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Cross-talk between two antioxidants, thioredoxin reductase-1 and hemeoxygenase-1 and therapeutic implications in multiple myeloma

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Multiple myeloma (MM) is characterized by an accumulation of abnormal clonal plasma cells in the bone marrow. Despite recent advancements in anti-myeloma therapies, MM remains an incurable disease with only a slight increase in the median survival rate to 5 years. Therefore, more effective therapies are needed. Antioxidant molecules are up-regulated in many human cancers, correlating with tumor proliferation, survival and drug-resistance and therefore, have been suggested as potential therapeutic targets. This study investigated the cross-talk between two major antioxidant molecules, thioredoxin reductase 1 (TrxR1) and hemeoxygenase-1 (HO-1) and their therapeutic implications in MM. We found that TrxR1 levels are up-regulated in MM cells compared to normal cells. We therefore tested the effect of TrxR1 inhibition using a specific inhibitor, auranofin, on MM cell growth. Although auranofin significantly inhibited TrxR1 activity at the lower concentrations, MM cell proliferation was only inhibited at the higher concentrations of auranofin. Inhibition of TrxR1 activity up-regulated another oxidative stress-responsive protein HO-1, which has been shown to act as a secondary anti-apoptotic protein. Inhibition of TrxR1 in conjunction with HO-1 significantly inhibited MM cell growth and induced apoptosis. Thus, HO-1 acts as a secondary anti-apoptotic mechanism in MM. Results showed that TrxR1 regulates HO-1 via the Nrf2 signaling pathway. These findings indicate that TrxR1 alone or in conjunction with HO-1 may serve as an effective therapeutic target to treat MM. Hence, this research highlights how understanding the cross-talk between these antioxidant systems may help in designing more effective therapeutic strategies to cure MM.

Biography

Prahlad V Raninga has completed M Res at University of East Anglia, England, and currently pursuing PhD at Griffith University, Australia. His main research interests include cancer biology, cell signaling and molecular cancer therapeutics. His current research is focused onto investigate the therapeutic potential of the antioxidant molecules to treat myeloma. He has published two first author papers in the reputed oncology journals during his early PhD candidature.

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