Editorial

Selenium: Not just another nutrient

Interest in the biological roles associated with the essential trace element selenium has been growing exponentially over the last few decades. Initially, most of the attention on selenium focused on its toxicity in both animals and people exposed to very high levels. Animals grazing in areas of very high soil selenium levels are susceptible to selenosis and may suffer from industrial exposure. Selenosis can also be triggered in people who overdose on nutritional supplements, thus dramatically exceeding safe levels of selenium. More recent events have seen the focus shift from toxicity to the benefits of adequate or supplemented levels of selenium in the diet.

Many of the benefits of selenium are likely to be due to its biological role as a constituent of proteins in forming the amino acid selenocysteine. Parallel work in prokaryotes by August Böck and eukaryotes by Dolph Hatfield revealed that the synthesis of selenium-containing proteins utilized unique translational machinery to synthesize selenoproteins. In prokaryotes, the investigation focused on complementation groups among bacterial strains unable to synthesize selenoproteins, while the eukaryotic story centralized on the selenocysteine tRNA. What followed was the discovery that selenoproteins were synthesized from mRNAs in which selenocysteine was encoded by the UGA stop codon that would otherwise result in translational termination. The use of the UGA codon as the codeword for selenocysteine in designated mRNAs in representatives of all of the Life Kingdoms is now generally considered to be an expansion of the universal genetic code to include UGA as the 21st naturally occurring amino acid. Genome-wide computational analysis from Vadim Gladyshev's group revealed that there are 25 human selenoproteins and many of these have known functions, including several with anti-oxidant enzyme activity and others involved with the synthesis of thyroid hormones.

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The focus of this Special Edition is the biological effects of selenium. Fueled by decades of animal studies showing that low, non-toxic doses of selenium provided in the diet of laboratory animals could reduce the incidence of cancer, the chemopreventive potential of selenium is now an area of intense study. Supported by human epidemiological studies showing an inverse association between selenium intake in cancer risk for several tissue types, as well as the results of preliminary supplementation trials, several selenium chemoprevention trials have been initiated world-wide, including the US-based SELECT trial investigating the efficacy of selenium supplementation, with and without vitamin E, to reduce the risk of prostate cancer. While human genetic studies have provided some support for a role of selenoproteins in the mechanism of chemoprevention with selenium, it is likely that there are selenoprotein-independent effects of selenium involving low-molecular weight selenium metabolites as well. This notion is supported by studies showing the growth-inhibiting and apoptosis-inducing effects of selenium on tumor cells which occur using concentrations of selenium well past those likely to enhance selenoprotein levels. Thus, selenoproteins, seleno-metabolites and perhaps selenium associated with less characterized peptides referred to as selenoprotein binding proteins all may influence cancer risk and etiology.

Whatever the form of selenium and the mechanism of action, selenium is likely to have significant actions in addition to those that influence cancer incidence. Effects on hormone metabolism, immunity, risk of heart disease and the pleotropic consequences of influencing diverse signaling pathways make selenium an important nutrient to consider in developing strategies to maintain and improve human health. The papers included in this Special Edition therefore are intended to serve as a useful primer for both those interested in using nutrition to minimize disease and those currently directly involved in the study of selenium biology.

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