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A Novel YC-1 Analogs, CLC, Induces MDA-MB-468 Human Breast Cancer Cell Apoptosis through Induction of G0/G1 Arrest and Up-regulation of Death-Receptor and Mitochondria Signaling Pathways

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In this study, we developed a novel YC-1 analog, CLC, to investigate the cell growth inhibition and apoptotic responses in MDA-MB-468 human breast cancer cells. CLC significantly reduced cell viabilities of MDA-MB-468 cells in time and dose-dependent manners. CLC caused G0/G1 arrest by inhibition cyclin-dependent kinase 2, 4 and 6 activities. CLC decreased the protein levels of Cyclin A, D and E by western blot. CLC induced DNA damage and apoptosis in MDA-MB-468 cells by using determination of morphologic changes and DAPI staining. Results from caspase activities assays and western blot analyses showed that activities of caspase-8, caspase-9 and caspase-3 were increased in CLC-treated MDA-MB-468 cells. HMJ-30-induced cell death was mediated both death-receptor and mitochondria-dependent apoptotic pathways in MDA-MB-468 cells. CLC induced early phosphorylation of p53Ser18 through ATM activation in MD-AMB-468 cells. In conclusion, CLC-induced G0/G1 arrest and apoptosis in MDA-MB-468 cells are involved in cyclin/CDK activities, death-receptor and mitochondria signaling pathways