

Emerging Role of Protein Tyrosine Phosphatases in Cancer Therapy Resistance

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Abstract

Tyrosine phosphorylation of intracellular proteins is a kind of post-translational modification that regulates the signal transduction in cellular process. The dephosphorylation of protein tyrosine phosphatases (PTPs) on signal transduction proteins contributed their role as a convergent node to mediate cross-talk between signaling pathways. In cancer, PTPs-mediated pathways served as signaling hubs through which cancer cells alleviated stress following the clinical therapy, via promoting constitutive activation of growth-stimulatory signaling pathways or influencing the immune-suppressive tumor microenvironment. Preclinical evidences suggested that anticancer drugs will release their greatest therapeutic potency when combined with PTP inhibitors, reversing drug resistance that was responsible for clinical failures during cancer therapy. Here, this review elaborated recent insights that substantiated the role of PTPs-mediated pathways in resistance to targeted cancer therapy and immune-checkpoint therapy, leading to the proposal of targeting PTPs inhibition in anticancer combination therapy for long-term disease regression. Clinical trials have been initiated to evaluate the safety and efficacy of combination therapy in advanced-stage tumors.

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