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Poster presentation

Tumor initiating activity of NO donor in two-stage mouse skin carcinogenesis and its role of cGMP

Harukuni Tokuda*[1], Fumio Enjo[1], Ayako Kumagai[1], Takao Konoshima[2], Midori Takasaki[2], Junko Takayasu[1] and Hoyoku Nishino[1]

Address: [1]Department of Biochemistry and Molecular Biology, Kyoto Prefectural University of Medicine, Kyoto, Japan and [2]Department of Pharmacology, Chiba Institute of Science Chiba, Japan

Email: Harukuni Tokuda* - htokuda@koto.kpu-m.ac.jp

* Corresponding author

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The important physiological roles of nitric oxide (NO) suggest that donation of NO may be useful for treatment of several disease states. Some pharmacological NO donors, that they may serve as natural strange and transport forms for bioregulatory NO and currently in use for the biological generation of NO. Other important feature of NO is a mutagenic compound that can cause mutations in bacteria as well as chromosomal aberrations in rat primary lung cells. To examine the possible role of tumorigenicity in mouse skin tumor initiating, we tested the effect of one NO donor, (±)-E-Methyl-2-[(E)-hydroxyimino]-5-nitro-6-methoxy-3-hexenamide (NOR1) in two-stage mouse skin carcinogenesis. SENCARmice were initiated with single dose of 390 nmol NOR1 and promoted with 1.7 nmol TPA twice weekly for 20 weeks. Mice developed an average of 5 or 6 skin tumors/mouse and an 100 % tumor incidence. On the course of studies of signaling pathway for carcinogenesis, western blotting analysis of qualified epidermal particule protein showed that H-Ras, MEK, p38 and cGMP expression in mouse skin were abnormal responsible for NOR1 treatment in a time- and dose-dependent matter. We posturate that these data suggest possible role of MAP pathway and cGMP as regulatory mechanism of potent activity in NO donor induced carcinogenesis.