

WALNUTS & CANCER

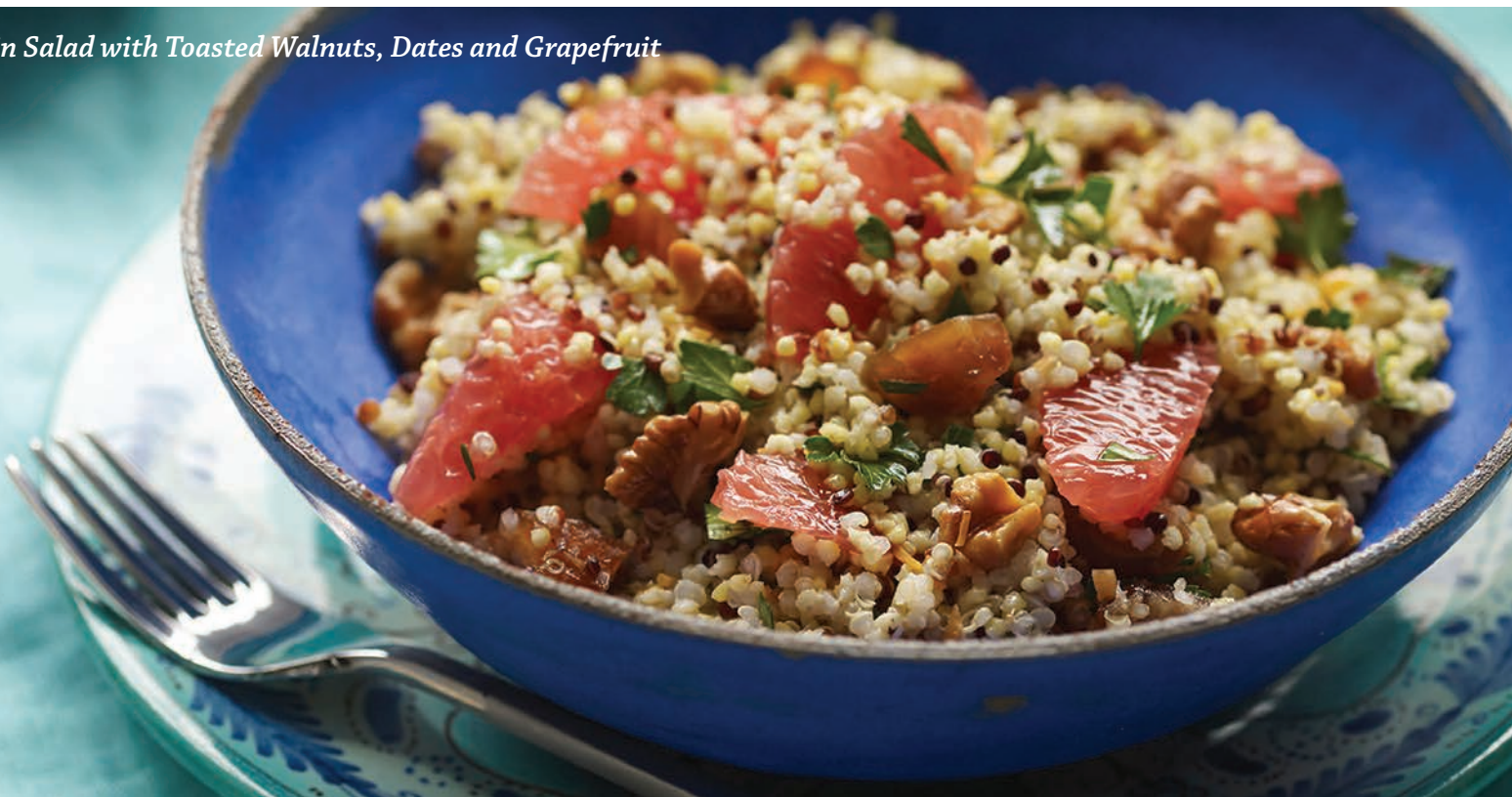
PRELIMINARY ANIMAL AND CELL model research has been investigating the potential benefit walnuts may have on a variety of cancers including breast, prostate and colorectal. Please note that the following animal and cell studies are provided as background and used to formulate hypotheses for additional research needed to determine the effects on humans.

A review of animal research published in *The Journal of Nutrition* demonstrates that walnuts may have multiple nutrients that could act in various ways to help decrease the risk of developing cancer. The studies reviewed suggest that these nutrients act together to provide more benefit than would be expected from the individual components.¹

BREAST CANCER

ANIMAL RESEARCH PUBLISHED in *Nutrition and Cancer* looked at the role of walnut consumption on potential breast cancer protection in maternal mice and their offspring. Researchers found that a diet including a modest amount of walnuts (equivalent to 2 ounces per day for humans) was associated with a decreased risk of breast cancer in mice.² Maternal mice were randomized to a control diet with corn oil or a diet containing walnuts, and both diets were designed to be isocaloric and isonutrient. The maternal mice were then bred with male mice and the offspring were randomized to the same two diets after weaning. The findings showed a significant reduction in tumor incidence, number and size in maternal and offspring mice that consumed walnuts compared to mice that did not consume walnuts. Although more research is needed to determine the specific components of walnuts and the mechanisms associated with tumor suppression, the findings demonstrate that walnuts may contribute to a healthy diet to reduce risk for breast cancer in mice.

Grain Salad with Toasted Walnuts, Dates and Grapefruit



COLORECTAL CANCER

AN ANIMAL STUDY PUBLISHED in *Cancer Prevention Research* found that eating walnuts could modify gut bacteria in a way that is beneficial to colon health, and may be associated with colon tumor suppression.³ In the study, researchers incorporated walnuts into two different diets, a standard mouse diet supplemented with 0, 15, 22.5, or 30.2 percent of calories from walnuts, and a Western diet, representing typical American intake, supplemented with 0, 5.2, 10.5, or 21.4 percent of calories from walnuts. Calories from fat sources were proportionally lowered in each diet to compensate for the addition of walnuts. Male mice fed a Western diet with 10.5 percent of total calories from walnuts, which translates to just over one ounce of walnuts in a human diet, showed a significant reduction in the number and size of tumors.

Animal research conducted at the Beth Israel Deaconess Medical Center and Harvard Medical School demonstrated that walnuts in the diet may inhibit colorectal cancer growth in mice by suppressing angiogenesis.⁴ In this study, mice with human colon cancer cells were randomized to diets containing approximately 19 percent of total energy from corn oil (control diet), flaxseed oil or ground walnuts (approximately 2 ounces of walnuts in a human diet). Compared with the corn oil diet, mice fed the walnut diet (equivalent to 2 servings of walnuts per day in humans) or flaxseed diet exhibited significantly slower tumor growth rates and lower tumor weights. The differences between walnut and flaxseed diets did not reach statistical significance. However, compared to the control-fed mice, consumption of walnuts significantly decreased angiogenesis which may be beneficial against the progression of colorectal cancer.

PROSTATE CANCER

WALNUTS CONTAIN SEVERAL BIOACTIVE compounds including ellagitannins (ETs), a type of polyphenol. After consumption, ETs are metabolized to release ellagic acid (EA), which is further metabolized by gut microbiota to form urolithins, such as A (UA) and B (UB).

A cell study published in the *European Journal of Nutrition* looked at gene expression in prostate cancer cells and found that UA, the main human metabolite of walnut polyphenols, may help to inhibit or reduce the risk of prostate cancer from developing.⁵ Similarly, another cell study showed that a diet rich in ET-containing foods, such as walnuts, could contribute to the prevention of prostate cancer by influencing the regulatory mechanisms in prostate cancer.⁶

Research published in *Cancer Investigation* showed that walnuts may help reduce prostate cancer risk in mice.⁷ In this experimental study,

mice were fed either a standard mouse diet (control diet) or a standard mouse diet enriched with walnuts (equivalent to 2 ounces of walnuts per day in humans). The final average tumor size in the walnut-fed mice was approximately 25 percent the average size of the prostate tumors that developed in the mice that consumed the non-walnut control diet.

¹Hardman, WE. Walnuts have potential for cancer prevention and treatment in mice. *J Nutr.* 2014;144(4 Suppl):555S-560S. ²Hardman WE, Ion G, Akinsete JA, et al. Dietary walnut suppressed mammary gland tumorigenesis in the C(3)1 TAg mouse. *Nutr Cancer.* 2011;63(6):960-70. ³Nakanishi M, Chen Y, Qendro V, et al. Effects of walnut consumption on colon carcinogenesis and microbial community structure. *Cancer Prev Res (Phila).* 2016;9(8):692-703. ⁴Nagel JM, Brinkoetter M, Magkos F, et al. Dietary walnuts inhibit colorectal cancer growth in mice by suppressing angiogenesis. *Nutrition.* 2012;28(1):67-75.

⁵Sánchez-González C, Ciudad CJ, Izquierdo-Pulido M, et al. Urolithin A causes p21 up-regulation in prostate cancer cells. *Eur J Nutr.* 2016;55(3):1099-112.

⁶Sánchez-González C, Ciudad CJ, Noé V, et al. Walnut polyphenol metabolites, urolithins A and B, inhibit the expression of the prostate-specific antigen and the androgen receptor in prostate cancer cells. *Food Funct.* 2014;5(11):2922-30. ⁷Reiter RJ, Tan DX, Manchester LC, et al. A walnut-enriched diet reduces the growth of LNCaP human prostate cancer xenografts in nude mice. *Cancer Invest.* 2013;31(6):365-73.