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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 †

Ajda Çoker Gürkan *, Merve Çelik, Merve Uğur, Elif Damla Arisan, Pinar Obakan Yerlikaya and Narçın Palavan Ünsal

Department of Molecular Biology and Genetics, Faculty of Science and Letters, Istanbul Kultur University, Istanbul 34156, Turkey

* Correspondence: a.coker@iku.edu.tr; Tel.: +90-(212)-498-45-65

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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 H_2O_2 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

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