

ブナシメジ由来ポリテルペンの HL-60 白血病細胞におけるアポトーシス誘導機構

Mechanism of Apoptosis Induced by Polyterpene from Buna-shimeji (*Hypsizigus marmoreus*) in HL-60 Cells

Hypsiziprenol A₉ is a polyterpene isolated from the fruiting body of the Japanese edible mushroom Buna-shimeji (*Hypsizigus marmoreus*). Although our recent studies revealed that hypsiziprenol A₉ has strong anti-tumor activity against tumor-bearing mice, its mechanism of action remains unclear. To elucidate further its anti-tumor action, we examined in detail hypsiziprenol A₉-induced apoptosis in human cancer cell lines.

We observed that hypsiziprenol A₉ strongly inhibited the growth of human promyelocytic leukemia HL-60 cells and several other cancer cell lines in a dose-dependent manner. Hoechst 33342 staining showed DNA fragmentation and condensation of chromatin in HL-60 cells treated with hypsiziprenol A₉. DNA laddering, a hallmark of apoptosis, was detected using agarose gel electrophoresis. In addition, flow cytometric analysis confirmed that hypsiziprenol A₉ increased sub-G₁/G₀ populations in a time-dependent manner. Hypsiziprenol A₉ also increased activities of caspase-2, -3, -8 and -9 in a dose-dependent manner in the apoptotic HL-60 cell. Furthermore, JC-1 fluorescent staining determined that hypsiziprenol A₉-induced apoptosis was associated with a loss of mitochondrial membrane potential.

These results suggest that hypsiziprenol A₉ inhibits the growth of HL-60 cells by inducing apoptosis that is mediated through mitochondrial membrane potential loss and caspase activation.