Sirtuin1 deacetylated and stabilized DNA damage repair (XRCC1) to promote chemoresistance in cancer

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Chemoresistance is one of the most important challenges in the clinical management of lung cancer. SIRT1 is a NAD dependent protein deacetylase and implicated in diverse cellular processes such as DNA damage repair, and cancer progression. SIRT1 is upregulated in chemo resistant lung cancer cells, genetic knockdown or chemical inhibition of SIRT1 reversed chemoresistance by enhancing DNA damage and apoptosis activation, accompanied with XRCC1 degradation. E3 ligase β-TrCP catalyzed the poly-ubiquitination of XRCC1 to promote its proteasome-dependent degradation. SIRT1 bound and deacetylated XRCC1 at lysine K260, K298 and K431, preventing it from β-TrCP-dependent ubiquitination. Mutations of these three lysine sites in XRCC1 abrogated the interaction with β-TrCP and prolonged the half-life of XRCC1 protein. Here we describe SIRT1 confers chemoresistance to lung cancer cells by deacetylating and stabilizing XRCC1. Therefore, targeting SIRT1 might be a new strategy to manage the chemoresistance of lung cancer, and probably other cancers.

Speaker Biography

Neelum Aziz Yousafzai has completed her PhD in Oncology from Zhejiang University, China. Her expertise in cancer diagnosis and therapy development approaches to improving human health. Her open and contextual evaluation model based on responsive constructivists creates new pathways for improving healthcare. She has great experience in research, clinical, teaching and administration, both in hospital and education institutions. She has published several research articles in well-known journals and delivered talks on national and international forum. Her areas of interest are oncology, molecular biology, immunology, biotechnology, pathology and genetics.

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