

## These Rodents See Red

JUST ONE EXTRA GENE IS ALL MICE NEED TO SEE VIBRANT COLORS.

Some lab mice can see the world in a whole new light, thanks to HHMI investigator Jeremy Nathans and his colleague Gerald H. Jacobs. Their findings provide insight into the remarkable plasticity of mammalian brains, and shed light on a plausible means by which humans may have acquired the ability to see many colors.

Nathans, at Johns Hopkins University School of Medicine; Jacobs, of the University of California, Santa Barbara; and their colleagues introduced the gene for a human red-light-sensing pigment into mice, and showed that the new photopigment functioned correctly, allowing the mice to distinguish colors they previously could not detect.

Most mammals have only two types of photopigments in the color-sensitive cone cells of their retinas. In mice, one pigment detects ultraviolet light, while the other sees yellowish-green wavelengths. Many primates, including humans, have three color-sensing pigments, which gives us our rainbow palette of color vision.

The researchers wondered whether the gene alone would alter sensory perception, or if additional changes in the nervous system would be necessary. Nathans and Jacobs showed that just the addition of the new photopigment endowed the mice with broader color vision. Using electrophysiological tests, the researchers determined that the rodents' retinas responded to red



Colored lights help show that the brains of genetically-altered mice can process information from new photoreceptors in their eyes. Here, a mouse deciding that the third colored panel looks different from the other two is rewarded with a drop of soy milk.

light. Then they subjected the mice to a series of behavioral tests, which confirmed that the mice could indeed see red.

In essence, says Nathans, the brains of the mice completed all the necessary rewiring to make their new color receptors function. He views the findings, published in the March 23, 2007, issue of *Science*, as a lesson on how color vision, and possibly other sensory traits, might have evolved in humans. "Maybe the principal way in which sensory systems evolve is by genetic change at the front end—at the receptor cells," he says, "and the brain is flexible enough to immediately take advantage of those changes." ■ —PAUL MUHLRAD

### IN BRIEF

The study, published May 1, 2007, in *Current Biology*, offers a new model for scientists to study transmission of infectious disease and could help identify therapeutic targets to block the spread of pathogens.

#### KEY ELEMENTS CONTROLLING PRION FORMATION IDENTIFIED

HHMI researcher Susan L. Lindquist at the Whitehead Institute for Biomedical Research and others have identified small regions within a yeast protein that control its conversion to infectious agents known as prions.

Prions are proteins that can fold into self-templating configurations, allowing proteins of the same type to adopt the same configuration. In the prion state, such proteins accumulate into masses known as amyloid, which can cause human disorders such as Creutzfeldt-Jakob disease.

Lindquist's group looked at *Saccharomyces cerevisiae* yeast protein Sup35, which normally regulates the flow of information from DNA into the cellular machinery that produces proteins. When Sup35 converts to a prion state, its activity is reduced, which changes expression of the yeast's DNA and alters biological function.

As described in their May 31, 2007, *Nature* article, the researchers attached Sup35 middle (M) and end (N) segments to a glass slide and exposed them to a solution containing fluorescently labeled copies of Sup35 in its nonprion state. The soluble Sup35 accumulated over a very small set of the peptides, which corresponded to two regions of the M and N segments previously found to be sites of protein-protein contact in assembled fibers. Under electron microscopy, these accumulated proteins showed fibers characteristic of amyloid prions.

Though the underlying process remains unclear, the researchers hypothesize that specific peptides cause the protein to adopt a prion configuration.

#### ANALYSIS REVEALS EXTENT OF DNA REPAIR ARMY

A database developed by HHMI investigator Stephen J. Elledge at Harvard Medical School and colleagues are providing the first detailed portrait of the army of more than 700 proteins that helps repair and maintain cellular DNA's integrity.

The DNA damage response is a routine event in the life of any cell. Stress caused

by environmental factors such as exposure to ultraviolet light, ionizing radiation, or other environmental phenomena can cause DNA to break apart or rearrange its nucleotide base pairs in unhealthy ways. Left unchecked, such mutations can accumulate over time and ultimately lead to conditions such as cancer and diabetes.

Elledge, senior author of a study published May 25, 2007, in *Science*, likened the DNA damage response to a command and control center. Two critical enzymes, known in scientific shorthand as ATM and ATR, act like sensors to detect trouble and initiate DNA damage response by engaging the cell's molecular repair apparatus. The researchers found this multiprotein army by looking at how these enzymes reacted to damage in human cells caused by ionizing radiation and ultraviolet light.

The revelation promises insight into a spectrum of diseases. In a companion paper published in the same issue of *Science*, Elledge's group used the database to identify two proteins, known as Abraxas and RAP80, critical to recruiting the breast and ovarian tumor-suppressing BRCA1 protein to sites of DNA damage.