transcription; these proteins include RNA polymerase and transcription factors. Transcription factors are proteins that initiate and regulate the transcription of genes. Transcription factors often regulate the rate of transcription for multiple genes involved in differentiation of specific types of cells such as muscle cells (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2861743/>). There are multiple interactions between transcription factors and epigenetic changes. For example, epigenetic mechanisms can turn on transcription of genes that code for transcription factors.⁵ During development, the epigenetic changes in each cell are influenced by chemical and physical signals from the tissue around the cell.

To help your students understand the term epigenetic, you may want to tell your students that epi is Greek for over, outside of, or around; this corresponds to the fact that epigenetic changes do not alter the sequence of nucleotides in the DNA. During the differentiation of red blood cells epigenetic changes include decreased methylation of the hemoglobin gene and increased acetylation of the histones in the region of DNA that plays a role in controlling the expression of this gene (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3398168/>).⁶ Epigenetic regulation of gene expression is typically quite complex (see the figure on page 4 of these Teacher Notes).

Question 6 asks the students to identify the arrows that represent epigenetic changes. To help your students understand the figures, you may want to ask them what the other arrows represent.

In the study described in question 7, the polluted air had levels of polycyclic aromatic hydrocarbons (PAH) that were at or slightly higher than air pollution levels in New York City (<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0110706>). Gene expression and

⁵ Gene expression is also regulated by mechanisms that act after transcription (e.g. effects of microRNAs on the stability of the mRNA; see <https://www.news-medical.net/life-sciences/Regulation-of-Gene-Expression.aspx>).

⁶ The Student Handout states that methyl groups on DNA repress transcription by preventing the proteins needed for transcription from binding to the DNA. For information about other mechanisms by which methyl groups on DNA repress transcription, see <http://birdlab.bio.ed.ac.uk/bird/sites/sbsweb2.bio.ed.ac.uk/bird/files/29.pdf>.

methylation of promoter DNA were assessed in fat tissue. Additional evidence for the proposed epigenetic mechanism comes from the finding that DNA methylation was inversely correlated with gene expression, body weight, BMI and amount of fat. The study reported similar results for the “grand-offspring” of the mice that were exposed to air pollution during pregnancy vs. the “grand-offspring” of the controls.

The findings from the mouse study may well be relevant for understanding one cause of human obesity. In humans, maternal exposure to PAH air pollution during pregnancy is associated with higher body mass index (BMI) and increased risk of obesity at ages 5-7. PAH are produced by incomplete combustion, with traffic responsible for about half of PAH air pollution levels.

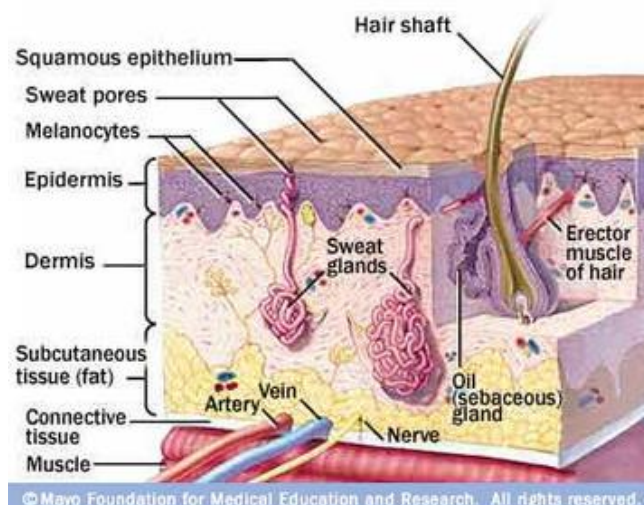
If you want your students to learn more about epigenetic regulation of gene expression and environmental influences on epigenetic changes, you can use the resources available at http://www.pbs.org/wgbh/nova/education/activities/3411_02_nsn.html and <http://learn.genetics.utah.edu/content/epigenetics/>.

Obviously, development involves much more than the processes of mitosis and cell differentiation. Information about other processes involved in development is available at:

- https://en.wikipedia.org/wiki/Prenatal_development
- <http://www.scholarpedia.org/article/Morphogenesis>
- <http://www.healthofchildren.com/P/Prenatal-Development.html>
- <https://www.youtube.com/watch?v=bEgygtbEo2A&feature=youtu.be>

The biology of skin is significantly more complicated than indicated in the Student Handout. For example, water loss is minimized not only by keratin, but also by special proteins in the cell envelope of fully mature keratinocytes and the barrier lipids surrounding these cells. Also, the figure on page 3 of the Student Handout shows only the epidermal layer of the skin between hair follicles. The figure below shows additional structures in human skin. The functions of the skin include:

- protection against water loss, invasion by microorganisms, and damage by UV light
- body temperature regulation (e.g. by sweating)
- sensing touch, temperature and painful stimuli (e.g. irritating chemicals)

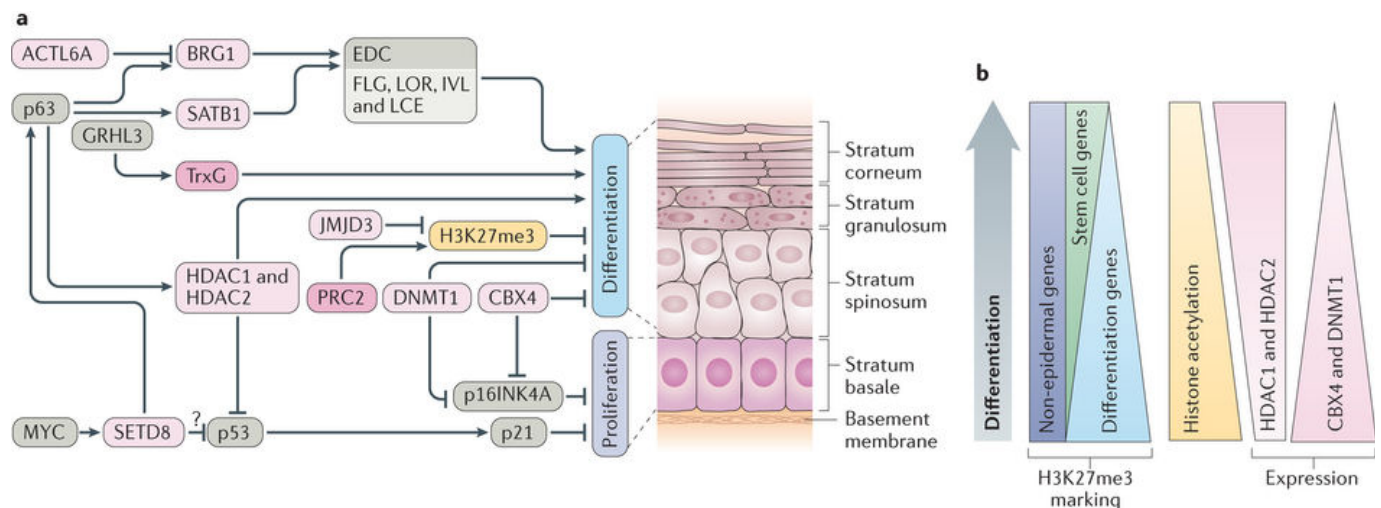


(https://healthscientechnology.wikispaces.com/file/view/skin_type.jpg/266829900/359x287/skin_type.jpg)

The figure on page 3 of the Student Handout refers to undifferentiated cells and does not introduce the more complicated concept of stem cells. In the epidermis, a stem cell divides to produce one replacement stem cell and one cell that divides a few more times before the resulting cells differentiate into keratinocytes. Typically, differentiated cells cannot undergo mitosis, so stem cells are needed to produce replacements for damaged differentiated cells. These stem cells in postnatal tissues should be distinguished from embryonic stem cells (<https://stemcells.nih.gov/info/basics.htm>).

As you discuss keratinocytes, you may want to mention that the dead keratinocytes that flake off the surface of the skin can be a source of DNA for crime investigations (<https://www.forensicmag.com/article/2013/04/touch-dna-crime-scene-crime-laboratory>).

This figure illustrates some of the complexity of the epigenetic regulation of the differentiation of keratinocytes. As the keratinocytes differentiate, there is a decrease in tri-methylation (H3K27me3) of the histones for the genes involved in keratinocyte differentiation and keratin production; this reduces the repression of transcription of these genes, so these genes become more active.



(<https://images.nature.com/full/nature-assets/nrm/journal/v17/n10/images/nrm.2016.76-f2.jpg>)

Sources for Figures in Student Handout

- Figure on the top of page 1, modified from Krogh, Biology – A Guide to the Natural World
- Figure on the top of page 2, modified from Krogh, Biology – A Guide to the Natural World
- Figure in the middle of page 2, modified from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3063335/>
- figure on the bottom of page 2, modified from https://www.researchgate.net/profile/Alberto_Passi/publication/264007308/figure/fig2/AS:282625391513602@1444394552053/Figure-2-Histone-acetylation-HATs-catalyze-histone-acetylation-Ac-using-acetylCoA-as.png
- Figure on page 3, modified from <http://singlecell.riken.jp/wp/wp-content/uploads/2016/09/research07-a-1-800x480.png>