If You Give a Mouse a Protein…
By Marshall Honorof

One blind mouse. It's not quite poetic enough to replace the time-tested "three blind mice," but it was recently at the center of a novel experiment involving mammalian vision. "The goal is to restore complete visual function in humans," says Hugh Cahill, who has been doing research with the Johns Hopkins Medical Institute's Neuroscience department for seven years. His latest research involves using a protein found in green algae to restore limited sight in mice. This development may seem astounding – and on some level, it is – but it might not be quite as useful as it sounds.

There's nothing particularly simple about the mammalian visual cascade, a series of chemical signals to the brain that turn an image into the eye into useful information in the brain. The two kinds of vision are non image-forming, which detects changes in light, and image-forming, which allows a mammal to actually see objects. In a healthy eye, the pupil constricts when exposed to light, and the retina records an image to send to the brain. Cahill and associates designed an experiment aimed towards restoring non-image forming vision in blind lab mice.

The catalyst for the experiment, surprisingly, wasn't a mammal. Actually, it wasn't even an animal at all. Rather, the JHMI researchers used a type of protein found in a certain kind of algae. Unlike mammals, whose light-sensitivity is linked to ten genes, these algae require only one protein, called channelrhodopsin-2, to be responsive to light.

After engineering a virus to express the channelrhodopsin-2, Cahill injected the virus into the eyeballs of thirty lab mice, genetically engineered to be blind and non-receptive to light. After a few days, some mice began to constrict their pupils after being

exposed to light, a sure sign of non image-forming vision. This means that the mouse, while still unable to see actual images, was able to detect changes in the level of light.

Even with this experiment done, the process of restoring human vision is not going to be a smooth train ride; a good deal of track hasn't even been laid yet. Although this experiment enabled mice to detect light sensitivities, all humans – even blind ones – can do that anyway. In nature, mammals – humans and mice included – can always detect light, even if they are blind. A receptor for light-sensitivity can be found in any blind human. Cahill's team solved an artificial problem with artificially-engineered animals. The experiment didn't produce the desired result in all mice, either. Of the thirty mice injected, about 90% showed no signs of change. Besides, the image-forming part of mammalian vision is a much more complex process, relating mostly to how the brain processes images, not how they eye receives them. "Therapeutically, [the experiment] has absolutely no value," Cahill admits.

Cahill's experiment has no real medicinal use yet, but he still hopes to use it as a springboard. "In a sense, it's kind of luck," he remarks, adding "99% of [these experiments] are failures. Absolute, total failures." This research, esoteric as it may be, was still successful, and could lead to bigger things in the future. After all, we all know how the old story goes: if you give a mouse a protein, he might want some eyesight to go with it.