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Young-Seuk Bae, J Clin Exp Oncol 2017, 6:6
DOI: 10.4172/2324-9110-C1-006

JOINT EVENT ON
20th Euro-Global Summit on
Cancer Therapy & Radiation Oncology
and
2nd International Oncologist & Diagnostics Conference
August 28-30, 2017 Brussels, Belgium

# Inactivation of the FoxO3a transcription factor is associated with the production of ROS during protein kinase CK2 downregulation-mediated senescence in human colon cancer and breast cancer cells

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Cellular senescence can be defined as an irreversible arrest at the G1 phase of the cell cycle. It can be triggered by telomere shortening or nontelomeric DNA damage. Various forms of stress, including reactive oxygen species (ROS) and oncogenic activation, induce DNA damage that results in the stabilization of p53 and subsequent overexpression of p21Cip1/WAF1 that proceeds to inhibit cell cycle progression. Therefore, it has been assumed that cellular senescence is a profitable, compensatory response aimed at avoiding the propagation of damaged and potentially tumorigenic cells. We previously showed that protein kinase CK2 downregulation mediates senescence through the reactive oxygen species (ROS)–p53–p21Cip1/WAF1 pathway in various human cells. In addition, because the number of senescent cells increases with organism aging, cellular senescence is widely believed to play an important role in aging. In the present study, we investigated whether the FoxO3a transcription factor is associated with ROS production during CK2 downregulation-induced senescence in human colon cancer HCT116 and breast cancer MCF-7 cells. FoxO3a overexpression suppressed ROS production and p53 stabilization induced by a CK2α knockdown. CK2α downregulation induced nuclear export of FoxO3a through stimulation of AKT-mediated phosphorylation of FoxO3a and decreased transcription of its target genes (Cu/ZnSOD, MnSOD, and catalase). In contrast, CK2α overexpression inhibited AKT-mediated FoxO3a phosphorylation. This resulted in nuclear accumulation of FoxO3a, and elevated expression of its target genes. Therefore, these data indicate for the first time that CK2 downregulation stimulates ROS generation by inhibiting FoxO3a during premature senescence in human colon and breast cancer cells.

## Biography

Young-Seuk Bae has his expertise in evaluation and passion in improving strategy for cancer chemotherapy. He has built this model after years of experience in research, evaluation, and teaching in Kyungpook National University, South Korea. He has shown a new senescence signaling pathway that specifically involves CK2. CK2 downregulation leads to ROS generation with subsequent activation of p53 and p21Cip1/WAF1. These observations are novel and will provide a new understanding of cellular senescence as well as novel diagnostic and therapeutic options for the treatment of various tumors.

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