

Intracellular generation of hydrogen peroxide by 6-formylpterin and induction of biological responses in transformed and non-transformed cells

Keisuke Makino¹ and Toshiyuki Arai²

¹International Innovation Center, Kyoto University, Yoshida-honmachi, Sakyo-ku, Kyoto 606-8501, Japan; ²Department of Anesthesia, Kyoto University Hospital, 54 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto 606-8507, Japan

6-Formylpterin is known as a potent XOD inhibitor with an inhibition constant (K_i) of approximately 0.6 nM (1, 2). Although 6-formylpterin does not usually occur in vivo, it is produced from folic acid in vivo in some pathological conditions, such as carcinoma (3). Recently, we showed that 6-formylpterin reacted with reducing agents in the cells, such as NADH, and intracellularly generated H₂O₂ which induced apoptosis in HL-60 cells, suppressed cell proliferation in PanC-1 cells and inhibited Fas-mediated apoptosis in Jurkat cells. The induction of apoptosis and the suppression of cell proliferation were observed when high concentrations of 6-formylpterin (greater than 1 mM) was applied to the cells and the inhibition of Fas-mediated apoptosis was observed when relatively low concentrations of 6-formylpterin (up to 500 mM) were applied (4). Although these biological responses were all observed in the transformed cell lines, we also showed that the intracellular H₂O₂ generation by 6-formylpterin occurred in human neutrophils and that the increased H₂O₂ restored the impaired bactericidal activity of the diphenyleneiodonium (DPI)-treated neutrophils (5). Further, now we just demonstrated that 6-formylpterin inhibits the drug-induced hepatocyte apoptosis and suppresses the T cell immune responses. These properties of 6-formylpterin may be serve as a therapeutic agent in some diseases.

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