Abstract

Autocrine Growth Hormone-Triggered Curcumin Resistance Abolished by NF-κB Signaling Pathway Dependent on Inflammatory Cytokines and Active Polyamine Catabolic Machinery in MCF-7, MDA-MB-453 and MDA-MB-231 Breast Cancer Cells †

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† Presented at the 2nd International Conference on Natural Products for Cancer Prevention and Therapy, Kayseri, Turkey, 8–11 November 2017.

Published: 16 November 2017

Abstract: Autocrine Growth Hormone (GH) induces cell growth, proliferation metastasis in breast cancer. Curcumin is a promising therapeutic agent in cancer through affecting different molecular targets. Our aim was to demonstrate the molecular machinery of curcumin-mediated apoptosis in autocrine GH + MCF-7, MDA-MB-453 and MDA-MB-231 breast cancer cells (BCCs). Stable GH expressing BCCs were generated by GH gene insert PC3.1 plasmid transfection and Neomycin selection. Although GH + cells are resistant to curcumin treatment, dose-dependent drug exposure decreased cell viability, inhibited colony formation, invasion-metastasis via suppressing GH expression in each BCCs. Anti-hormonal concentration of curcumin (20 µM for MCF-7, MDA-MB-453 and 25 µM for MDA-MB-231) inhibited NF-κB p65 (Ser 536) phosphorylation and decreased DNA binding activity of NF-κB p65 in autocrine GH expressing BCCs. In addition, autocrine GH-mediated IL-1α, IL-6, IL-1β pro-inflammatory cytokine expressions downregulated by curcumin treatment. Moreover, curcumin overcome autocrine GH triggered drug resistant and induced caspase-mediated apoptotic cell death through activating Polyamine (PA) catabolic pathway enzymes which led to generation of toxic by-products such as H2O2 in MCF-7, MDA-MB-453 and MDA-MB-231 GH + BCCs. In conclusion, curcumin could overcome GH-mediated resistant phenotype via modulating NF-κB-mediated inflammatory cytokine expression and PA catabolic machinery activation in breast cancer cells.

Keywords: breast cancer; curcumin; Polyamine; NF-κB; apoptosis

Conflicts of Interest: The authors declare no conflict of interest.