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The Physiological Effect of Cold Atmospheric Pressure Plasma on Cancer Cells, Cancer Stem Cells, and Adult Stem Cells

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Abstract : Cold Atmospheric Pressure Plasma (CAPP) is defined as a partially ionized gas with electrically charged particles at room temperature and atmospheric pressure. CAPP generates reactive oxygen species (ROS) and reactive nitrogen species (RNS), and has potential as a new apoptosis-promoting cancer therapy. With an annular type dielectric barrier discharge (DBD) CAPP-generating device combined with a helium (He) gas feeding system, we showed that CAPP selectively induced apoptosis in various cancer cells while it promoted proliferation of the adipose tissue-derived stem cell (ASC). The apoptotic effect of CAPP was highly selective toward p53-mutated cancer cells. The intracellular ROS was mainly responsible for apoptotic cell death in CAPP-treated cancer cells. CAPP induced apoptosis even in doxorubicin-resistant cancer cell lines, demonstrating the feasibility of CAPP as a potent cancer therapy. With the same device and exposure conditions to cancer cells, CAPP stimulated proliferation of the ASC, a kind of mesenchymal stem cell that is capable of self-renewing and differentiating into adipocytes, chondrocytes, osteoblasts and neurons. CAPP-treated ASCs expressed the stem cell markers and differentiated into adipocytes as untreated ASCs. The increase of proliferation by CAPP in ASCs was offset by a NO scavenger but was not affected by ROS scavengers, suggesting that NO generated by CAPP is responsible for the activated proliferation in ASCs. Usually, cancer stem cells are reported to be resistant to known cancer therapies. When we applied CAPP of the same device and exposure conditions to cancer cells to liver cancer stem cells (CSCs) that express CD133 and epithelial cell adhesion molecule (EpCAM) cancer stem cell markers, apoptotic cell death was not examined. Apoptotic cell death of liver CSCs was induced by the CAPP generated from a device with an air-based flatten type DBD. An exposure of liver CSCs to CAPP decreased the viability of liver CSCs to a great extent, suggesting plasma be used as a promising anti-cancer treatment. To validate whether CAPP can be a promising anti-cancer treatment or an adjuvant modality to eliminate remnant tumor in cancer surgery of vestibular schwannoma, we applied CAPP to mouse schwannoma cell line SC4 Nf2 -/- and human schwannoma cell line HEI-193. A CAPP treatment leads to anti-proliferative effect in both cell lines. We are currently studying the molecular mechanisms of differential physiological effect of CAPP; the proliferation of ASCs and apoptosis of various cancer cells and CSCs.

Keywords : cold atmospheric pressure plasma, apoptosis, proliferation, cancer cells, adult stem cells
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