Apoptotic Effects of Niclosamide and Chemotherapies, with Potential to Overcome Drug Resistance in Triple Negative Breast Cancers

Lakhanpal, Geeta

Triple-negative breast cancers (TNBCs) are one of the most aggressive subtypes of breast cancer. They have a higher concentration of cancer stem cells, which leads to chemoresistance and a lower cure rate compared to non TNBC. Apoptosis, or programmed cell death is mediated by caspases (cysteine-aspartic proteases),through activation of procaspase(s), a self-amplifying cascade. This eventually leads to cleavage of several key proteins in cytoplasm and the nucleus, leading to apoptosis. PARP(polyADP-ribose polymerase)plays an important role in repair of single stranded DNA and is one of the substrates cleaved by both caspase activation.The presence of cleaved PARP(c-PARP),is a popular diagnostic tool for demonstration of apoptosis, since it indicates a functional caspase activation. Niclosamide, an FDA approved tenicide, inhibits Wnt-beta catenin pathway, an active pathway in TNBC and in stem cells signaling. I sought to compare levels of apoptosis induced by Niclosamide and other FDA approved drugs used in breast cancer treatment-Adriamycin, Taxol, Platinum compounds, in 2-LMP TNBC cell line, using cytotoxicity assay and c-PARP on Western Blot. Niclosamide induced apoptosis even at 1uM concentration. Taxol was more active than Niclosamide at 10uM concentration. Platinum compounds did not have any significant apoptotic effect in 2-LMP cell line. There may be a potential role for combining Niclosamide with other agents.

Awards Won: