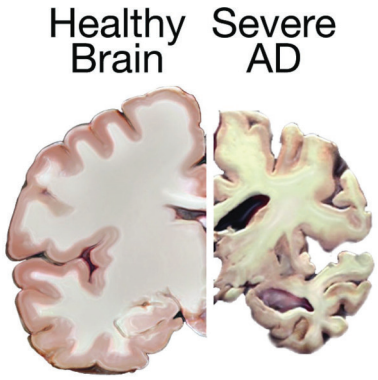
MODEL ORGANISMS

TEACHING THE GENOME GENERATION

SCIENTIFIC BREAKTHROUGH?

The Jackson Laboratory
Leading the search for tomorrow's cures

In this exercise, you will explore Alzheimer's Disease, a devastating neurodegenerative disorder that affects more than 4 million Americans, and assess the validity of a possible therapy that can halt or even reverse symptoms of Alzheimer's.
Model organisms are a great resource for scientists, but not all models are created equal. Was the mouse used in this study a good one? the best one? to represent human Alzheimer's Disease?



Molecular pathologies in Alzheimer's patient's brains lead to the death of neurons. In severe cases, the brain will appear to have shriveled up.

Using Google, Wikipedia and/or OMIM, answer the following questions:

What are the outward symptoms of a patient with Alzheimer's Disease (AD)?

What are the defining characteristics of the brain in Alzheimer's Disease?

Is there a *cure* for AD? Are there any *treatments* available for Alzheimer's patients?

Model organisms, much like model airplanes, are a representation/imitation/example of another (often larger or more complex) thing. In experimental biology, organisms like bacteria, flies and even mice are used as simplified representations of human biology and disease. These organisms can be more easily housed and fed, controlled for genetics and manipulated in experimental situations than humans. While technology is rapidly advancing scientists ability to understand human disease in the human, model organisms are still the preferred vehicle for rapid results. However, some model organisms are better representations of specific human systems or conditions than others. Scientists must choose which organism will be the best model for their research.

THE BREAKTHROUGH

Read the following science news article:
Roberts (2016) 'Flashing light therapy' for Alzheimer's,
BBC News online. www.bbc.com/news/health-38220670

Find the primary paper the news article discusses.

Dr. Tsai in her lab at MIT

What information in the article did you use to find the paper?

What search engine did you use to find the paper?

What terms or phrases are unknown or confusing to you?

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While watching a video www.youtube.com/watch?v=O_p4QWkE2Ls (5 min) or listening to a podcast www.radiolab.org/story/bringing-gamma-back (27 min) about the study, answer the following questions:

What defining characteristics of Alzheimer's Disease was assessed in this study?

What kind of cells in the brain helped to clear the amyloid beta plaques?

What mouse model was used in this study?

In order to apply this breakthrough in mouse models of AD to humans with AD, what parts of the experiment would you want to test further?

What brain region was assessed?
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ASSESSING SCIENTIFIC BREAKTHROUGHS

Let's dive deeper to understand the mouse model that Dr. Tsai used in the experiment.

1. Go to Mouse Genome Informatics, www.informatics.jax.org
2. Do a search for 5XFAD (the mouse used in the Tsai study).
3. Click on the first hit with the complicated long name Tg(APP...).

   Note: This is a transgenic mouse that carries two "humanized" genes, APP and PSEN1. Humanized means that the genes carry human-like mutations, in this case, mutations specifically found in patients with Alzheimer's Disease. These transgenes, genes from one species that are inserted into the genome of another, are specifically expressed in the brain. The transgenic mouse also has App and Psen1 mouse genes that function normally.
4. Scroll down to the Phenotypes and Disease Models tables.
5. Click on a few of the phenotype buttons (colored boxes at the top of each column, ex: cx2, cx4, tg7, etc.)

List some of the phenotypes associated with this mouse model.

Do the phenotypes of this transgenic mouse reflect the symptoms and brain characteristics of a human affected by AD?

Is this mouse a good model for Alzheimer's disease in humans? If not, how could it be better?

Do model organisms need to recreate all features of a human disease to be useful?

Revisit the BBC article about this breakthrough. Was the impact of the Tsai study on future human AD treatments reported to the public appropriately (in the context of the mouse model that was used for the experiment)? Explain your thinking.