

Investigating Prenatal Arsenic Exposure and Altered Gene Expression

Student Worksheet

Name:

UNC scientist Rebecca Fry, PhD, and her research team are studying children's health effects related to prenatal exposure to arsenic. Arsenic is a toxic metal that poses a threat to children's health. Pregnant women can be exposed to arsenic by ingesting arsenic contaminated foods or drinking water. **“There is evidence that maternal exposure to arsenic may leave marks on the baby's DNA that could result in altered birth outcomes and/or in long term health effects/disease later in life and be passed on to future generations,”** Fry explains.

Part I. What is the relationship between prenatal arsenic exposure and changes to gene expression?

1. In your own words, state the central question guiding Dr. Fry's research.

Dr Fry collected newborns' cord blood leucocytes (white blood cells) at birth to see examine the relationship between their prenatal exposure to arsenic, changes to DNA methylation and functional epigenetic changes, which would be revealed through altered mRNA expression.

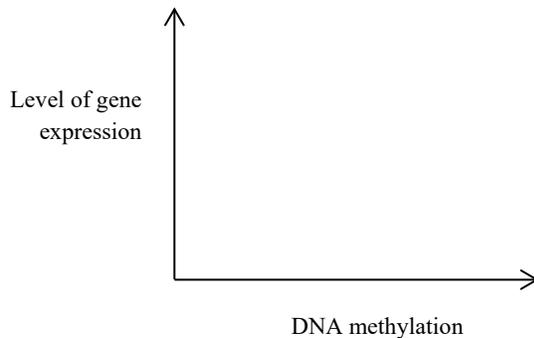
Next, you will learn how to interpret a *visual representation* of these resulting data, referred to as a **heat map**. Use the following questions as a guide as you view the heat map provided by your teacher.

2. Notice that the map is organized into rectangles that form columns and rows:
How many rectangles are in a vertical column?
What do these rectangles represent?

How many rectangles are in a horizontal row?
What do these rectangles represent?
3. What does a green rectangle represent? A yellow rectangle?
4. What conclusion can you make about the data from the bottom 110 rows? How about rows 111-334?
5. Draw a conclusion about this heat map: what does this heat map reveal about infants exposed to high levels of maternal arsenic?
6. Do these data prove that arsenic causes differential gene expression *in utero*? Why or why not?
7. Where might Fry and her research team direct future research to expand upon these findings?

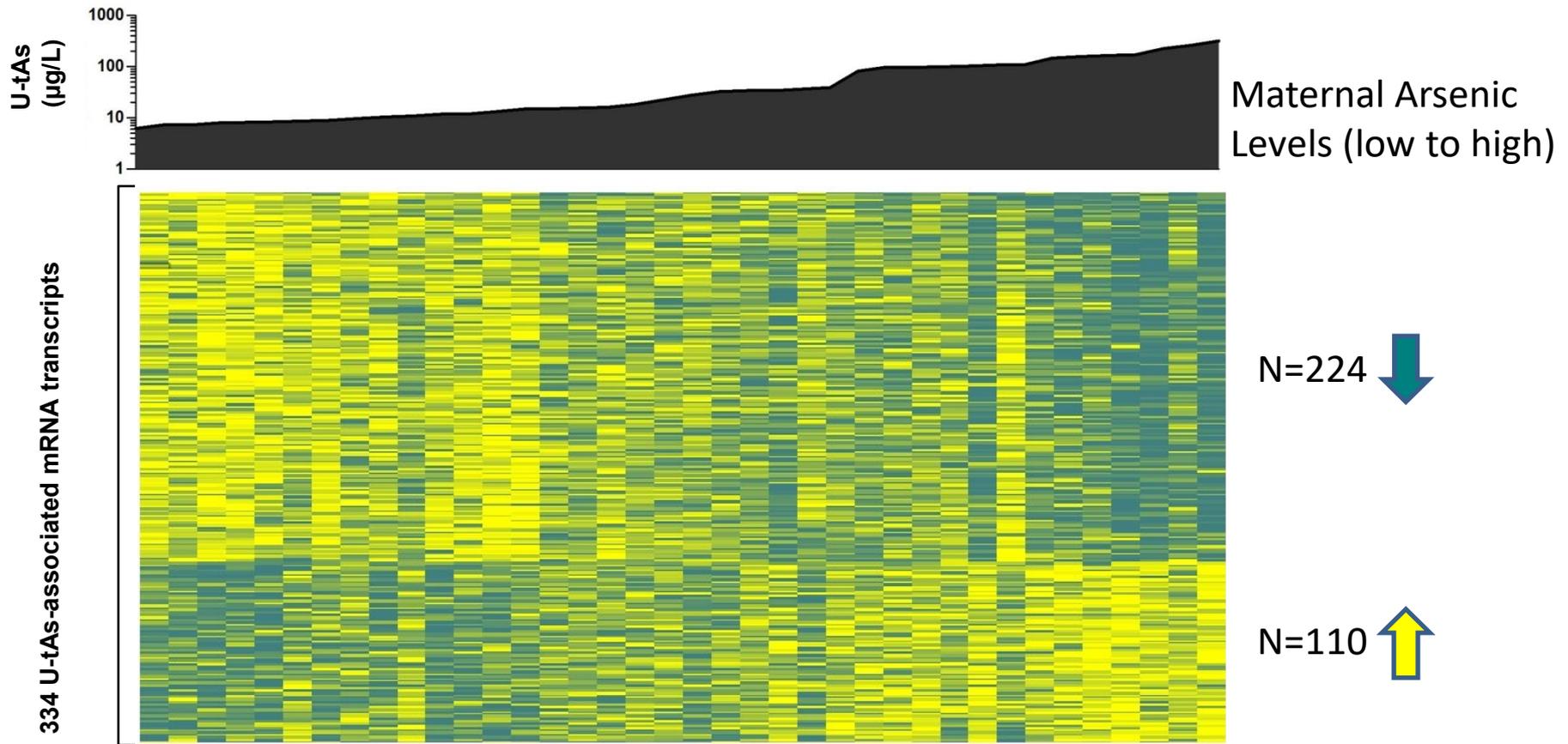
Part II. Are any of the genes that are altered in association with arsenic exposure controlled (turned on/off) by changes to DNA methylation?

8. Based on what you have learned about gene expression and DNA methylation, for each scenario below circle the *expected impact* on gene expression if arsenic exposure leads to a change in DNA methylation.
- a. A gene that gets more methylated in response to arsenic exposure would be expected to have:
Increased gene expression Decreased gene expression
- b. A gene that gets less methylated in response to arsenic exposure would be expected to have:
Increased gene expression Decreased gene expression
9. If DNA methylation controls expression of a particular gene, use a pen or pencil to depict what you perceive to be the *expected relationship* between DNA methylation (x axis) and gene expression (y axis) on the blank graph below.



10. Dr. Fry and her team identified a subset of seven genes that were differentially methylated *and* differentially expressed *and* associated with differences in birth outcomes. One of these genes is KCNQ1 which encodes a potassium- voltage-gated potassium channel and plays a role in development. Your teacher will show you a graph depicting the data Dr. Fry obtained for KCNQ1 in response to arsenic exposure; each dot represents the KCNQ1 gene for one infant (38 infants total). Observe the graph and answer the questions below.
- a. Does the displayed graph depict the trend you predicted in question 9 above?
- b. What does this graph tell you about KCNQ1 expression in response to arsenic exposure?
11. In summary, Dr. Fry’s findings revealed that 2,919 genes exhibited differential methylation in response to arsenic exposure, and 334 gene exhibited corresponding changes in gene expression (mRNA transcripts) while only 16 genes exhibited a significant linear relationship between methylation and gene expression. What do these data suggest about the other genes that were differentially expressed in response to arsenic exposure?
12. Where might Dr. Fry and her research team direct future research to expand upon these findings?

Heat Map Analysis | Identifying genomic changes associated with prenatal arsenic exposure



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N=38 subjects with range of arsenic exposure, cord blood (vein) isolated