

5th Asia-Pacific Summit on
Cancer Therapy

July 20-22, 2015 Brisbane, Australia

Inverse regulatory role of p53 modulating human sodium iodide symporter gene expression in breast cancer

Madhura G Kelkar, Sushmita Chatterjee, Abhishek Derle and Abhijit De
Advanced Centre for Treatment Research and Education in Cancer, India

Human Sodium Iodide Symporter mediated (NIS) radio iodide accumulation is the basis of effective targeted radio iodide therapy in differentiated thyroid cancers. NIS is aberrantly expressed in majority of the breast cancer (BC) subtypes although its relevance and regulation is poorly understood. To get an insight on NIS transcriptional regulation, we have identified the presence of three putative regulatory p53-binding sites on full-length human NIS promoter by genome wide *in silico* analysis. Since p53 mutations in BC are frequently observed, we have investigated the role of p53 in NIS regulation. Over expression of wild type p53 as a transgene or activation of endogenous p53 by doxorubicin (DR) treatment in BC cell lines results in significant reduction of promoter activity. Further the siRNA-mediated p53 knockdown effect shows reversal on reduced transcript ($p < 0.005$). Abrogation of p53 binding sites by site directed mutagenesis also results in significant increase in promoter activity ($p < 0.05$) indicating NIS-promoter repression is p53-dependent. Further, direct binding of p53 to human NIS promoter is also confirmed by chromatin immunoprecipitation analysis. As a result of endogenous p53 activation by DR, cellular NIS protein content is also reduced and thus impacting NIS-mediated iodide uptake significantly ($p < 0.05$). Further, DR drug effect is validated in breast cancer xenograft model by optical bioluminescence imaging. This study provides novel information revealing complete biochemical and functional basis to show that human NIS is a direct target of p53 in BC cells. Our study opens up a scope for establishing link between aberrant NIS expression and p53 mutations in BC patients.

Biography

Madhura G Kelkar has completed her Master's degree in Life Sciences from Mumbai University. She has cleared national level entrance exams including GATE and CSIR-UGC-NET. Currently, she is enrolled to Homi Bhabha National Institute (HBNI) for the Doctorate study. During her PhD course, she has published papers in peer-reviewed reputed journals like *Current Opinion in Pharmacology* and *Cell*. She had also attended national and international conferences.

mkelkar@actrec.gov.in

Notes: