

9,10-フェナンスリジン類による HCT-116 および HL-60 細胞のアポトーシスの誘導

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Effect of the Orthoquinone Moiety in 9, 10-Phenanthrenequinone on the Ability to Induce in HCT-116 and HL-60 Cells

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ABSTRACT: 9, 10-Phenanthrenequinone (9, 10-PQ) is one of the most abundant quinones among diesel exhaust particulates. Recent data have suggested that quinones induce apoptosis in imine, epithelial and tumor cells, leading to respirator illness; however, the mechanisms by which quinones induce apoptosis and the structure required for this remain unknown. We studied the antitumor activity of 9, 10-Q analogs against two human tumor cell lines, HCT-116 colon tumor cells and HL-60 promyelocytic leukemia cells. The loss of the cis-orthoquinone unit in 9, 10-PQ abrogated its ability to induce apoptosis in the two tumor cell lines, and the IC₅₀ values of these analogs were indicated over 10 μM. An analog of 9, 10-PQ in which the biaryl unit had been deleted displayed a reduced ability to induce tumor cell apoptosis, while the analogs 1, 10-phenanthroline-5, 6-dione and pyrene-4, 5-dione, which also had modified biaryl units, exhibited increased tumor cell apoptotic activity. The cis-orthoquinone unit in 9, 10-PQ was identified as essential for its ability to induce apoptosis in tumor cells, and its biaryl unit is also considered to influence orthoquinone-mediated apoptotic activity.

抄録 排気ガスの有害物質の一つである9,10-フェナンスレンキノン (9,10-PQ) は、癌細胞などのアポトーシスを誘導することが近年報告されてきているが、その活性発現構造などの詳細については未だ不明である。本報告において、ヒト大腸癌由来のHCT-116細胞およびヒト骨髄腫由来のHL-60細胞に対する9,10-PQ類の抗腫瘍活性発現構造について解析した結果、オルトキノ部位が *cis* 配置であること、さらにオルトキノ部位への芳香環が重要であることが明らかとなった。抗腫瘍活性の認められた9,10-フェナンスリジン類について、その活性発現機序を解析したところ、caspase-3の活性化に伴うアポトーシスの誘導によることが示唆された。

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