Targeting the AKT/mTOR/STAT3 pathways through a ROS-dependent Ubiquitin proteasome degradation in breast cancer by the natural polyphenol compound, carnosol

Rabah Iratni, Hussain El Hasasna and Halima Al Samri
Department of Biology, College of Science, United Arab Emirates University. Po. Box: 15551, Al Ain, UAE

Abstract

We have previously showed that carnosol significantly inhibited the viability and colony growth of triple negative breast cancer cells and induced ROS-dependent Beclin-1-independent autophagy and subsequent apoptotic cell death. Here were analyzed the molecular mechanism through which carnosol exerts its anti-cancer activity. Mechanistically, we found that carnosol inactivated the AKT/mTOR pathway by promoting the proteasome-dependent degradation of both proteins. Strikingly, we also found that carnosol target Stat3 to degradation. Proteasome inhibition restored these proteins to level comparable to control cells. The proteasomal degradation of mTOR, which occurred as early as 30 minutes post-carnosol treatment was concomitant with an overall increase in the level of ubiquitinated proteins and translated stimulation of proteolysis by the proteasome. Interestingly, we found that treatment of the breast cancer cells with N-acetylcysteine, a ROS inhibitor, not only restored AKT/mTOR/Stat3 proteins to level comparable to control cells, but also dramatically reduced carnosol-induced cell death and blocked the activation of autophagy and apoptosis. Our findings demonstrate that carnosol exerts its anti-breast cancer activity through stimulation ubiquitin proteasome system which consequently triggers both autophagy and apoptosis, making it a potential and valuable source of novel therapeutic cancer drug.

Biography

Prof. Rabah Iratni has completed his PhD in Cellular and Molecular Biology from University Joseph Fourier Grenoble 1 (France) and postdoctoral studies from University of Medicine and Dentistry of New Jersey (USA). He is currently a professor at the the United Arab Emirates University. His lab focuses on the discovery of new biologically active natural products, to evaluate their potential as therapeutic agents against breast cancer and determine their mechanism(s) of action. He also have a strong interest in the understanding of the epigenetic basis of cancer with focus on breast cancer. He has authored several papers in prestigious journals including Cell, Science, Molecular Cell, Genes & Development, PNAS etc.

Presenting author details
Full name: Rabah Iratni
Contact number:+971 713 6526
Email: R_iratni@uaeu.ac.ae
Category: (Oral presentation or Poster presentation)

جامعة الإمارات العربية المتحدة
United Arab Emirates University UAEU