Resveratrol protects embryonic mesencephalic cells from *tert*-butyl hydroperoxide: EPR spin trapping evidence for a radical scavenging mechanism

Mark J. Burkitt[1], Jenny Karlsson[2], Mia Emgård[2] and Patrik Brundin[2]

[1]Gray Cancer Institute, PO Box 100, Mount Vernon Hospital, Northwood, Middlesex, HA6 2JR, United Kingdom; and [2]Section for Neuronal Survival, Wallenberg Neuroscience Center, Department of Physiological Sciences, Lund University, S-223 62 Lund, Sweden

In recent years, the antioxidant and other pharmacological properties of resveratrol (3,5,4′-trihydroxy-*trans*-stilbene), a polyphenol present in grapes and wine, have attracted considerable interest from the biomedical research community. In an examination of the potential neuroprotective properties of the compound, we have investigated the ability of resveratrol to protect rat embryonic mesencephalic tissue, rich in dopaminergic neurones, from the pro-oxidant *tert*-butylhydroperoxide. Using the EPR spin-trapping technique, the main radicals detected in cell suspensions were the *tert*-butoxyl and methyl radical-adducts of the spin trap 5,5-dimethyl-1-pyrroline-*N*-oxide, indicating one-electron reduction of the peroxide followed by a β-scission reaction.

The appearance of EPR signals from the trapped radicals preceded the onset of cytotoxicity, which was almost exclusively necrotic in nature. The inclusion of resveratrol in incubations resulted in the marked protection of cells from the peroxide. In parallel spin trapping experiments, we were able to demonstrate the scavenging of radicals by resveratrol, which involved direct competition between resveratrol and the spin trap for reaction with the radicals. To our knowledge, this is the first example in which cytoprotection by resveratrol has been demonstrated by EPR spin-trapping competition kinetics to be due to its scavenging of the radicals responsible for the toxicity of a pro-oxidant.

Supported by Pharmascience Inc. and the Cancer Research Campaign