

## **Theory on Aging is Tested, Adding 30% to Flies' Lives**

**By Gina Kolata**

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Testing a leading theory of the cause of aging, researchers say that by giving flies new genes they have been able to extend their lives by 30 percent and to keep them more nimble and robust.

The theory says that a group of unstable and damaging molecules called *free radicals* bombard cells throughout life, inflicting steady damage. Eventually, the injuries are so great that cells no longer function properly, organ systems fail, diseases like cancer or heart disease occur, cataracts cloud the eyes, and finally the organism dies. Vitamins C and E, and beta carotene, can help mop up free radicals, and so those who believe in the theory often take them as dietary supplements.

In a study being published today in Science magazine, Dr. Rajindar S. Sohal and Dr. William C. Orr, biologists at Southern Methodist University in Dallas, gave fruit flies *extra copies* of genes that are normally used to rid cells of free radicals.

What resulted, Dr. Sohal said in a telephone interview, was "the first direct evidence" that improved defenses against free radicals can extend life and improve its quality. He added that the flies that received the added genes were so much more vigorous that "we could tell which ones they were just by looking at them."

### **Similar System in Humans**

Dr. Sohal noted that humans have an almost identical system for defusing free radicals. While the test in flies does not prove that people could live longer and better if they controlled free radical damage in their own cells, it does give new weight to the theory, some experts said.

Dr. Earl Stadtman, chief of the laboratory of biochemistry at the National Heart, Lung and Blood Institute in Bethesda, Md., said scientists had already demonstrated that free radical damage accumulated in cells as people and animals aged. But he said, "The big question has always been, What is cause and what is effect?"

That question is answered with the new study, Dr. Stadtman said. "It's almost a proof for the free radical theory of aging," he said.

But Dr. Gene Cohen, director of the Washington, D.C. Center on Aging, cautioned that it was not clear how, if at all, those results would apply to people. "These are flies and not humans" he said.

The idea behind the experiment was to strengthen cells' natural defenses against free radicals. Cells use one enzyme, *superoxide dismutase*, to convert free radicals to hydrogen peroxide. Then they use a second, *catalase*, to convert hydrogen peroxide to water. Dr. Sohal and Dr. Orr *genetically altered* the flies so that they made excess amounts of both enzymes.

### **Longer-Living Flies**

Flies with the extra enzymes lived longer on average and had a longer maximum life span. The longest an untreated fly lived was 71 days, while the longest a treated fly lived was 92 days.

Dr. Sohal said he had determined the flies' vigor by knocking them to the bottom of a cylinder and then measuring how quickly they climbed back up the sides. Until 35

days of age – middle age for a fruit fly – flies with the extra enzymes were faster than those in the comparison group. After that, the treated flies, though not faster, were more active, with rates of oxygen consumption about 40 percent higher than those of flies in the comparison group, the researchers reported.

Dr. Sohal said that after doing research on free radicals and aging for two decades, he finally had proof of the theory. And the crucial piece of the puzzle, he said, was preventing the most dangerous of the free radicals from forming in the first place, rather than mopping them up afterward with vitamins C or E. That allowed him to see a more pronounced effect and showed that it was the lack of free radicals and not some other effect of vitamins that made the difference.

While no one is proposing that people alter their genes, it may be possible to inject or use some other method to supply superoxide dismutase and catalase to body tissue, said Dr. Robert N. Butler, the Brookdale Professor of Gerontology at the Mount Sinai School of Medicine in Manhattan. It does no good to eat the enzymes because they are proteins and are degraded in the stomach.

### Theory Gains Converts

Dr. Butler said that the 50-year-old free radical theory was “often disparaged” but that as evidence for it mounted it was fast gaining converts among scientists who studied aging. So convinced are researchers that many, if not most, did not wait for direct proof but *began taking vitamins C and E and beta carotene anyway*, hoping to prevent free radical damage from spreading in their own cells.

Dr. Carl Cotman, who directs the Irvine Brain Aging Research Unit at the University of California at Irvine, is one. His specialty is the aging brain, but about a year ago, after reading research papers on the free radical theory of aging, he was convinced. “It was so compelling,” he said, that he immediately began taking vitamins C and E.

Dr. Huber Warner, deputy associate, director of the biology of aging program at the National Institute on Aging, said he began taking supplements about two years ago. When he saw data showing that proteins, as well as DNA and fats, could be damaged by free radicals, he said. “I became convinced.” Proteins, unlike DNA and fats, cannot be repaired if they are damaged. “When proteins get damaged, then you are damaging the machinery of the cell, the stuff that has to do the work.” Dr. Warner said.

Deis Comment:

Superoxide catalyzes  $O_2^- + O_2^- \rightarrow H_2O_2 + O_2$

Catalase:  $H_2O_2 + H_2O_2 \rightarrow 2 H_2O + O_2$

Beta carotene supplements can cause liver damage and are not worth the risk.

In the Dec. 15, 2000 issue of *Science*, Helfand et al. published a paper on the “Indy” gene, which helps take up nutrients in the gut. *Lowering* the activity of the gene leads to longer life spans. “Indy” comes from a scene in Monty Python and the Holy Grail, “I’m Not Dead Yet.”