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A novel therapeutic approach for triple-negative breast cancer

Triple–negative breast cancer (TNBC) is frequently diagnosed in younger women and is highly aggressive with early pattern of metastasis, limited treatment options, and poor prognosis. A recent study showed that blocking glucocorticoid receptor (GR) activity could potentiate chemotherapy-induced cytotoxicity in TNBC. However, due, in part, to mainly targeting GR's activation function domain, AF2 and largely overlooking AF1 activity, cell/tissue-specific efficacy of GR antagonists has been low. It thus is axiomatic that attempts to precisely control GR activity in TNBCs without controlling AF1 activity will be of limited success. We recently showed that the antagonist-bound receptor, which blocks coactivator interactions with AF2, opens AF1 surfaces for such interactions with coactivators including SRC-1. We also reported that TBP-induced AF1 conformation suits for SRC-1 interaction and subsequent transcriptional activity. Our western blot data also showed that the level of TBP and SRC-1 are higher in MDA-MB-231, TNBC cells compared to MCF-7 cells. Increased Expression of TBP and SRC-1 have been suggested to contribute to oncogenesis in breast cancers. Interestingly, the level of GR expression is constitutively higher in the nucleus of MDA-MB-231 cells compared to MCF-7 suggesting that the GR in TNBC may be transcriptionally active even in the absence of an endogenous hormone. Therefore the role of TBP/SRC-1/AF1 in modulating GR-mediated specific gene regulation in TNBCs may be critical. We have identified a small peptide that can block GR AF1/TBP/SRC-1.It is expected that the results from these studies may provide a novel therapeutic strategy to inhibit TNBC tumor growth.

Biography

Raj Kumar received his PhD degree in Neuro-toxicology and is currently a Professor of Biochemistry at The Commonwealth Medical College, Scranton, PA, USA. His research area is focused on the therapeutic targeting of the steroid receptors (SRs) for endocrine-related cancers. Currently, his laboratory is working on a novel therapeutic strategy that could provide cell/tissue-specific target gene regulations in current SHR-based endocrine therapies. In addition to more than 100 publications to his credit, he has also served as Editorial Board Member of more than two-dozen scientific journals, and as expert reviewer on more than two-dozen grant review panels.

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