

Analysis of Her2 Dependent Molecular Mechanisms which Cause Tamoxifen Resistance

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Abstract

Introduction: Tamoxifen resistance is the consequence of interactions between environmental factors, host factors and molecular mechanisms. There are various molecular mechanisms involving in the Tamoxifen resistance. In this review we will focus on receptor Her2 over expression and over activation and its' cytoplasmic growth signaling cascades and finally gene transcription alterations.

Methods: Near 50 articles about the role of Her2 in Tamoxifen resistance from 1994 to 2015 were studied. After denoting their eligibility, they were categorized in 3 parts; cell lines studies, animal models, and clinical studies.

Results: Activation of the components of Her2 growth signaling cascade including AKT, mTOR, SRC and Hh proteins family and suppression of PTEN has a notable effect on Tamoxifen resistance. Research results do not elucidate any significant difference between PIK3CA changes in resistant and sensitive tumor cells.

Discussion: Breast cancer cell growth relies on estrogen and estrogen receptor. Tamoxifen inhibits the cell proliferation as a result of estrogen receptor inhibition. On the other hand, Her2 growth signaling cascade over activity results in cell proliferation even in the presence of Tamoxifen. At last there are some evidences revealing that Tamoxifen acts as an agonist in breast cancer cells in such a specific circumstance.

Keywords: Breast Cancer, Tamoxifen Resistance, Her2 Signaling Cascade.