



CALIFORNIA
TABLE GRAPE
COMMISSION

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November 5, 2009

Dear Researcher:

Enclosed please find the California Table Grape Commission's 2010-11 request for Letters of Intent (LOI) to submit a proposal for its Annual Research Grant Program. The commission welcomes Letters of Intent from you and other researchers at your institution and asks that you notify other interested researchers about the LOI. Feel free to post the document if appropriate. The document is also available on the commission's website at www.grapesfromcalifornia.com. Deadline for submission of letters is Thursday, December 3, 2009.

Once again, we are soliciting Letters of Intent first. Following the review of submitted Letters of Intent, finalists will be invited to submit a complete proposal to the commission. This year we will be reviewing Letters of Intent for \$30,000 grants that may be applied toward any relevant health issue.

The major goal of this program is to fund studies that examine the potential health benefits of grape consumption. To facilitate such studies, the California Table Grape Commission developed a freeze-dried grape powder made from fresh California table grapes, which is to be used for work funded by this grant program. The powder is a composite of seeded and seedless red, green and blue-black California grapes. As with fresh grapes, the powder is known to contain simple phenolics, resveratrol, flavans (including catechins), flavonols (including quercetin) and anthocyanins.

Thank you very much for your interest in California grapes.

Regards,

Jim Howard
Vice President
jim@grapesfromcalifornia.com

California Table Grape Commission Request for Letters of Intent (LOI) 2010-11 Research Grant Program

Issue Date:

Thursday, November 5, 2009

Letter of Intent Due Date:

Thursday, December 3, 2009

Purpose: The California Table Grape Commission seeks to encourage research projects to assess the potential benefits of table grapes to human health, using a freeze-dried powder made from fresh grapes.

Background: Fruits and vegetables contain a large number of naturally occurring nutritive and non-nutritive constituents, and have been shown to help maintain health and prevent chronic illnesses such as certain cancers, heart disease, stroke and obesity. Preliminary studies of grapes and grape products such as grape juice indicate potential cardiovascular protection. Additionally, preliminary studies of grapes and/or isolated grape constituents such as resveratrol, catechins, procyanidins, flavonols and anthocyanins indicate that these may help protect against certain cancers, heart disease, nerve and brain disorders, arthritis and an array of other conditions.

Freeze-Dried Grape Powder

In 1999, the California Table Grape Commission began production of a freeze-dried whole grape powder made from fresh California grapes; it is not an extract. The powder was created to provide researchers with a grape sample that would be available on a continuous basis, to further the study of grapes and health. Research results observed using the grape powder are thus the result of grape consumption and research proposals should be titled and written to reflect this.

The grape powder is a composite of whole red, green and blue-black California grapes, seeded and seedless varieties, in a freeze-dried powder form. It was created using Good Manufacturing Practices (GMP) and precautions to preserve the integrity of the biologically active compounds found in fresh grapes. As with fresh grapes, the grape powder is known to contain anthocyanins, catechins, resveratrol, flavonols (including quercetin), flavans and simple phenolics as well as sugars. An information sheet about the grape powder is included with this request for LOIs. Methods are available for the preparation of extracts that are suitable for cell culture studies, if needed.

Grape Powder Placebo

The California Table Grape Commission has developed a placebo for human consumption, which is available for those researchers conducting human studies, to encourage the development of well-controlled studies.

Specific Objectives: The emphasis of this research program is to facilitate research that will increase our understanding of the potential effects of grape consumption on human health. Research projects should be designed to provide a foundation for subsequent, large-scale studies in humans, and where appropriate, the development of pilot human studies is

encouraged. This does not exclude cell or animal studies that may make a significant contribution to the current body of knowledge about grapes and health. Specifically, the grants are to be used to encourage research, using the freeze-dried grape powder as a stand-in for fresh grapes, to examine the link between consumption of grapes and health, including protection against diseases such as heart disease, cancer and diseases associated with the aging process such as age-related macular degeneration, Alzheimer's/brain health, arthritis, etc. Chronic diseases of national concern such as metabolic syndrome, obesity, etc. would also be appropriate.

Please note: the use of a severely compromised subject population in proposed human studies is not appropriate for this research grant program.

Grapes and Health Grant: three to four awards of \$30,000 each are anticipated.

Examples of relevant research areas include, but are not limited to:

- Examining the impact of grape consumption (via grape powder) on prevention of heart disease, cancer, nerve and brain disorders, arthritis, diabetes or other chronic diseases
- Determining the effect of grape consumption on the activity of known disease-causing agents
- Evaluating the effects of grape consumption on risk factors and subclinical markers of disease in small human or animal studies

A list of previously funded projects is attached.

In addition to the grant monies, the California Table Grape Commission will provide a sufficient quantity of the freeze-dried grape powder to the Principal Investigator for completion of the proposed studies, which is of significant value at \$535/kg. For those conducting human studies, placebo will also be provided.

Funds Available: Three to four awards of \$30,000 each – grant amounts cover total costs (including direct and indirect costs) for one year and will be committed specifically to fund individual proposals submitted in response to this RFP. It is expected that competitive awards will not require overhead (indirect costs) in excess of 20 percent of total costs. It is anticipated that several awards will be made, however this level of support is dependent on the receipt of a sufficient number of proposals of high scientific merit. Although this initiative is provided for in the programs of the California Table Grape Commission, awards are contingent upon the availability of funds for this purpose. Funding does not carry with it the obligation for continuation beyond the year, although researchers can re-apply.

Deadline for Submission of Letters of Intent: Thursday, December 3, 2009.

Terms: Each research grant will provide funds for a one-year period. The year will begin on August 1, 2010 and end on July 31, 2011. Grant recipients will receive 75 percent of the grant amount at the time of the award, and the other 25 percent upon completion of the study and delivery of the final report. A no-cost extension may be possible if needed. Funding is intended for direct application to conducting the research studies, including funding for relevant laboratory supplies and technical personnel. Responsibility for the planning, direction and execution of the

This form, the grape powder information sheet and a list of previously funded studies are available online at www.grapesfromcalifornia.com

proposed project within the established timeframe will be solely that of the Principal Investigator and the applicant organization. Recipients will be required to submit a written progress statement at mid-year and a final report on the research outcome. The Principal Investigator should be prepared to present the results of their research at the California Table Grape Commission's annual meeting if requested. (If asked to present, travel expenses associated with attending would be borne by the commission.) The commission reserves the right to view research results prior to presentation or publication in whole or part (including abstracts). Additionally, grant awardee names, proposal title and institution may be posted on the California Table Grape Commission's website.

Eligibility: Candidates must have a medical or other doctoral degree and be a faculty member or project leader at a college or university, teaching hospital, or established research institute or organization. Preference will be given to researchers with previous experience in related research.

Review Considerations: Letters of Intent must be received by December 3, 2009. The commission's scientific advisory panel, which is comprised of distinguished researchers, will evaluate letters for scientific and technical merit. The scientific advisory panel will also examine the provisions made for the safety of the research environment including the protection of human subjects and laboratory animals, where applicable.

Review Criteria:

- Scientific, technical, or medical significance and originality of proposed research
- Appropriateness and adequacy of the experimental approach (including use of the freeze-dried grape powder) and methodology proposed to carry out the research
- Qualifications and research experience of the Principal Investigator and staff, particularly, but not exclusively, in the area of the proposed research
- Availability of the resources necessary to perform the research
- Appropriateness of proposed budget and duration in relation to the proposed research

Award Criteria: Scientific merit and programmatic priorities will be considered in selecting finalists to submit complete proposals. Finalists will be notified in December 2009, and invited to submit a full proposal. It is expected that final proposals will be due the first week of February, specific date to be determined. Awardees will be notified in June 2010. Disbursement of funds will be withheld until all approvals are granted for human subject and animal usage and a Material Transfer Agreement is signed by the recipient institution.

Letter of Intent Guidelines:

Format and Size Limit: Your entire narrative should be no more than three pages (two additional pages are allowed solely to highlight investigator qualifications), using an 11 or 12 point font. Narratives exceeding the page limit will not be reviewed.

Topic: Your project must explore the link between consumption of grapes (freeze-dried grape powder) and protection of human health.

Please include:

1. Contact information that is clearly visible and that includes name, title, phone number, email address and mailing address
2. Brief description of the topic to be addressed and its relevance/implications
3. Specific aims of the project

4. Description of the applicable research methodology
5. Project limitations
6. Names and qualifications of principal investigator and key staff (up to two pages in addition to narrative)
7. Estimated timetable and abbreviated budget for completion of the project
8. Estimated quantity of grape powder needed for research

Submission of Letter: Complete Letter of Intent (original + 10 copies) must be received no later than Thursday, December 3, 2009.

Send letter to:

Mr. Jim Howard
Health Research Grant Committee
California Table Grape Commission
392 W. Fallbrook, Suite 101
Fresno, CA 93711-6150

Phone: 559.447.8350
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California Table Grape Commission Information Sheet

Freeze-Dried Table Grape Powder (Y2006)

Updated 9/08

Fresh Grapes

Fresh grapes contain about 82% water, 12-18% sugar and 0.2-0.8% acid, mainly tartaric and malic acid. Grapes also contain numerous phenolic compounds, including simple phenols, simple phenolic acids, cinnamic acids, stilbenes, flavonoids, flavans, flavonols and anthocyanins. A standard serving size of fresh grapes is approximately 3/4 cup (126 grams).

Grapes are high in flavonoids and are particularly good sources of flavans. For example, the major phenolic compound in grapes is catechin, and they contain epicatechin, gallic acid and epigallocatechin. Grapes also contain high concentrations of leucoanthocyanidin flavans of varied structure. Grapes are good sources of flavonols, primarily quercetin. Red and blue-black grapes contain high amounts of anthocyanins.

Freeze-Dried Grape Powder

The freeze-dried grape powder is to be used for research purposes only. It is a composite of fresh red, green and blue-black California grapes (seeded and seedless varieties), that have been frozen, ground with food-quality dry ice, freeze-dried and re-ground using Good Manufacturing Practices for food products throughout. The powder was processed and stored to preserve the integrity of the biologically-active compounds found in fresh grapes. As with fresh grapes, the powder is known to contain resveratrol, flavans (including catechin), flavonols (including quercetin), anthocyanins and simple phenolics.

To estimate the amount of fresh grapes represented by the powdered preparation, moisture content must be taken into account. The dry powder contains approximately 1% moisture and fresh grapes contain approximately 82% moisture. Therefore, 100 grams of fresh grapes corresponds to approximately 18.2 grams powder. The powder is hygroscopic and should be stored in moisture-proof containers at -70°C.

Phytochemicals Analyzed in Freeze-Dried Preparation

Note: The following analysis does not represent the complete phytochemical profile of grapes

Compounds	Total	Individual
Catechins	57.2 mg/kg	
Catechin		36.4 mg/kg
Epicatechin		20.8 mg/kg
Anthocyanins	566 mg /kg	
Peonidin		38.3 mg/kg
Cyanidin		266 mg/kg
Malvidin		261.7 mg/kg
Flavonols		
Quercetin		16 mg/kg
Kaempferol		3.4 mg/kg
Isorhamnetin		3.5 mg/kg
Stilbenes		
Resveratrol		1.8 mg/kg
Total Polyphenols		448 mg/100g

Nutrient Analysis of Freeze-Dried Table Grape Powder (Y2006)

Nutrient	Amount (per 100 g powder)	Units
Calories	384.0	kcal
Total Fat, acid hydrolysis	0.45	g
Total Carbohydrate	91.2	g
Protein (N x 6.25)	3.9	g
Beta Carotene	0.064	mg
Vitamin A from Carotene	106.0	IU
Vitamin C	1.3	mg
Calcium	61.0	mg
Iron	2.62	mg
Sodium	30.6	mg
Potassium	1070.0	mg
Thiamin HCl	0.18	mg
Folic Acid	30.4	mcg
Phosphorus	121.0	mg
Magnesium	39.1	mg
Zinc	0.472	mg
Copper	0.488	mg
Manganese	0.366	mg
Moisture	1.3	g
Ash	3.1	g
Total Polyphenols	448.0	mg

Nutrient analyses were performed using standard methods of analysis. References available by request.

Microbiological Analysis of Freeze-Dried Table Grape Powder (Y2006)
(9/08)

Microorganism Analyzed	Result	Units
Standard plate count	1300	CFU/g
Coliform		
<i>E. coli</i>	<10	CFU/g
<i>Salmonella</i> (rapid method)	Negative/25g	+/-
Staphylococcus	<10	colonies/g
Yeast and mold count	1120	CFU/g

MPN: Most probable number

"Neither pathogenic nor harmful bacteria species were identified or found to be associated with this sample." Microbial Analysis report from Covance Laboratories, Inc.
9/08

California Table Grape Commission
Previously Funded Research Topics
1999 - 2009

1. *Vasoprotective Effects of a Standardized Grape Product, John Bauer, Ohio State University*
2. *Grapes and Cardioprotection, Dipak Das, University of Connecticut*
3. *Therapeutic Effect of Grape Intake in Animal Models of Neurodegeneration, Giovanni Manfredi, Weill Medical College of Cornell University*
4. *Anti-Atherogenic Activity of Grapes in Hypercholesteremic Transgenic Mice, Kathryn McMahon, Texas Tech University of Health Sciences Center*
5. *Evaluation of Cancer Chemoprevention Potential of Standardized Grape Extract, John Pezzuto, University of Illinois at Chicago*
6. *Absorption, Metabolism, and Antioxidant Capacity of Grape Polyphenols, Ronald Prior, Arkansas Children's Nutrition Center*
7. *Bioavailability of Grape Constituents, Chung Yang, College of Pharmacy, Rutgers University*
8. *Inhibition of Metalloproteinase Gene Expression by Extract of Fresh Grapes, Constance Brinkerhoff, Dartmouth Medical School*
9. *Favorable Effects of Grapes on LDL Oxidation and Atherosclerotic Lesions. Studies in Ovariectomized Guinea Pigs, a Model for Menopause, Maria Luz Fernandez, University of Connecticut*
10. *The Effects of Standardized Grape Preparation on Presbycusis, Michael Seidman, Henry Ford Health System*
11. *Polyphenolic Grape Constituents Increase Bioavailability of L-DOPA: Benefits in the Treatment of Parkinson's Disease, Bao Ting Zhu, University of South Carolina*
12. *Prevention of Atherosclerosis by Standardized Grape Preparation: Mechanical Studies in Cell Culture, Atherosclerotic Mice, and Humans, Bianca Fuhrman, Lipid Research Lab, Rambam Medical Center Israel*
13. *Oral Administration of Freeze-Dried Powder to Prevent Photodamage to Skin, Donald Godwin, University of New Mexico Health Sciences Center*
14. *Can Grapes Prevent Brain Aging? Robert Klein, University of Kansas Medical Center Research Institute*

15. *The Neuroprotective Effects of Grape Polyphenols*, Albert Sun, University of Missouri School of Medicine
16. *Inhibition of Different Stages of Skin Carcinogenesis with Freeze-Dried Grape Powder*, Margaret Hanausek, AMC Cancer Research Center
17. *Protection of Urinary Bladder Function by Grape Extracts*, Robert Levin, Albany College of Pharmacy
18. *The Protective Effect of Standardized Grape Preparation Against Cancer/Anticancer Activity of grape and grape skin extracts combined with catechins based on inhibition of tNOX and growth of HeLa cells in culture and 4T1 mouse mammary tumors in mice*, Dorothy Morre, Purdue University
19. *Cardioprotective Effects of Grape Polyphenols in Pre- and Post- Menopausal Women*, Maria Luz-Fernandez, University of Connecticut
20. *Inhibition of PhIP-DNA Adduct Formation in Female F344 Rats by Dietary Freeze-Dried Grape Powder*, Herman Schut, Medical College of Ohio
21. *Effects of Grape Powder on Inflammation Markers in Post-Menopausal Women*, Johanna Slavin, University of Minnesota
22. *Interactive and Synergistic Effects of Grape Powder, Grape Seed Proanthocyanidins, Resveratrol, and Quercetin in a Colon Cancer Model*, Jerry Exon, Holm Research Center, University of Idaho
23. *Ischemic Bladder Dysfunction: Protection by Grape Suspension*, Robert Levin, Albany College of Pharmacy
24. *Cardioprotection by Resveratrol and Freeze-Dried Grape Preparation*, Joseph M. Wu, New York Medical College
25. *Grape Antioxidant Impact on Heart Failure Pathogenesis*, Steven Bolling, University of Michigan
26. *Effects of Freeze-Dried Powder on WNT Signaling and Colon Cancer*, Randall Holcombe, University of California, Irvine
27. *Age-Related Blindness: Possible Prevention or Delay by Grape Powder*, Silvia Finneman, Weill Medical College
28. *Evaluation of Aromatase Inhibition Potential of Standardized Grape Powder*, Janet Olson, Mayo Clinic
29. *Effects of Resveratrol and/or Grape Powder on Estrogen Dependent Modulation of Lesion Area in a Rodent Model for Atherosclerosis and Restinosis*, Tammy Dugas, Louisiana State University
30. *Freeze-dried Grape Powder as a Potential Adjuvant in the Treatment of Rheumatoid Arthritis*, Srinvasa Raja, John Hopkins Hospital

31. *Effects of Freeze-Dried Table Grape Powder on Vascular Health in Post-Menopausal Women*, Carl Keen, University of California, Davis
32. *Effect of Grape Powder Supplementation on Inflammation Biomarkers in Human Volunteers*, Ishwarlal Jialal, UC Davis and Veteran's Administration Northern California Healthcare System
33. *Grape-Enriched Diets Reduce Metabolic Syndrome in Rats*, Stephen Bolling, University of Michigan
34. *Protective Effects of Grape Phytonutrients in a Model of Alzheimer's Disease* Jason Eriksen, University of Houston
35. *Neuroprotection in Age-Related Macular Degeneration (AMD) by Grape Extract*, Baerbel Rohrer, Medical University of South Carolina
36. *Grape Consumption Prevents Age-Related Blindness: Optimizing Course of Therapy and Identifying Target Organelles*, Silvia C. Finneman, Fordham University
37. *Are Grapes Neuroprotective in a Mouse Model of Stroke and Alzheimer's Disease?* Richard Hartman, Loma Linda University
38. *Does Grape Consumption Have Potential to Inhibit Hyperproliferative Effects of Colon-Specific Growth Factor/Infectious/inflammatory Agents?* Pomila Singh, University of Texas Medical Branch
39. *Anti-Inflammatory Activities of Grapes in Humans at Risk for Cardiovascular Disease*, Susan Zunino, USDA ARS Western Human Nutrition Research Center
40. *Chemoprevention of Esophageal Cancer with Grape Consumption: A Clinical Investigation in China*, Tong Chen, Ohio State Comprehensive Cancer Center
41. *Characterization of Critical Physical and Mechanical Properties of Lyophilized Grape Powder Required for Patient Delivery System*, Ken Morris, University of Hawaii , Hilo
42. *Grape Consumption Improves Joint Mobility and Relieves Pain Associated with Knee Osteoarthritis*, Shanil Juma, Texas Woman's University
43. *Grapes and Alzheimer's*, Edward Neafsey, Loyola University, Chicago