Activity 4
Long-Term Effects of Drug Addiction

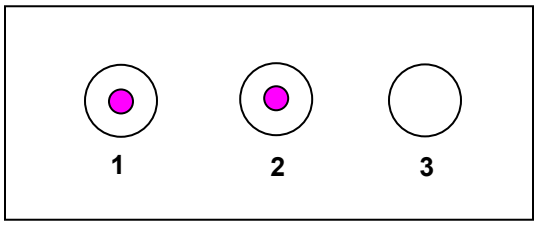
Core Concept:
Addictive drugs may lead to long-term changes in brain function.

Class time required:
Approximately 60-80 minutes

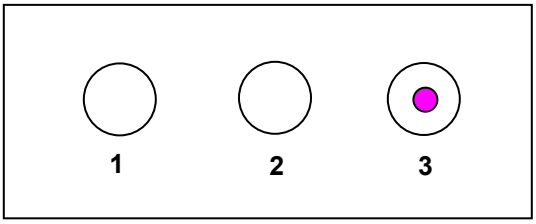
Teacher Provides:

- Copy of student handout entitled "**Long-term Effects of Drug Addiction**" for each student.
- COLOR copies of PET scans, Figures 1 and 2. One copy per student. These may be laminated or placed in sheet protectors for use with multiple classes.
- Safety goggles for each student
- Kit of lab materials for each team of 2-3 students that includes:
  - Microtube containing 1 ml of pH 10 buffer labeled "RNA—NO drug abuse"
  - Microtube containing 1 ml of pH 10 buffer labeled "RNA—Drug Abuse"
  - Disposable plastic dropper labeled "RNA—NO drug abuse"
  - Disposable plastic dropper labeled "RNA—Drug abuse"
  - Half sheet with papers for spotting RNA for rats that were exposed and not exposed to drugs. See page 4. Print on card stock. Use a cotton swab to apply small spots of a 1% solution of phenolphthalein (Wards Natural Science, catalog # 951 V 1504) to the gene spots on the microarrays (NOTE: The pink circles below show you where to apply the spots of phenolphthalein solution):

Use for RNA from a rat that was NOT exposed to drugs



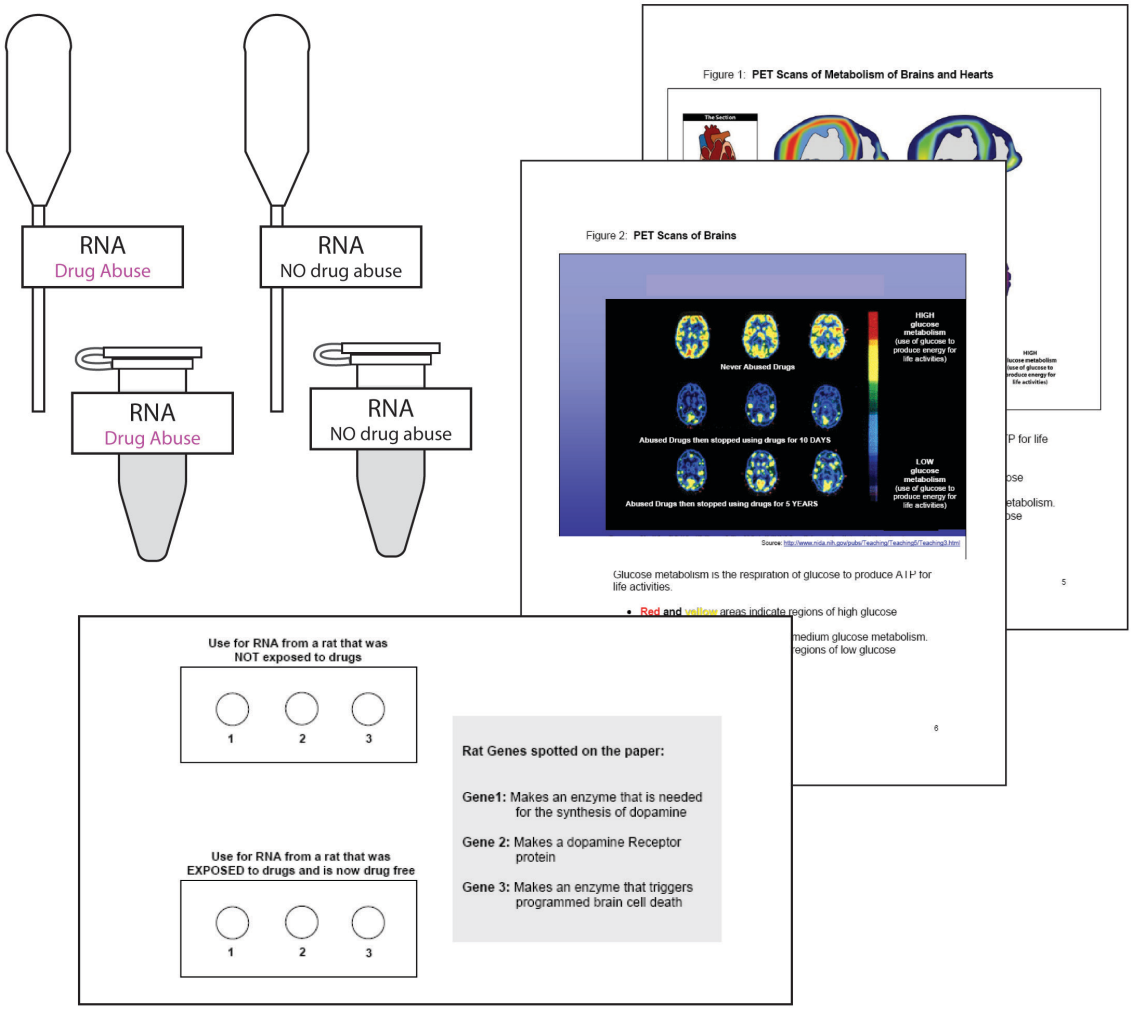
Use for RNA from a rat that was EXPOSED to drugs and is now drug free



This project was generously funded by Science Education Drug Abuse Partnership Award R25DA021697 from the National Institute on Drug Abuse. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute on Drug Abuse or the National Institutes of Health.

Copyright © 2010, University of Rochester
May be copied for classroom use

Quick Guide:



Copyright © 2010, University of Rochester
May be copied for classroom use

Suggested Class Procedure:

1. Explain to students that this activity is a simulation. NO real drugs are used in this activity.

2. Distribute copies of the student handout entitled "**Long-term Effects of Drug Addiction**" and **Figures 1 and 2 PET Scans** to each student.

3. Read the information in the Part 1 box aloud to the class. Students should complete the questions in Part 1 and then share their answers.

4. Read the information in the first box in Part 2 aloud to the class and ask students to complete question 1.

5. Read the information in the first box in Part 2 aloud to the class and ask students to complete question 1.
   - If the concept of gene expression has not been introduced in prior instruction, consider discussing the information with your students before they begin the hands-on activity. Refer to the information and illustration on page 3.
   - If the concept of RNA binding to complementary DNA has not been introduced in prior instruction, consider discussing the information with your students before they begin the hands-on activity. Refer to the information and illustration on page 5.

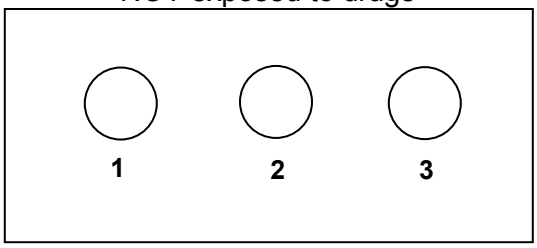
6. *Note: Knowledge of DNA and RNA and genes is helpful but not essential for Part 2. If students have not had prior instruction in molecular genetics, you may need to provide additional support as students work on Part 2.*

7. Distribute safety goggles and kits of lab materials to teams of students. Ask students to complete Part 2. Encourage the students to refer to the information on pages 4-5. when they are answering questions in the lab instructions.

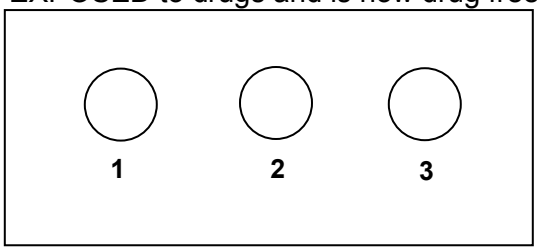
8. If time permits, have students share and discuss their answers to the questions in Part 1 and Part 2. Possible additional questions for discussion in class might include:
   - Why do scientists use rats, rather than humans, for these experiments?
   - Does the information from these rat experiments also apply to drug addiction in humans?

Copyright © 2010, University of Rochester
May be copied for classroom use

Use for RNA from a rat that was NOT exposed to drugs



Use for RNA from a rat that was EXPOSED to drugs and is now drug free



Rat Genes spotted on the paper:

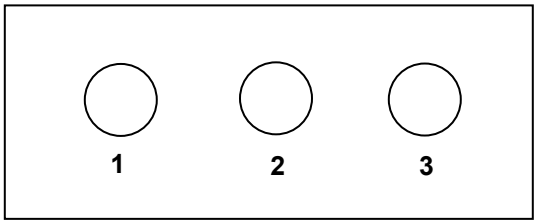
Gene1: Makes an enzyme that is needed for the synthesis of dopamine

Gene 2: Makes a dopamine Receptor protein

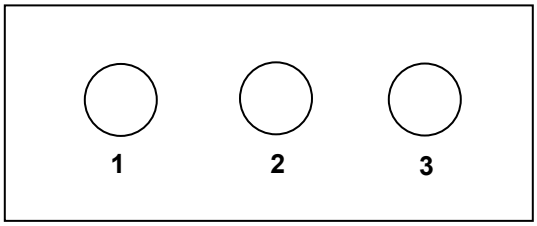
Gene 3: Makes an enzyme that triggers programmed brain cell death

---

Use for RNA from a rat that was NOT exposed to drugs



Use for RNA from a rat that was EXPOSED to drugs and is now drug free



Rat Genes spotted on the paper:

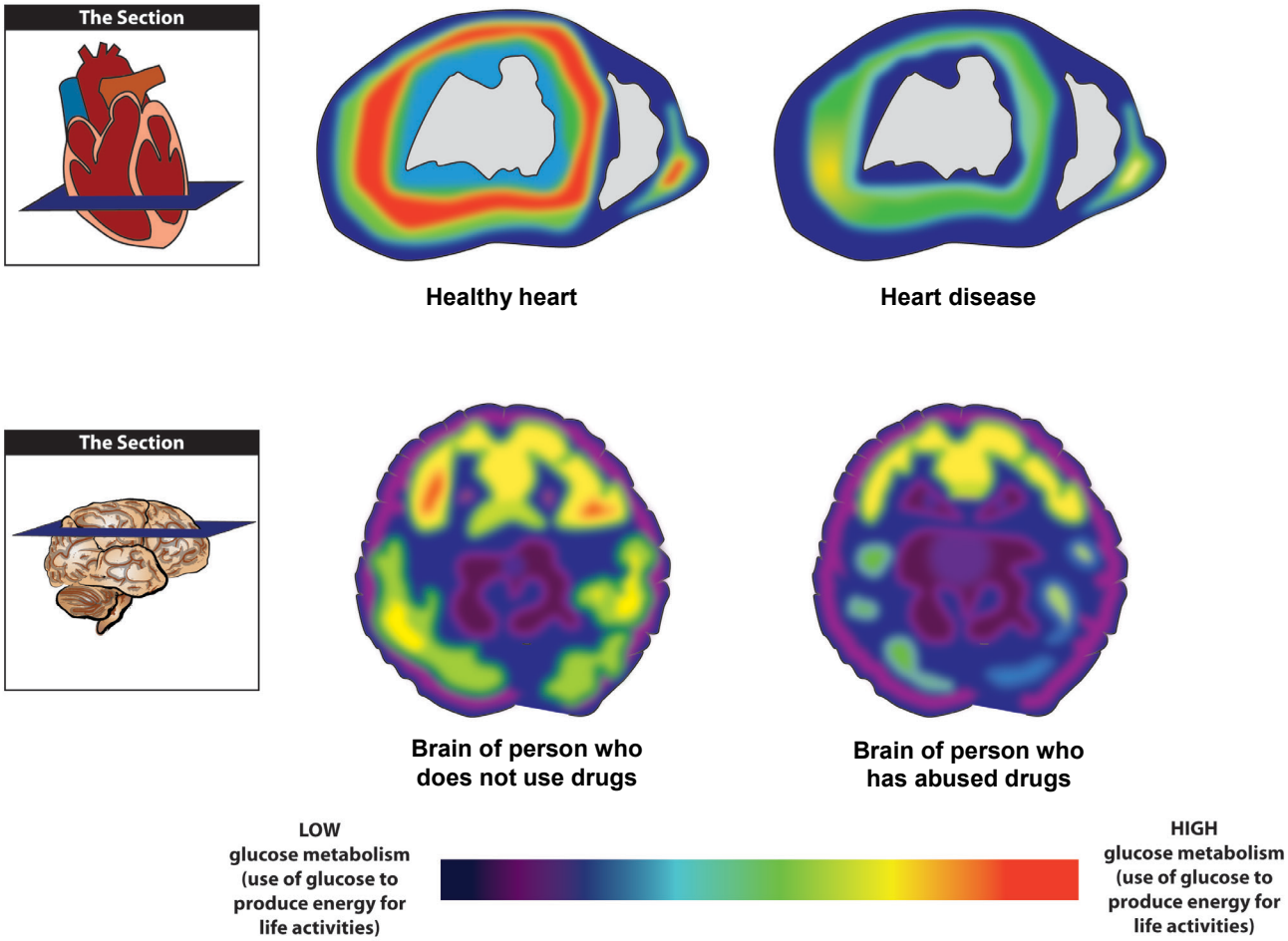
Gene1: Makes an enzyme that is needed for the synthesis of dopamine

Gene 2: Makes a dopamine Receptor protein

Gene 3: Makes an enzyme that triggers programmed brain cell death

Copyright © 2010, University of Rochester
May be copied for classroom use

Figure 1: **PET Scans of Metabolism of Brains and Hearts**

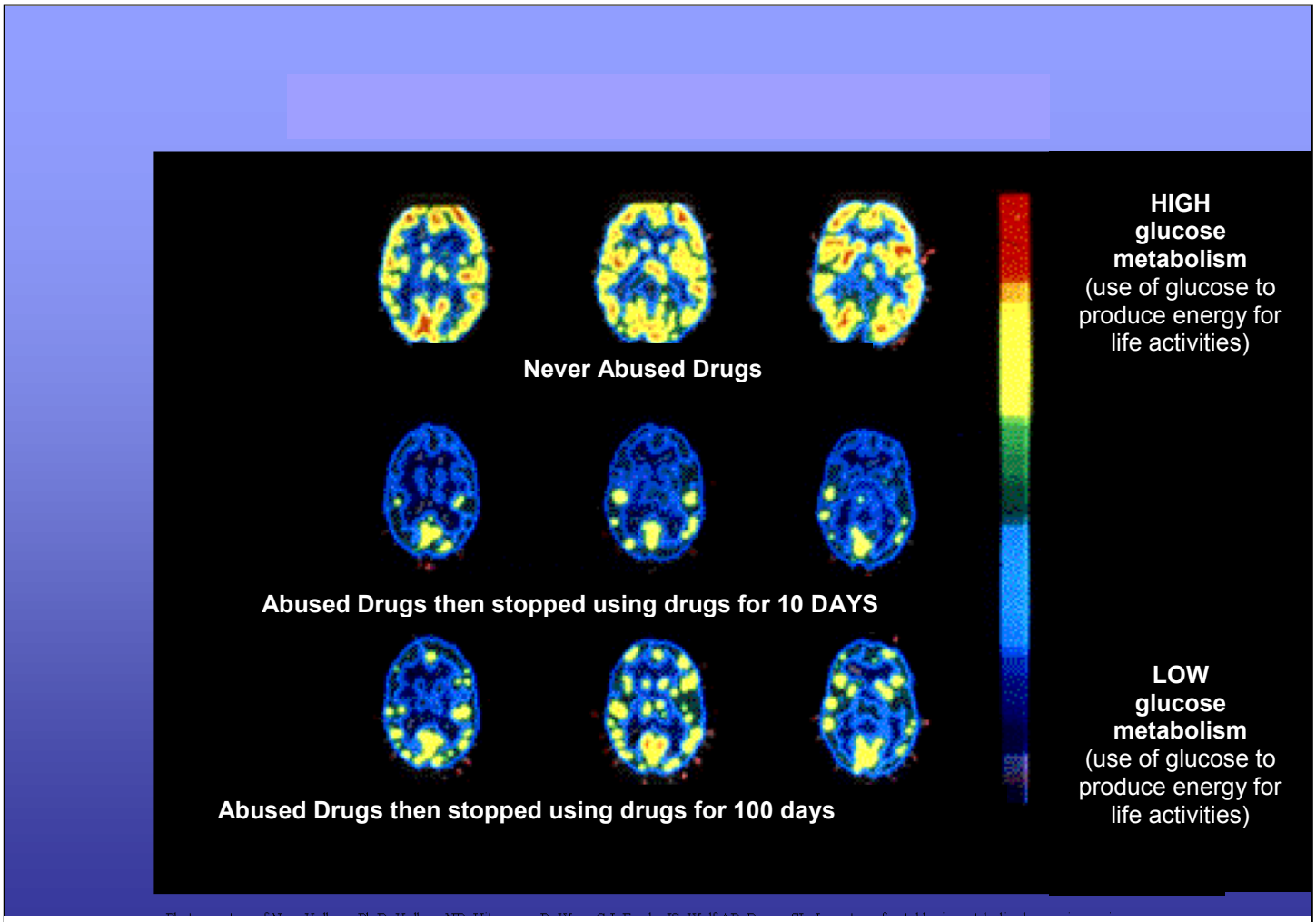


Glucose metabolism is the respiration of glucose to produce ATP for life activities.

- **Red and yellow** areas indicate regions of high glucose metabolism.
- **Green** areas indicate regions of medium glucose metabolism.
- **Blue and purple** areas indicate regions of low glucose metabolism.

Copyright © 2010, University of Rochester
May be copied for classroom use

Figure 2: **PET Scans of Brains**



Source: modified from http://www.nida.nih.gov/pubs/Teaching/Teaching5/Teaching3.html

Glucose metabolism is the respiration of glucose to produce ATP for life activities.

- **Red** and **yellow** areas indicate regions of high glucose metabolism.
- **Green** areas indicate regions of medium glucose metabolism.
- **Blue** and **purple** areas indicate regions of low glucose metabolism.

Copyright © 2010, University of Rochester
May be copied for classroom use

Activity 4
Long-Term Effects of Drug Addiction

Part 1: Addiction is a chronic disease

Drug addiction is considered a chronic brain disease because drugs cause long-lasting changes in brain structure and function. Addiction is similar to other chronic (long lasting) diseases, such as heart disease. Both disrupt the normal, healthy functioning of an organ. Both drug addiction and heart disease may be prevented or treated but they cannot be cured. In most cases, chronic diseases cause long-term changes in body functions and will require a lifetime of regular treatment.

A positron emission tomography (PET) scan is a medical test that helps doctors identify abnormal from normal functioning organs and tissues. A PET scan can measure such vital functions as glucose metabolism - the use of sugar to produce energy for life activities. This information can help doctors determine whether organs are healthy or diseased.

2. Both drug addiction and heart disease are "chronic diseases." What is meant by the term "chronic disease?"

   A chronic disease is one that can be controlled, but not cured. In most cases, a chronic disease cause long-term changes in body functions and will require a lifetime of regular treatment.

3. The top half of Figure 1 shows PET scans for the heart of a healthy person (on the left) and for a person with heart disease (on the right). Refer to the color scale for glucose metabolism shown on the bottom of Figure 1. Compare the metabolism of a healthy heart with the metabolism of a diseased heart.

   The healthy heart has more red and yellow active regions. The metabolism in healthy hearts is higher than the metabolism in the diseased hearts.

In a PET scan:

- **Red and yellow** indicate **more active** regions with high metabolism (high use of food and oxygen to produce ATP needed for life activities).
- **Blue and purple** indicate less active regions with low metabolism (low use of food and oxygen to produce ATP needed for life activities).

Copyright © 2010, University of Rochester
May be copied for classroom use

4. The bottom half of Figure 1 shows PET scans for the brain of a person who does not use drugs and for a person who has abused drugs. Compare the glucose metabolism levels in the brains of the person who did not use drugs and the person who abused drugs.

   The metabolism in brain of a drug user is higher than the metabolism in a person who abused drugs.

5. Explain three ways in which heart disease and drug addiction are similar.

   Both heart disease and drug addiction:
   - ***Disrupt normal, healthy functioning of organs***
   - ***Have serious harmful consequences if left untreated***
   - ***Are preventable***
   - ***Are treatable***
   - ***Decrease organ metabolism***

Part 2: Drug abuse causes long-term changes in brain function

Scientists would like to know whether the brain can recover from drug addiction. They can use PET scan studies and gene studies to determine whether the brain returns to normal when an individual stops abusing drugs.

A. PET Scan Studies

Scientists can use PET scans to determine if drug addiction results in long-term changes to the brain. Figure 2 shows PET scans from:

- 3 individuals who never abused drugs
- 3 individuals who abused drugs for 6 months and then stopped using drugs for 10 days
- 3 individuals who abused drugs for 6 months and then stopped using drugs for 100 days

1. Based on the information in the brain PET scan photos, what conclusions can you draw?

   Drug abusers showed some improvement in brain function after 10 days, but their brains were not completely back to normal after 100 days.

Copyright © 2010, University of Rochester
May be copied for classroom use

B. Gene Expression Studies

Cells contain thousands of different genes. Not all of these genes are active (turned on) at any one time. Some genes are **expressed (turned on)** and others are **silenced (turned off).** Environmental factors, such as drugs, can influence which genes are expressed or silenced.

Scientists suspect that the long-lasting changes in brain function associated with drug abuse may be due to changes in **gene expression** in brain cells. If scientists can identify which genes are affected by long-term drug abuse, they may be able to use this information to develop treatments that could be used to restore normal brain functions.

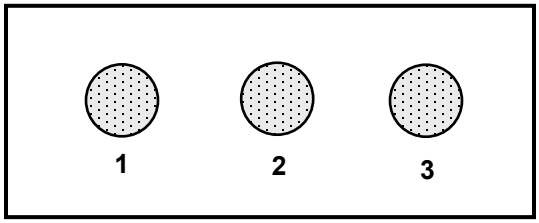
2. Scientists identified **three genes that they hypothesized might be responsible for the long-term brain damage in drug abusers**. They placed spots of DNA from these three genes on a strip of paper.

Rat Genes spotted on the paper:

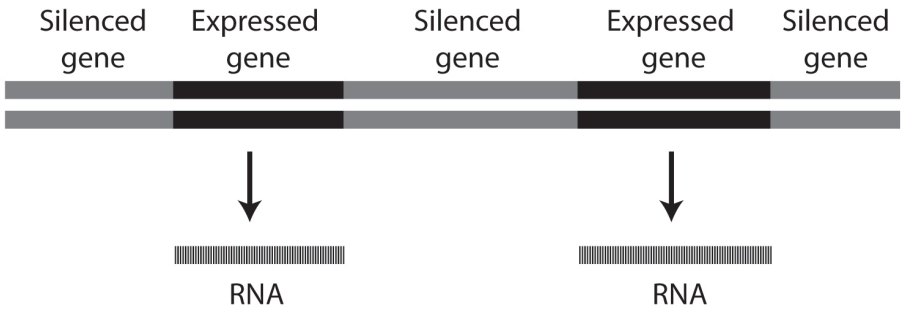
Gene 1: Makes an enzyme that is needed for the synthesis of dopamine

Gene 2: Makes a dopamine Receptor protein

Gene 3: Makes an enzyme that triggers programmed brain cell death



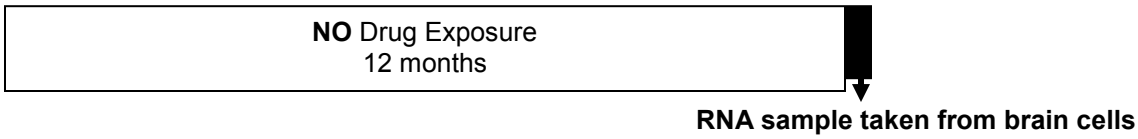
3. The scientists knew that active (expressed genes) produce RNA. Inactive (silenced genes) do not make RNA.



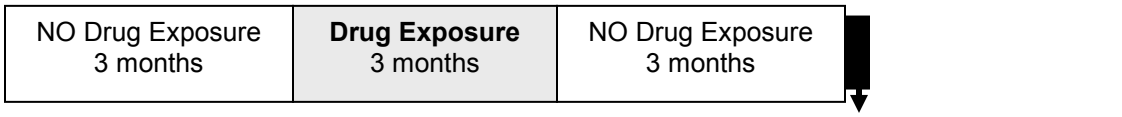
Copyright © 2010, University of Rochester
May be copied for classroom use

4. To compare the gene expression in rats that had been exposed to drugs with rats that had not been exposed to drugs, scientists isolated **RNA** samples from the brains of two types of rats.

   - Rats that were never exposed to drugs:



   - Rats that were exposed to drugs for 3 months and have been drug free for 3 months:



5. The RNA molecules in the samples from both types of rats were then labeled with a pink label.
   - If a gene is **expressed,** the RNA will stick to the corresponding spot on the paper causing a pink color.
   - If a gene is **silenced**, the RNA will not stick to the corresponding spots on the paper and the spot will remain white.

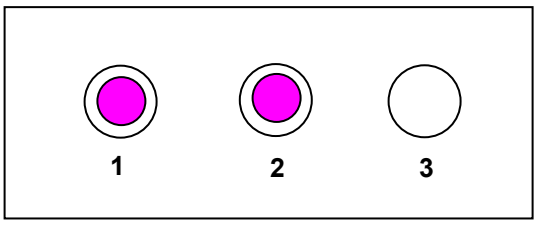
6. What color would a gene spot be if that gene in a brain cell is being expressed (turned on)?

   The spot will be pink.

7. Obtain a tube containing RNA from the brain cells of a rat that was **NOT exposed to drugs**.

8. Use the paper that is labeled "Use for RNA from Rat that was NOT exposed to drugs". Place one drop of this RNA onto each of the circles (DNA spots) on the paper. Record your observations in the diagram below.

Use for RNA from a rat that was NOT exposed to drugs



9. List the numbers of the genes that are **expressed** in the brain cells of a rat that was NOT exposed to drugs.

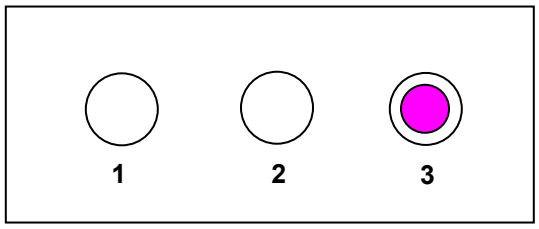
   Genes 1 and 2

Copyright © 2010, University of Rochester
May be copied for classroom use

10. Obtain a tube containing RNA from the brain cells of a rat that was **EXPOSED to drugs and then was drug free**. This rat was exposed to drugs in the past, but has been drug-free for 3 months.

11. Use the paper labeled "Use for RNA from Rat that was EXPOSED to drugs". Place one drop of this RNA onto each of the circles (DNA spots) on the paper. Record your observations in the diagram below.

Use for RNA from a rat that was EXPOSED to drugs and is now drug free



12. List the number of the gene that is expressed **only in rats that were exposed** to drugs. Also describe the function of this gene.

    Gene 3: Enzyme involved in programmed cell death

Rat Genes spotted on the paper and their functions:

Gene1: Makes an enzyme that is needed for the synthesis of dopamine

Gene 2: Makes a dopamine Receptor protein

Gene 3: Makes an enzyme that triggers programmed brain cell death

13. How might expression of this gene affect the functioning of rat brain cells?

    Expression of this gene could lead to increased brain cell death.

14. List the numbers and the functions of the genes that are **silenced only in rats that were exposed** to drugs.

    1 Enzyme needed for synthesis of dopamine

    2 Receptor for dopamine

15. How might silencing of these genes affect the functioning of rat brain cells?

    The brain cells would not make normal amounts of dopamine or dopamine receptors. This would interfere with the neuron's ability to communicate with other neurons.

Copyright © 2010, University of Rochester
May be copied for classroom use

16. Do the results of your microarray experiments support the conclusion that drug abuse causes long term changes in brain cells? Explain why or why not.

Yes, because the rats exposed to drugs expressed different genes. The changes in the genes could lead to decreased ability to respond to rewards and increased brain cell death.

17. Scientists hope to use information from this type of research to develop ways of preventing or treating brain damage that results from drug abuse and addiction. To do this they might try to identify drugs that turn off or turn on the expression of specific genes.

- What genes would they want to turn **on** to treat brain damage that results from drug abuse and addiction?

Genes 1 and 2

- What gene would they want to turn **off** to treat brain damage that results from drug abuse and addiction?

Gene 3

Copyright © 2010, University of Rochester
May be copied for classroom use