19th International Conference on Traditional Medicine and Acupuncture
10th International Conference on Pharmaceutical Research and Drug Discovery
25th Global Biotechnology Conference

October 25, 2022 | Webinar

Abdelkader E Ashour

King Salman International University, Egypt

CARP-1 functional mimetics are novel pro-apoptotics and inhibitors of cancer cell growth and metastasis

CARP-1/CCAR1 is a peri-nuclear phospho-protein which functions as a co-activator of the cell cycle regulatory anaphase promoting complex/cyclosome (APC/C) E3 ligase. CARP-1 functional mimetics (CFMs) are a class of small molecule compounds that inhibit CARP-1 binding with APC/C subunit APC-2. CFM-4, a lead compound, was found to be a potent antitumor agent that suppresses growth and metastasis of various tumor cells including medulloblastoma, neuroblastoma, malignant pleural mesothelioma, lung and breast cancers, in part by stimulating apoptosis. Recently, we examined the possible inhibitory effects CFM-4 against proliferation and metastasis of colorectal cancer (CRC). CRC constitutes one of the most aggressive malignancies worldwide. Existing anti-tumor treatments clinically applied for CRC include surgery, radiotherapy and chemotherapy. The high incidence of metastasis and toxic side effects of therapies, as well as low response rates of CRC to chemotherapy indicate that existing treatment methodologies remain unsatisfactory. Thus, it is crucial to develop more efficient and less noxious treatment modalities for this disease. In this recent study, we investigated the growth inhibitory potential of the CFM-4 on CRC and found that CFM-4 inhibits colon cancer cell proliferation in a dose and time dependent manner. To molecularly assess the effects of CFM-4 as antitumor agent against human colorectal HT-29 cells, mRNA expression analysis by qPCR was also utilized. Results revealed upregulation of expression of caspase-8 and caspase-9, as well as p53 and its downstream targets, PUMA, Noxa, Smac which play a crucial part in promoting mitochondrial apoptotic pathway. These results suggest that CFM-4 induces both intrinsic and extrinsic pathways of apoptosis. The influence of CFM-4 on mRNA expression of the NF-?B signaling inhibitor A20-binding inhibitor protein (ABIN1) was also assessed and revealed upregulated. Although CFM-4 did not significantly affect the expression of the PI3K downstream effector AKT, it remarkably upregulated the PI3K negative regulator PTEN. Moreover, we examined CFM-4 effects on colon cancer cell cycle and observed that CFM-4 has significantly induced G2/M phase arrest and dose-dependent increase in sub-G1 peak, indicative of apoptosis, of the cell cycle of the colon cancer HT-29 cells, further substantiating our Annexin V/PI apoptosis results. Furthermore, western blot analysis results revealed that CFM-4 enhanced expression of CARP-1, as well as the initiator caspase, caspase-8, and the executioner caspase, caspase-3. On the other hand, metastatic properties of the HT-29 CRC cells were reduced by CFM-4 through blocking their capabilities to form colonies, migrate and invade through the matrix-coated membranes. These results revealed that the potent antitumor and anti-metastatic properties of CFM-4 against CRC are due to collective pro-apoptotic, anti-proliferative and anti-invasive activities. Together our data warrants further investigations of CFM-4 as potential anti-tumor agent for CRC malignancy and metastasis.

Biography

Abdelkader E Ashour has obtained his PhD degree from the University of Nebraska Medical Center (UNMC) at Omaha, NE, USA in 2006 and performed postdoctoral studies at UNMC. During his stay at USA, He received numerous awards, including the prestigious Harris Award for Excellence and Outstanding Work in Cancer Research. He was and still is collaborating with top-notch scientists, including Dr. Arun K. Rishi from Wayne State University at Detroit, MI, USA. He has published 72 research papers in reputed journals plus 5 submitted/in preparation manuscripts.

aeashour@gmail.com

Received Date: September 6, 2022; **Accepted Date:** September 8, 2022; **Published Date:** October 31, 2022