



CALIFORNIA
TABLE GRAPE
COMMISSION

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October 30, 2019

Dear Researcher:

The California Table Grape Commission (commission) is pleased to announce its request for Letters of Intent to submit a proposal for its 2020-21 Health Research Grant Program. Letters of Intent are sought for \$35,000 grants toward clinical research in the area of grapes and gastrointestinal (GI) health.

The role that GI health plays in overall health is significant and understanding the role of the intestinal microbiome is a growing area of scientific research. The anti-inflammatory, antioxidant, and antimicrobial properties of the nutrients and phytochemicals found in grapes potentially influence intestinal and systemic health. Grapes and grape polyphenols appear to influence intestinal bacteria, with subsequent metabolic consequences. Preliminary research suggests that grapes may act in the following ways to positively impact intestinal health: act as prebiotic agents; serve as antimicrobial agents; neutralize pro-oxidants that damage DNA and proteins; reduce populations of gut microbes that produce pro-oxidants; and modulate inflammation. Grapes may also play a role in maintaining the health of colon tissue, protecting against cancer-promoting genes.

The commission has funded several studies (animal and human) that suggest the consumption of grapes may contribute to GI health by modulating gut bacteria, and also inhibiting target genes known to promote colon cancer in normal colonic mucosa. The commission would like to expand work in the area of gut health with clinical studies. Areas of interest include the effects of grape consumption on: the gut microbiome; colon polyps, colon cancer, irritable bowel syndrome, colitis, diverticular diseases, and Crohn's disease. See Attachment A for a summary of the research to date.

All details concerning the submission of a Letter of Intent can be accessed on the commission website at www.grapesfromcalifornia.com/grapes-health/health-research-grants/. Available documents include the Letter of Intent Solicitation Letter – GI Health, the Letter of Intent Guidelines – GI Health, the Freeze-Dried Table Grape Powder Overview, the Guidelines for Use of California Table Grape Powder in Health Research Studies, and the Funded Research Studies 1999-2019.

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Published studies or final reports resulting from previously funded GI health research can be accessed for review by the applicant. The purpose of making this information available is to help ensure that new proposals in an area previously studied appropriately continue and expand on that work, with effective doses and protocols.

The major goal of this program is to fund studies that examine the potential health benefits of grape consumption on gut health. To facilitate such studies, the California Table Grape Commission developed a freeze-dried table grape powder made from fresh California table grapes that is to be used for work funded by this grant program. It is not an extract. The powder is a composite of seeded and seedless red, green, and black California grapes. As with fresh grapes, the powder is known to contain simple phenolics, resveratrol, flavans (including catechins), flavonols (including quercetin), and anthocyanins.

Following the review of submitted Letters of Intent, finalists will be invited to submit a complete proposal to the commission. Please note: the Letter of Intent must be submitted electronically, in a single PDF file.

Deadline for submission of a Letter of Intent is Monday, December 2, 2019 at 5 p.m. Pacific Standard Time (PST). For the Letter of Intent Guidelines – GI Health please visit www.grapesfromcalifornia.com/grapes-health/health-research-grants/.

The commission Health Research Grant Program is overseen by a scientific advisory panel of distinguished scientists who will be reviewing the Letters of Intent. In the meantime, inquiries regarding this process should be directed to healthresearch@grapesfromcalifornia.com.

Thank you for expressing interest in the health benefits of California grapes.

Regards,

A handwritten signature in blue ink that reads "Courtney Romano". The signature is fluid and cursive, with a long horizontal line extending to the right.

Courtney Romano, MBA, RD
Health Research Grant Program Director
for the California Table Grape Commission

enclosure

cc: Kathleen Nave, president

Summary of California Table Grape Commission GI Health Studies

All studies supported by the California Table Grape Commission studied the effects of a whole grape freeze-dried powder.

PUBLISHED RESEARCH

Nguyen, A.V., Marinez, M., Stamos, M.J., Moyer, M.P., Planutis, K., Hope, C., & Holcombe, R.F. (2009). Results of a phase I clinical trial examining the effect of plant-derived resveratrol and grape powder on Wnt pathway target gene expression in colonic mucosa and colon cancer. *Journal of Cancer Management and Research*, 1, 25-37.

In a phase-1 human pilot trial normal colonic mucosa and colon cancer tissue examined pre- and post-exposure to grape powder by oral consumption. Grape powder inhibited target gene expression in normal colonic mucosa. The greatest effect was seen following ingestion of 80 g grape powder/day.

Nguyen, A.V., Marinez, M., Stamos, M.J., Moyer, M.P., Planutis, K., Hope, C., & Holcombe, R.F. (2009). Effect of a grape-supplemented diet on proliferation and Wnt signaling in the colonic mucosa are greatest for those over age 50 and with high arginine consumption. *Journal of Cancer Management and Research*, 1, 25-37.

In this study, healthy subjects were assigned to eat either 1/3, 2/3 or 1 lb. of grapes every day for two weeks. Researchers found that grape consumption at all levels inhibited the activities of target genes involved in cancer promotion. The benefits observed were most significant for two groups of people with a higher incidence of colon cancer: older individuals and those whose diet was high in arginine, a specific amino acid. This study reinforces previous findings that suggest a potential protective role for grapes against colon cancer.

Baldwin, J., Collins, B., Wolf, P.G.,...& McKintosh, M.K. (2015). Grape consumption reduces adiposity and markers of hepatic lipogenesis and alters gut microbiota in butter fat-fed mice. *J of Nutritional Biochemistry*, Jan; 27:123-35.

Animals consuming a grape-enriched diet (3%) for 11 weeks exhibited an increase in some beneficial gut bacteria (*Akkermansia muciniphila*) and a decrease in detrimental bacteria (sulfidogenic *Desulfobacter* spp. and the *Bilophila wadsworthia*-specific dissimilatory sulfite reductase gene.) Further, the grape-enriched diet mitigated high-fat-induced impairment to the intestine, commonly known as “leaky gut.” Grape-fed mice at either the 3 or 5% diet showed reduced total body and inguinal fat, and displayed lower liver weights and triglyceride levels. The grape diet had a minor effect on impact on markers of inflammation or lipogenesis in adipose tissue or intestine.

UNPUBLISHED RESEARCH

Focus: Suppression of colon carcinogenesis by grape powder through mitigation of inflammation and induction of apoptosis of colon cancer stem cells. PI: Vanamala, Jairam K.P., Penn State University.

In this study, a grape-enriched diet (at either 3% or 6% w/w) decreased the number of intestinal polyps by 55%, providing greater protection than aspirin (at 200 ppm; human equivalent dose), which decreased colon polyps by 42%. The grape-enriched diet also ameliorated the weight loss typically seen with colon tumor development. Control mice displayed significant weight loss, but the aspirin-consuming mice had the greatest amount of weight loss. The animals consuming the grape-enriched diet also displayed improved neurological functioning and behavior compared to the control and aspirin mice.

Focus: Evaluation of cancer chemoprevention potential of standardized grape preparation. PI: Pezzuto, JM, University of Illinois at Chicago.

Dose-selection studies showed that up to 5000mg/kg grape powder could be added to the animal diet with no adverse effects. No significant effect was observed against the carcinogen.

Focus: Interactive and synergistic effects of grape powder, grape seed extract, proanthocyanidins, resveratrol and quercetin in a colon cancer model. PI: Exon, J.H., University of Idaho.

In this study animals were treated with a carcinogen at the onset of starting a grape-enriched diet. A trend toward decreased number of Aberrant Crypt Foci was observed, but not statistically significant.