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Stop that oxidation! What fruit flies teach us about human health Featured scientist: Biz Turnell from Technische Universität Dresden

Research Background:

Have you ever eaten an apple and noticed that, after a while, the core turns brown? This color change happens because of **oxidation** – a chemical reaction between the oxygen in the air and the inside of the apple. The same thing is happening inside our own bodies all the time.

Each of our cells is home to mitochondria, tiny factories whose job is to turn the food we eat into the energy we need to live. But mitochondria also make molecules called **reactive oxygen species**, or **ROS**. As the name suggests, these molecules contain oxygen and tend to react with the things around them. Like the oxygen in the air reacting with the apple core and turning it brown, ROS react with different parts of the cell, causing **oxidative**



Biz with one of their favorite scientists in training.

damage. Everything in the cell, including our DNA, can be damaged by ROS molecules. Too much damage contributes to diseases including cancer, heart disease, diabetes, and Parkinson's.

Bodies can prevent oxidative damage in two ways. First, they can use antioxidants. **Antioxidants** work by reacting with ROS to stop them from harming cells. Some antioxidants come from the food we eat, while others are made inside the body. If a body doesn't have enough antioxidants, it can get sick. One example is a genetic mutation called **DJ-1**. It stops the body from producing antioxidant molecules. Many people with Parkinson's disease, a neurological illness, have this DJ-1 mutation.

Some living things have evolved a second way to stop oxidative damage: their mitochondria actually make fewer ROS! These species have a special protein called **alternative oxidase**, or **AOX**. It works by shortening the pathway that mitochondria use to turn food into energy. A shorter pathway means fewer ROS are made. Scientists have been able to take the AOX gene and move it into other species.

Biz, a scientist studying oxidative damage, wanted to study the effects of the DJ-1 mutation and the AOX gene. To do their research, Biz uses fruit flies. Fruit flies are useful because they are easy to work with and scientists can control the types of mutations and genes they have in the lab. Some of these mutations are the same as

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those found in humans, so scientists can use them to study human disease. In one study, scientists were able to take the AOX gene and put it into the fruit fly. Fruit flies can also have the DJ-1 mutation that stops antioxidants from being made. Biz used these genetic tools to work with flies that have less oxidative damage (AOX mutants), more oxidative damage (DJ-1 mutants), or normal levels (controls).



Left: Biz's colleague hard at work in the fly lab. Right: Laboratory fruit flies in a vial. Photo Credits: Conni Wetzker.

Biz was interested in how AOX and DJ-1 affect reproductive cells – sperm and eggs. Oxidative damage is even more dangerous for reproductive cells than for other cells. Whereas most cells can iust self-destruct or stop replicating when they build up too much damage. sperm and eggs have to stay healthy up until the moment of fertilization. This wait can last a long time. In many species, females store the male's

sperm inside their own bodies for days, months, or even years after mating! In addition to making their own ROS and antioxidants, sperm and egg cells stored inside the female can be damaged or protected by ROS and antioxidants made by the female's reproductive tract. Either way, damage to reproductive cells is very important because it can be passed on to future generations or can cause the offspring to die.

Biz wanted to test whether the level of oxidative damage in eggs and stored sperm would influence how many offspring a female had. If cells with oxidative damage do not produce healthy offspring, then fruit flies with less damage should have more offspring. Biz also expected that fruit flies with more damage should have fewer offspring. To test these ideas, Biz mated normal male fruit flies to three groups of females: females with the AOX gene, females with the DJ-1 mutation, and normal ("control") females. Aside from having the AOX or DJ-1 gene, the females in all treatments were genetically the same. The males used in the experiment were also genetically identical. After the males and females mated, Biz counted the number of surviving offspring from each group.

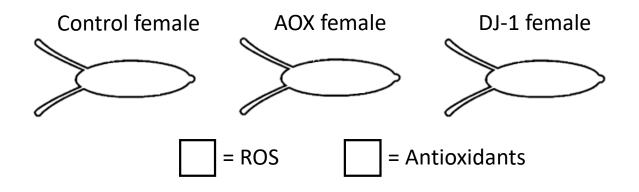
<u>Scientific Question</u>: How does the level of antioxidants or ROS in reproductive cells affect female fruit flies' reproductive success?

<u>What is the hypothesis?</u> Find the hypothesis in the Research Background and underline it. A hypothesis is a proposed explanation for an observation, which can then be tested with experimentation or other types of studies.

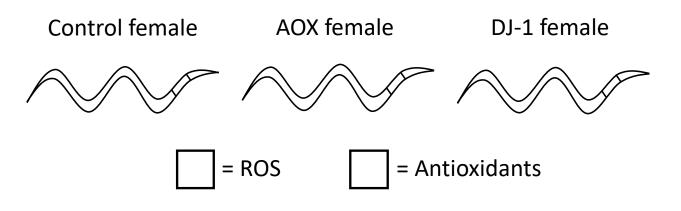
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Draw Your Predictions:

1. For each egg cell below, draw your predictions for the amount of ROS and antioxidants the cell is exposed to. Use one color for ROS (leading to increased oxidative damage) and another for antioxidants. Fill in the legend to show which colors you used.

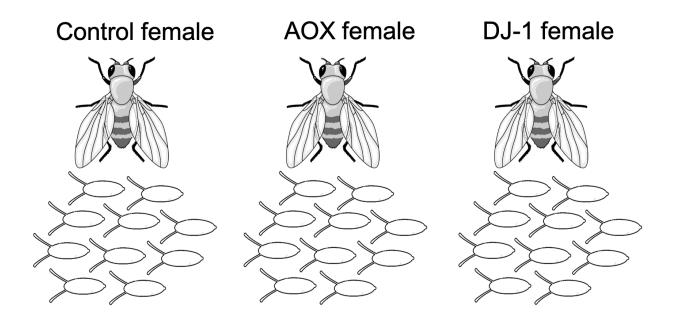


2. For each sperm cell <u>stored inside the female</u>, draw your predictions for the amount of ROS and antioxidants the cell is exposed to. Use one color for ROS and another for antioxidants. Remember that even though all the males were genetically identical and produced a normal amount of ROS and antioxidants, their sperm can still be affected by both ROS and antioxidants from nearby cells in the female's body. Fill in the legend to show which colors you used.



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3. For the egg clutches from each of the three female flies, put a check mark on the eggs you predict will grow into adult flies and an X on the eggs you predict are damaged from ROS.



Scientific Data:

Number of adult offspring			
Control	AOX	Mutation DJ-1	
88	161	62	
85	194	73	
76	121	21	
55	146	21	
87	162	45	
91	114	38	
70	140	21	
126	66	4	
90	121	89	
63	56	11	
Control	AOX	Mutation DJ-1	

Use the data below to answer the scientific question:

	Control	AOX	Mutation DJ-1
Average number			
of adult offspring			

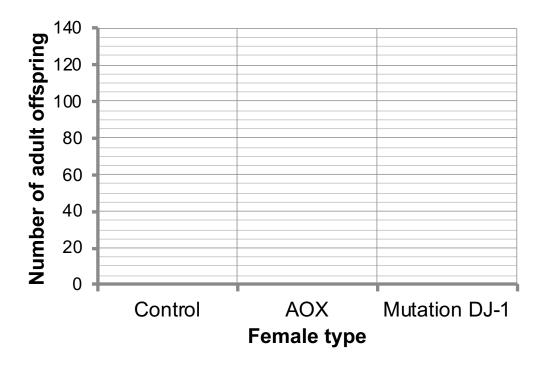
Which data will you graph to answer the question?

Independent variable:

Dependent variable:

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<u>Draw your graph below</u>: Identify any changes, trends, or differences you see in your graph. Draw arrows pointing out what you see, and write one sentence describing what you see next to each arrow.



Interpret the data:

Make a claim that answers the scientific question.

What evidence was used to write your claim? Reference specific parts of the table or graph.

Explain your reasoning and why the evidence supports your claim. Connect the data back to what you learned about how antioxidants and ROS affect oxidative damage.

Did the data support Biz's hypothesis? Use evidence to explain why or why not. If you feel the data was inconclusive, explain why.

<u>Your next steps as a scientist</u>: Science is an ongoing process. What new question do you think should be investigated? What future data should be collected to answer your question?