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| **Title** | Molecular Biology – Will Research Using Mice Help Find a Cure for Obesity? |
| **Introduction** | The 21st Century Research lab depends on the needs of society to drive and fund their science endeavors and society depends on the technology and research to fulfill their needs. It is a dependency relationship that has gone on for many years. One of the latest trends in research is investigating hot topic, big money, human conditions like obesity and cancer. Biotechnology has responded through molecular biology and using genetically engineered knockout mice. The human condition of obesity stems from the body’s ability to metabolize and store nutrients in food. The molecular biologist is looking for a way to inhibit fat storage through gene therapy. Don’t grab that fry yet- it is still in early laboratory stages.This lesson explores how scientists are using molecular research to find a remedy for weight gain in humans. Students will exercise to burn calories, discuss the relationship between societies on biotechnology, and then finally read a scientific article on the Wnt10b protein transgenic mouse.As part of the multi-unit lesson, this activity relates the mice created in lesson 1 to the research findings on obesity and genetic modifications. **Lesson EQ**: How is biotechnology used to affect living organism? |
| **Curriculum Alignment** | North Carolina Science Essential Standards    8th Grade Science  8. L. 2 Understand how biotechnology is used to affect living organism.  8 L.2.1 Summarize aspects of biotechnology including:  Specific genetic information available  Careers  7th Grade Science  7. L. 1. Understand the processes, structures and functions of living organisms that enable them to survive, reproduce and carry out the basic functions of life.   * Compare structures and functions of plant and animal cells, including major organelles   7. L. 2 Understand the relationship of the mechanisms of cellular reproduction, patterns of inheritance and external factors to potential variation among offspring.  High School Biology  Essential Standard Clarifying Objectives  Bio.1.1 Understand the relationship between the structures and functions of cells and their  Organelles.  Bio.1.1.3 Explain how instructions in DNA lead to cell differentiation and result in cells specialized to perform specific functions in multicellular organisms.  Bio.3.1 Explain how traits are determined by the structure and function of DNA.  Bio.3.1.1 Explain the double-stranded, complementary nature of DNA as related to its function in the cell.  Bio.3.3 Understand the application of DNA technology.  Bio.3.3.1 Interpret how DNA is used for comparison and identification of organisms.  Bio.3.3.2 Summarize how transgenic organisms are engineered to benefit society. North Carolina Career and Technical Essential Educational StandardsStrands of this topic are discussed in the following High School Courses:Exploring Biotechnology – Course Number 6828Biotechnology and Agri-science Research I - Course Number: 6871Biomedical Technology- Course Number: 7200  * Exploring Biotechnology in Health Science- Course Number: 7205 * PLTW Biomedical Innovations- Course Number: 7273 * PLTW Principles of Biomedical Sciences- Course Number: 7270 |
| **Learning Outcomes** | Student will demonstrate understanding of the driving forces of biotechnology to research and society through class discussion.Using their mice models – the students will apply knowledge of knockout genes to actual research in biotechnology by creating scenarios using WNtb10 proteins.Students will demonstrate their knowledge of the pros (treatments)/ and cons (side effects) in biomedical research through creating a graphic organizer.Through reading a scientific article, the students will use context clues to understand technical vocabulary. |
| **Time Required and Location** | One, 50-minute class period |
| **Materials Needed** | Engage Activity:Stopwatch or clock Balance ScoopVarious Carbs/ Lipids/ proteins and Salt to measure amounts- sugar, butter, protein powder and saltExplanation Activity:[Lesson](#Lesson) 3 Student Handout: Scientific ReadingPoster paper |
| **Participant Prior Knowledge** | The students will need to have access to their mice, or the mice information from Lesson 1 for the extension activity. |
| **Facilitator Preparations** | The scientific article used in this lesson should be pre-read and technical vocabulary research for understanding.The chart should be written on the board for the students to copy. |
| **Activities** | Engage:1. The teacher will set the stage for the discussion of obesity by getting the students involved in exercise.Select a volunteer(s) to start jogging as you ask these questions: The student should jog approx. 5 minutes to burn 1 bite of a cheeseburger. (To burn 300 calories the student would need to job 30 minutes. To include more people – have 30 people jog 10 minutes = 1 cheeseburger)2. Teacher says:How many calories are in a fast food cheeseburger? (300)How many grams of fat? (12g)How many grams of carbohydrates? (33g)How many grams of protein? (15g)How many milligrams of salt? (750 mg)3. If a balance is available – ask students to measure out the amounts using butter (fat), carbohydrates (sugar), protein (protein powder), and salt. This will extend their knowledge and give them a real world connection to the amounts and figures listed on nutrition charts for foods.Exploration:4. The teacher should ask the class and discuss the following:“What if you never had to exercise again to burn off the calories of a cheeseburger, or fries, or any other food that was high in calories and fat?”“If a biomedical facility could give you medicine, or change your body so you would never gain weight what would you take advantage of their offer?If you answered “yes,” then at what cost? How much would you pay?What about side effects (other things that could happen – like thicker skin or loss of hair) would you still jump at the chance to be thin forever?Why do scientist want to find a quick fix for what makes people gain weight. (Researchers and Society are in a dependency relationship5.) The teacher should draw a Biotechnology Triangle on the board that represents the connection between Science/Biotechnology/ and SocietyScience   SocietyBiotechnology  The teacher says:   * Society demands science to find cures and treatments for human problems and conditions. They also depend on biotechnology to make their life easier and better. * Science needs funding and support from society and biotechnology to help in their research. * Biotechnology is driven by society and invented and used by scientists.   **Explanation**  To explore one of the most society driven topics of research, obesity, the students will read an article about creating transgenic mice that do has the a knockout gene for fat production.  **Scientific Literature- Title: The mouse diet: More high-fat chow, but less body fat**  Students can read the article silently, or it can be read aloud by the teacher.  6. Using a graphic organizer- the students willdistinguish among facts, reasoned judgment  based on research findings, and speculation in a text.    In the large square – the students should write the topic of the scientific article  In the smaller squares – the words: FACT (Left Square), Judgment based on research (Middle Square), Speculation in text (right square)  Teacher note – Definitions of terms  Fact – science has determined that the results cannot be questioned   * Reasoned judgment based on research findings – The scientific findings suggest a link or correlation between cause and effect * Speculation – the research doesn’t support nor refute the scientist’s claim or idea. (It is just a hunch or educated guess on the part of the researcher.)   7. Using the article the students can work collaboratively to think/pair/share- or work independently to locate a fact given in the article, or a reasonable judgment based on research, or finally just speculation by the researcher. They write their answers under the appropriate boxes.  **Extension –**  8. The teacher can use the mice created from Lesson 1 to relate the scientific finding and create a scenario. For example: Those students with black mice – have a gene sequence of DNA called WNt10b which is a protein that represses fat cell growth in tissue.Those students with white/grey mice – have an artificial sequence of 2 genes, WNt10b and another gene called the FABP4 promoter. The promoter increases the effect of WNt10b by 50 %. (It makes cells repress even more fat tissue growth)The students with brown mice – have been given the ob gene. The ob gene strand stimulates fat cell growth.The students with white mice – digest the food normally. 9. Based on the information presented in the article; “The mouse diet: More high-fat chow, but less body fat.” Have the students hypothesize what would happen over an extended period of time to their mouse and the other mice in the experiment if they are givenA high fat dietA low fat dietJust the chow mix daily10. Using poster paper, students can record their ideas in a chart and post on the wall for a Gallery Walk. Students should be allowed to present their chart to the class and defend their hypothesis.  |  |  |  |  |  | | --- | --- | --- | --- | --- | | Mouse Type | High Fat diet | Low fat diet | Chow only diet | Appearance | | Black |  |  |  |  | | White/Gray |  |  |  |  | | Brown |  |  |  |  | | White (control) |  |  |  |  | |
| **Assessment** | Student understanding of the information presented in this lesson will be evaluated on their ability to add at least 2 facts, 2 judgments, and 2 speculations from the article on the graphic organizer.Using the article information, students will be able to complete a chart describing the physiological effect of the new DNA on mouse development and fat processing.Answers may vary but may include:Large Square Topic: The Effect of Wnt10b on Mouse Weight Gain Fact (Left Square) - The transgenic mice in this study have underdeveloped mammary glands, an inability to generate body heat and skin that's twice as thick as normal.    Judgment based on research (Middle Square) - The Wnt10b protein had significant impact on mice health. The results of research suggest the Wnt10b gene causes mice to stay lean and healthy when fed high calorie fatty foods...  Speculation in text (Right square)- Humans may one day benefit from this research never becoming fat after gene therapy using Wnt10b. Thick skin may be the only noticeable side-effect of this DNA change.  Assessment Rubric for the Graphic Organizer:   |  |  |  |  | | --- | --- | --- | --- | | 3 | 2 | 1 | 0 | | The student’s chart has each section complete and the answers are 100% correct, concise and critical interpretations of the topic headings. Two examples of each type listed. | The student’s chart is 70% complete and the answers provided are correct interpretations of the topic headings. | The student’s chart is partially complete (50%). One or more of the answer groups are inappropriate interpretations of the topic heading. | Students did not complete a chart. | |
| **Critical Vocabulary** | Metabolism- the sum total of the chemical processes that occur in living organisms, resulting in growth, production of energy, elimination of waste material, etc.  Metabolic disorder- a disorder or defect of metabolism  adipose tissue- loose connective tissue in which fat cells accumulate.  Adipocytes – fat cells  Repress - to keep under control, check, or suppress  therapeutic – of or pertaining to treating or curing a disease |
| **Modifications** | A student that is physically unable to run in place for up to 5 minutes should not be required to participate in the Engage activity.  The scientific journal article has technical vocabulary that will be difficult for English as a Second Language Learners and Learning Disabled Students. In classes where these students may be present, the teachers should read the entire article aloud to the class.  If time prohibits a Gallery Walk for displaying and discussing student charts – post them after school for a quick Gallery Walk lesson review on the next day. |
| **Alternative Assessments** | A student that does not participate in the engage physical activity can be encouraged to help weigh the ingredients to show amounts per serving. |
| **References** | Vocabulary Definitions-  www.dictionary.com  Nutrition Obesity Center-  <http://www.sph.unc.edu/cnrc/>  Graphic Organizer Templates-  <http://www.bing.com/images/search?q=Graphic+Organizer+Template&view=detail&id=0B576F1BCC96D593BD64BD2DB3D86A40E0B408D6&first=0&FORM=IDFRIR>  Michigan University Scientific Article  www.ur.umich.edu/0304/July06\_04/02.shtml  MacDougald Research Lab information-  http://macdougaldlab.physiology.med.umich.edu/ |
| **Supplemental Information** | There are many medical facilities in North Carolina that research and treat the condition of obesity. Most concentrate on nutrition and public health. For example, UNC- Chapel Hill’s Nutrition Obesity Research Center has a wealth of information on hot topics like low-fat foods, and childhood obesity. |
| **Comments** | The Scientific Article appeared in the University of Michigan Newsletter called: The University Record Online. It was written by Sally Pobojewski on staff for medical school communications. The actual investigator in the project was Ormond MacDougald, associate professor of molecular and integrative physiology in the Medical School. He was assisted by Kenneth Longo a research fellow in physiology. Their assistants were: Wendy Wright, research associates; Sona Kang, graduate student; Isabelle Gerin and Shian-Huey Chiang, post-doctoral fellows; Dr. Peter Lucas, lecturer in pathology; and Mark Opp, associate professor of anesthesiology and of molecular and integrative physiology.  In a biomedical lab, numerous people support the Primary Investigator, who in this case was MacDougald. After further research into the work presented by this researcher, I found he was invited to present his findings on Mice and Fat at the 2006 Nobel Symposium in Sweden.  The findings were also published in numerous other journals-  Discover Magazine (<http://discovermagazine.com/2004/oct/all-you-can-eat-gene>)  Innovations Report (http://www.innovations-report.com/html/reports/medicine\_health/report-30714.html)  Further information can be found concerning the research conducted at the MacDougald Research Lab from the website: http://macdougaldlab.physiology.med.umich.edu/links.html |
| **Author Info** | This lesson was written by Martha Tedrow. She teaches eighth grade at Jefferson Middle School in Winston-Salem, NC. She has been teaching for 28 years, has Bachelors in Education from UNC – Chapel Hill and Masters in Education from Gardner Webb University. In 2004, she became Nationally Board Certified in Science. This curriculum module lesson was designed as part of a Kenan Fellowship and in cooperation with Carol Kent and Dr. Lawrence Rudel, molecular biologists at Wake Forest Baptist Medical Center’s Biotechnology Center. Martha’s mentor for the Fellowship was Robert Sox, a Professional Development Leader with North Carolina’s Department of Public Instruction. |

**Lesson 3: Scientific Article**

**Title: The mouse diet: More high-fat chow, but less body fat**

*By Sally Pobojewski  
Medical School Communications*

Genetically engineered mice created at the Medical School are living every dieter's dream. They eat unlimited amounts of high-fat mouse chow, but have about 50 percent less body fat than normal mice on a low-fat diet.

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| http://www.ur.umich.edu/0304/July06_04/img/040706_mouse.jpg |
| *This experimental mouse from the study has 50 percent less body fat and fewer fat cells than a normal mouse. (Photo by Kenneth Longo, Medical School)* |

And they show no signs of diabetes or other metabolic disorders, which are common in animals with too little fat.

But don't stock up on potato chips and ice cream just yet. The genetically altered mice are leaner than normal mice, but they also have some less-than-desirable characteristics—such as underdeveloped mammary glands, an inability to generate body heat and skin that's twice as thick as normal.

All these changes appear to be caused by a protein called Wnt10b, which is present in artificially high amounts in fat tissue from the experimental mice. Wnt10b is one of a family of 19 related proteins. Wnts (pronounced "wints") regulate the complex changes that take place as an embryo grows. Part of this process is the development of fatty adipose tissue, which contains fat cells called adipocytes.

Ormond MacDougald, associate professor of molecular and integrative physiology in the Medical School, has spent years studying the effects of Wnt10b on the development of adipocytes. In August 2000, MacDougald and his colleagues published a paper in Science, showing that Wnt10b gene activity repressed fat cell development in tissue cultures.

Now, in the first study in living animals, MacDougald and Kenneth Longo, a research fellow in physiology, have demonstrated that Wnt10b has the same effect on fatty tissue in mice.

"High levels of Wnt10b expression produced animals with 50 percent less body fat and fewer fat cells, regardless of whether the mice ate a high-fat or low-fat diet," MacDougald says.

Results of the experiments were posted last month on the Journal of Biological Chemistry's JBC Online Web site.

"To determine the effect of the gene on adipose tissue development, we created an artificial sequence of DNA called a transgene linking Wnt10b to another gene called the FABP4 promoter, which is expressed only in adipose tissue," Longo says. "We injected the transgene DNA into fertilized mouse eggs and bred mice that inherited the new gene to create the animals used in our study. Under the control of the FABP4 promoter, fatty tissue in the transgenic mice contained 50 times the amount of Wnt10b found in adipose tissue from normal mice."

Longo and MacDougald discovered that Wnt10b had a different effect on the two types of fat found in normal mice. White fat is a storage reservoir for excess energy. Brown fat is a specialized form of adipose tissue, found in small mammals and human newborns, which generates heat to keep the animal warm. While the transgenic mice in the U-M study had half as much white fat as normal mice, they had virtually no brown fat. This made it impossible for them to maintain their core body temperature, leaving them vulnerable to cold.

For reasons U-M scientists don't understand, the transgenic mice had skin that was twice as thick as and much heavier than normal mice. Another puzzling and unexpected finding from the study was that the transgenic mice consumed slightly less oxygen.

But perhaps the most surprising thing about the transgenic mice was their general state of robust good health.

"When we started making these animals, we thought they would have reduced amounts of fat, and thus suffer from metabolic complications, including diabetes," Longo says.

"In fact, the insulin sensitivity and glucose tolerance of transgenic mice on a high-fat diet was better than that of normal mice on a low-fat diet. We don't know why, but additional research should provide some answers," MacDougald says.

But don't look for Wnt10b diet pills to be on the market any time soon, caution Longo and MacDougald.

"Pharmaceutical companies are interested in the potential therapeutic role of Wnts genes in decreasing fatty tissue, but finding the right drug to selectively target this pathway without complications will be a considerable challenge," MacDougald says.

"We've seen the potent effect of Wnt10b on fat in mice, but we don't know if it would work the same way in humans," Longo adds. "And, if the results we see in the skin of the transgenic mice are any indication, I'd say we have to tread carefully. I think we'd all like to be thicker-skinned, but only in the figurative sense."

The research was funded by the National Institutes of Health, the U-M Center for Integrative Genomics, and the U-M Center for Organogenesis, the Diabetes Research and Training Center, and the American Diabetes Association.

The experimental mice used in the study were produced in U-M's Transgenic Animal Model Core facility. The University has filed for patent protection on the Wnt10b transgenic mouse.

Study collaborators from U-M included Wendy Wright, research associate; Sona Kang, graduate student; Isabelle Gerin and Shian-Huey Chiang, post-doctoral fellows; Dr. Peter Lucas, lecturer in pathology; and Mark Opp, associate professor of anesthesiology and of molecular and integrative physiology.