Murphy Cancer Foundation presents Cutting Edge Research at Ehrlich II – 2nd World Conference on Magic Bullets in Nürenberg, Germany October 3 - 5, 2008

When More is Not Necessarily Better: Interdisciplinary Inquiry into the Implications of U-Shaped Dose Responses for Personalizing Anticancer Interventions

David J. Waters, PhD, DVM, Purdue University Center on Aging and the Life Course, and the Gerald P. Murphy Cancer Foundation, West Lafayette, IN, USA.

Background: The perception that is pervasive among the public is that, when it comes to taking cancer-fighting dietary supplements, more is better. Whether or not this concept is valid is especially relevant to health-conscious men and women, who are ironically at highest risk for the ill-effects of oversupplementation because they are already consuming high quality diets rich in vitamins and minerals. In 2001, the National Cancer Institute launched SELECT to evaluate whether daily supplementation with selenium (Se) or vitamin E prevents prostate cancer. But very little was known about what dose of Se might offer the most potent cancer-protective effects. We hypothesized that Se regulates the accumulation of genotoxic damage within the prostate and that the relationship is non-linear, i.e. more Se is not better.
Methods: We conducted a randomized feeding trial in which 69 elderly beagles (equivalent to 65 year-old men) received adequate or supranutritional Se intake for 7 months. We used the aging dog prostate to mimic the aging human prostate, enabling us to study the effects of Se on prostatic cells in an appropriate context.
Results: Se supplementation significantly decreased the accumulation of DNA damage in the prostate (alkaline Comet assay). When we examined the relationship between toenail Se level and prostatic DNA damage, we discovered an intriguing U-shaped dose response curve; more was not better. Further, we showed that the Se level that minimizes DNA damage in the aging dog prostate remarkably parallels the Se level that minimizes prostate cancer risk in 2 large human studies.
Conclusions: Now, more than ever, we need a new approach to cancer prevention — personalized cancer prevention (*Waters et al, Nutrition and Cancer 2008; 60:1-6*). Defining the U-shaped relationship between DNA damage and cancer-modulating nutrients addresses one of the major obstacles to developing personalized cancer-reducing interventions. It follows from this understanding that not all individuals will necessarily benefit from increasing their nutrient intake. Baseline nutrient status should be required for all individuals in prevention trials to avoid oversupplementation.