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Qiou Wei

University of Kentucky College of Medicine, USA

Targeting sulfiredoxin in colorectal cancer

Colorectal cancer is the third most common cancer and the second leading cause of cancer death in both men and women. Sulfiredoxin (Srx) is a unique reductase that restores the peroxidase activity of peroxiredoxins (Prxs) by reducing the hyperoxidized, inactive form of Prxs back to their active, reduced form. To understand the role and mechanism of Srx in colorectal cancer development, we studied the functional significance of Srx in colon tumorigenesis, cancer invasion and metastasis using human patient primary specimens, cell culture as well as mouse models. We demonstrate that Srx is highly expressed in primary specimens of human colorectal cancer patients, and such abnormally high expression of Srx enhances cancer invasion in culture and drives cancer metastasis in a mouse orthotopical implantation model. Moreover, we also demonstrate that genetic depletion of Srx protects mouse from carcinogen-induced colon cancer development. Mechanistically, we reveal that loss of Srx sensitizes cancer cell to oxidative stress induced cell death, whereas the presence of Srx enhances the activation of mitogen activated protein kinase signaling through increasing the C-terminal tyrosine phosphorylation levels of the epidermal growth factor receptor (EGFR). This function of Srx is mediated through its inhibition of EGFR acetylation, a novel post-translational modification of EGFR in human CRC cells identified by liquid chromatography-electrospray ionization-tandem mass spectrometry analysis. Taken together, our data suggest that Srx promotes CRC cell invasion and metastasis through a novel mechanism of enhancing EGFR signaling, and it may thus be used as a potential target to develop molecular therapeutics for the treatment of colorectal cancer in patients.

Biography

Qiou Wei after obtaining his MD from Chongqing Medical University and PhD from the University of South Dakota, did his Post-doctoral training at Harvard Medical School and National Cancer Institute. Currently, he is a tenure-track Assistant Professor at the Department of Toxicology and Cancer Biology and an active Member of the Markey Cancer Center, the University of Kentucky College of Medicine. He studies the fundamental mechanisms of cancer invasion and metastasis with the ultimate goal of identifying small molecules that can be used to block the process of tumorigenesis and cancer metastasis.

qiou.wei@uky.edu

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