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Novel 1,5-diphenyl-6-substituted 1H-pyrazolo[3,4-d]pyrimidin-4(5H)-ones induced apoptosis in RKO colon cancer cells

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Novel 1,5-diphenyl-6-substituted-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-ones were synthesized and characterized. All compounds were screened for their anti-proliferative activities in five different cancer cell lines. The results showed that compounds 7a and 7b comprising aminoguanidino or guanidino moiety at position 6 inhibited proliferation of RKO colon cancer cells with IC50 of 8 and 4 μM, respectively. Compounds 7a and 7b induced apoptosis in RKO cells, which was confirmed by TUNEL and annexin V-FITC assays. Flow cytometric analysis indicated that compounds 7a and 7b arrested RKO cells in the G1 phase and the most active compound 7b increased levels of p53, p21, Bax, ERK1/2 and reduced levels of Bcl2 and Akt. Compound 7b also activates release of cytochrome c, which is consistent with activation of caspase-9. Additionally, compound 7b increased caspase-3 activity and cleaved PARP-1 in RKO cells. Collectively, these findings could establish a molecular basis for the development of new anti-cancer agents.

Biography

Ahmed M Malki received his PhD in Biochemistry in 2006 in the field of Molecular Oncology from Edison Institute of Biotechnology, Biochemistry Department, Ohio University in USA. Dr Malki awarded best publication from Biochemistry Department, Ohio University in 2005. Dr Maki held postdoctoral position at University of California Berkeley, USA via NIH grant in 2007. Dr Malki has more than 20 years of experiences in academia teaching undergraduate, graduate courses, supervising students and applied research. Dr Ahmed M Malki received his PhD in Biochemistry in 2006 in the field of Molecular Oncology from Edison Institute of Biotechnology, Biochemistry Department, Ohio University in USA. Dr Malki awarded best publication from Biochemistry Department, Ohio University in 2005. Dr Maki held postdoctoral position at University of California Berkeley, USA via NIH grant in 2007. Dr Malki has more than 20 years of experiences in academia teaching undergraduate, graduate courses, supervising students and applied research.. Dr Malki was appointed as Head of Molecular therapeutics laboratories at centre of excellence at City of Research and Technology in 2009 in Egypt and Associate Professor of clinical biochemistry in Alexandria University. Dr Malki also received Best Research Award, Global Breast Cancer conference, 2011, Seoul, South Korea and Alexandria University Award for Scientific encouragement in 2012. Dr Malki has received best poster award at Annual research Day 2014, QU research forum 2015 and 2016. Dr Malki awarded international and national grants for discovery of novel small molecules targeting cancer cells; he has many peer reviewed international publications and He is serving in editorial board member in number of international journals. Dr Malki presented his research as invited speaker at international conferences and professional meetings. The central theme of Dr Malki' s research focuses on the understanding of the signaling pathways that regulate cell proliferation, cell death and designing novel anticancer drugs targeting p53. Dr Malki supervised more than 25 master students in the field of molecular therapeutics. Dr Malki was appointed as coordinator of Master Biomedical Science program from 2013-2015 and he is currently appointed as Acting Associate Dean for Academic Affairs for the college of Health Sciences.) Dr Malki was appointed as Head of Molecular therapeutics laboratories at centre of excellence at City of Research and Technology in 2009 in Egypt and Associate Professor of clinical biochemistry in Alexandria University. Dr Malki also received Best Research Award, Global Breast Cancer conference, 2011, Seoul, South Korea and Alexandria University Award for Scientific encouragement in 2012. Dr Malki has received best poster award at Annual research Day 2014, QU research forum 2015 and 2016. Dr Malki awarded international and national grants for discovery of novel small molecules targeting cancer cells; he has many peer reviewed international publications and He is serving in editorial board member in number of international journals. Dr Malki presented his research as invited speaker at international conferences and professional meetings. The central theme of Dr Malki' s research focuses on the understanding of the signaling pathways that regulate cell proliferation, cell death and designing novel anticancer drugs targeting p53. Dr Malki supervised more than 25 master students in the field of molecular therapeutics. Dr Malki was appointed as coordinator of Master Biomedical Science program from 2013-2015.

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