Anti-tumor effect of arsenic trioxide in murine xenograft model

Mariko Kito, *[1]Kenji Matsumoto, *[1]Naoko Wada, *[2]Shoji Futatsugawa, *[3]Kouichiro Sera, *[1]Yoshinori Nozawa, *[1]Yukihiro Akao

Institute of Applied Biochemistry
Yagi Memorial Park Mitake Kani-gun Gifu 505-0116 Japan

*1 Gifu International Institute of Biotechnology
1-1 Naka-fudogaoka Kakamigahara Gifu 504-0838 Japan

*2 Takizawa Laboratory, Japan Radioisotope Association
348-1 Tomegamori Takizawa 020-0173 Japan

*3 Cyclotron Research Center, Iwate Medical University
348-58 Tomegamori Takizawa 020-0173 Japan

Abstract

Arsenic trioxide, As_2O_3 (ATO), has been established to be an effective agent for acute promyelocytic leukemia but its effect on solid tumors has not been fully explored. In the present study of murine xenograft system, we found that ATO significantly inhibited tumor growth of human hepatocellular carcinoma cell line HuH7 by both of intravenous and intratumor injection. Pathological examination revealed that ATO induces severe cell death in the tumor cells and affects the tumor angiogenesis. Some of dead cells showed the characteristic features of apoptosis, which was evaluated by TUNEL in intratumor ATO-treated mice. The measurment by using Particle induced X-ray emission revealed that after intravenous injection of ATO, arsenic accumulated in tumor than in brain, kidney or liver. Thus, the effects of ATO on tumor *in vivo* are multiple which include inhibition of tumor growth, induction of apoptosis, and inhibition of angiogenesis, suggesting that ATO has a great potential for the treatment of solid tumors as a novel chemotherapeutic agent.