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How antioxidants defend cells

Antioxidants in the body act as chemical scavengers, intercepting reactive molecules called free radicals before they have a chance to damage cells. Two recent studies shed some light on how such protective mechanisms work.

In one study, researchers examined how vitamin E, vitamin C, and carotenoids such as beta carotene collaborate to get rid of free radicals, whose harmful effects arise from their readiness to grab an electron from another molecule. The scheme the chemists propose works something like a bucket brigade, with the dangerous chemical property being passed from one molecule to the next.

First, vitamin E reacts with the free radicals, restoring them to their less harmful state. This reaction, however, turns vitamin E into a potentially damaging radical, which the carotenoids then inactivate. Finally, vitamin C repairs the resulting carotenoid radicals, and the water-soluble vitamin C radicals eventually wash out of the body.

The mechanism, says T. George Truscott of Keele University in England, may help explain the puzzling results of clinical studies showing that beta carotene supplements boost the incidence of cancer in smokers. The Beta Carotene and Retinol Efficacy Trial (CARET), funded by the National Institutes of Health, was halted early because of this finding (SN: 1/27/96, p. 55).

According to the researchers' proposed scheme, smokers tend to be low in vitamin C, so they don't have enough of the vitamin to scavenge carotenoid radicals. Giving smokers supplements of carotenoids only adds to the radicals in the body, he says.

"This [cascade] occurs in test tubes, but the proof will be in human trials" using combinations of antioxidants, Truscott says. He and his colleagues report their findings in the Jan. 22 JOURNAL OF THE AMERICAN CHEMICAL SOCIETY.

Beta carotene, for example, seemed very promising in the laboratory, says Gilbert S. Omenn of the Fred Hutchinson Cancer Research Center in Seattle, but its effect was radically different in people. Truscott carried his study out in an organic solvent, so it's difficult to predict whether the mechanism would be the same in a physiological system.

Nevertheless, Omenn says, "I think it's terrific that trials have generated chemical research like this to try and explain the clinical results."

The second study addresses a very different kind of protection against free radicals—one built into proteins themselves. Rodney L. Levine, Earl R. Stadtman, and their colleagues at the National Heart, Lung, and Blood Institute in Bethesda, Md., propose that the amino acid methionine may function as a protein's last-chance defense against free radical damage. Their study appears in the Dec. 24, 1996 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

"It's just an initial concept, but we think it has good logic," Stadtman says. "Almost all [free radicals] we've studied have a preference for attacking methionine." Free radical attack turns the amino acid into methionine sulfoxide. That change didn't affect the structure or function of the particular protein they studied, however, suggesting that "perhaps methionine was put there to protect." The situation is similar in other proteins, he adds.

Moreover, earlier studies have shown that some enzymes can restore methionine sulfoxide to its original state, thereby setting up a cycle that allows its antioxidant activity to be renewed.

The group is now trying to create mutant strains of yeast that produce variable amounts of such enzymes. By looking at whether the yeast mutants are more or less sensitive to free radical damage, the researchers hope to lend further support to their theory.

— C.W.