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Presentation Title:	Resveratrol and muscadine grape extract reduce radiation-induced bone marrow PU.1 gene loss and chromosome aberration frequency
Presentation Start/End Time:	Sunday, Apr 19, 2009, 1:00 PM - 5:00 PM
Location:	Hall B-F, Poster Section 2
Poster Section:	2
Poster Board Number:	19
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The purpose of this study was to 1) investigate if resveratrol (*trans*-3,5,4'-trihydroxystilbene) or a muscadine grape extract (MGE) containing resveratrol could reduce the frequency of radiation-induced PU.1 gene loss, 2) determine the optimal dose of resveratrol as a single agent for reducing radiation-induced chromosome aberration frequencies, and 3) determine the optimal MGE resveratrol dose for reducing radiation-induced chromosome aberrations in mouse bone marrow cells. Male CBA/CaJ mice, 9-10 weeks old, were divided into groups for the following treatments: 1) no treatment, 2) resveratrol only 3) MGE only, 4) radiation only, 5) resveratrol initiated before radiation (Res+RAD), 6) MGE started before radiation (MGE+RAD), and 7) resveratrol started 2 hours or 2 days after radiation (RAD>Res 2hrs or RAD>Res 2 days+). Irradiated mice received a 3-Gy dose of whole body gamma-radiation. The Res+RAD group received resveratrol (100 mg/kg) daily by gavage for 2 days prior to radiation exposure, with the third resveratrol dose administered 30 minutes before irradiation. Resveratrol administration continued mixed in the drinking water at a daily dose of 100 mg/kg. The MGE+RAD group received the MGE consistent with a total *trans*-resveratrol dose of 5.73 µg/kg by gavage for 2 days prior to irradiation as for Res+RAD. For the RAD>Res 2hrs, resveratrol (100 mg/kg) was a single dose 2 hours after irradiation and for RAD>Res 2 day+, resveratrol (100 mg/kg) was initiated 2 days after irradiation and continued. Bone marrow from groups of 5 mice was collected at 1 and 30 days post-irradiation and processed for fluorescent in-situ hybridization (FISH) PU.1 detection. Slides were blinded and 100 cells per mouse were scored. For the dose response studies, groups of 10 mice received doses of 5.75µg/kg and 1.50, 3.12, 6.25, 25, 50, or 100 mg/kg of resveratrol as a single agent or 0.9, 2.10, 5.73, 7.13, or 10.70 µg/kg of total *trans*-resveratrol in the MGE given for 2 days prior to irradiation. Bone marrow was harvested at 1 day and processed for cytogenetic evaluation with a total of 250 cells scored. Resveratrol and MGE initiated before irradiation and resveratrol started after irradiation significantly ($p<0.0001$) reduced PU.1 gene loss at 1 and 30 days. The optimum dose range of resveratrol for reducing chromosome aberrations was 3.12-25 mg/kg and for the MGE it was 2.10-7.13 µg/kg. These results demonstrate that resveratrol alone, or as found in combination with other bioactive factors in MGE is capable of significantly reducing radiation-induced PU.1 gene loss. The µg/kg doses of MGE resveratrol are superior to resveratrol alone in mg/kg or equivalent µg/kg doses of resveratrol as a single agent. Reduction of PU.1 gene loss and chromosome aberration frequencies in irradiated bone marrow cells suggests that resveratrol and MGE may protect against development of radiation-induced acute myeloid leukemia.

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