

392 W. Fallbrook, Suite 101 Fresno, California 93711-6150

phone: 559.447.8350 fax: 559.447.9184

grapesfromcalifornia.com

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 eye health.

Increased oxidative stress is associated with many eye diseases, including the progression of Age-Related Macular Degeneration (AMD), the leading cause of blindness in the elderly. The retina is extremely vulnerable to oxidative damage. The incidence of cataracts and glaucoma is also linked to oxidative stress, and diabetic retinopathy, while initially caused by uncontrolled high blood sugar over time, is exacerbated by oxidative stress as well.

The commission has funded a number of studies (animal and human) that suggest the consumption of grapes may contribute to eye health by promoting antioxidant actions that protect the retina's structure and function; preventing activation of inflammatory pathways and inhibiting abnormal and harmful blood vessel growth in the eye. The commission would like to expand work in this area with clinical studies. Areas of interest include the effects of grapes on macular degeneration, cataracts, and glaucoma. 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 – Eye Health, the Letter of Intent Guidelines – Eye Health, the Freeze-Dried Table Grape Powder Overview, the Guidelines for Use of California Table Grape Powder in Health Research Studies, and the Funded Health Research Studies 1999-2019.

Published studies or final reports resulting from previously funded eye 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 eye 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 – Eye 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,

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 Eye Health Studies

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

Yu, C.-C, Nandrot, E.F., Dun, Y., & Finnemann, S.C. (2011). Dietary antioxidants prevent agerelated retinal pigment epithelium damage and blindness in mice lacking the $\alpha\nu\beta$ 5integrin, *Free Radic. Biol. Med.*, 52:660-670.

In an animal model of vision loss similar to human macular degeneration, the grape powder diet significantly decreased HNE-adduct content, lipofuscin granule buildup and prevented age-related cone and rod photoreceptor dysfunction. The grape diet was protective when fed at a younger age (3-6 months or 6-9 months), but offered no protection when fed at 9-12 months. The grape powder was significantly more protective than lutein.

Kanavi, M.R., Darjatmoko, S., Wang, S., Azari, A.A., Famoodian, M., Kenealey J.D...& Polans, A.S. (2014). The sustained deliver of resveratrol or a defined grape powder inhibits new blood vessel formation in a mouse model of choroidal neovascularization. *Molecules*, 19:17578-17603.

In a controlled feeding trial in mice grape powder significantly reduced the formation of harmful blood vessels (choroidal neovascularization) associated with models of the exudative form of age-related macular degeneration (AMD), a leading cause of blindness in the industrialized world

Patel, A.K., Davis, A., Esperanza Rodriguez, M., Agron, S., & Hackam, A.S. (2016) Protective Effects of a grape supplemented diet in a mouse model of retinal degeneration. Nutrition, 32:384-390.

In a mouse model of retinal degeneration, freeze-dried grape powder (FDGP) preserved retinal structure and function compared to a sugar-matched control. In addition, retinal thickness and photoreceptor numbers were preserved by the FDGP-supplemented diet compared to controls.

Unpublished Work

Focus: Effects of grapes on retinal microvascular function. PI: Lott, Mary E.J., Penn State University, Hershey

This study examined the short-term effects of grape ingestion on microvascular function and oxidative stress across the diabetes continuum in humans. In this study grape consumption resulted in improvements in microvascular vasodilation of the retinal blood vessels in individuals with prediabetes and type 2 diabetes; reductions in diastolic blood pressure in

healthy middle-aged individuals; and reductions in oxidative stress in healthy individuals and those with prediabetes. Consuming grapes led to no change in glucose homeostasis of individuals with prediabetes and diabetes but did improve the secretion of insulin in Type 2 diabetics.

Focus: Grapes and Cataract Prevention. PI: Hongli Wu, University North Texas Health Center

This study looked at the impact of grape consumption for 3 months on cataract formation in mice. A dose responsive protective effect was seen at all levels, where a 15% grape diet significantly inhibited the onset and severity of cataracts, resulting in clear lenses.

Focus: Neuroprotection in age-related macular degeneration with grapes. PI Rohrer, Medical University of South Carolina.

This study found that mice consuming a 10% grape diet showed significant improvement in photoreceptor function and were protected from photoreceptor cell loss.