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New insights into the pathogenesis of ovarian cancer: Oxidative stress

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Lack of prognostic markers for the early detection of ovarian cancer as well as for chemoresistant ovarian cancer remains a major challenge in the treatment of this disease. Understanding the biological significance of the relationship between oxidative stress and ovarian cancer will highlight potential mechanisms for the pathogenesis of this disease. We hypothesize that oxidative stress plays an important role in the pathogenesis of ovarian cancer, as it induces genotypic modifications of tumor cells that not only contribute to the maintenance of the oncogenic phenotype but also to the acquisition of chemoresistance. We have characterized epithelial ovarian cancer to manifest a persistent pro-oxidant state through alteration of the redox balance, which is further enhanced in their chemoresistant counterparts. Forcing ovarian cancer cells to undergo oxidative phosphorylation rather than glycolysis has been shown to be beneficial for eliminating cells via apoptosis. Collectively, our data indicated a causal relationship between the acquisition of chemoresistance and chemotherapy-induced genetic mutations in key redox enzymes, leading to a further enhanced oxidative stress in chemoresistant EOC cells. This concept was further confirmed by the observation that induction of point mutations in sensitive EOC cells increased thier resistance to chemotherapy. Also, a combination of antioxidants with chemotherapy significantly sensitized cells to chemotherapy. Identification of targets for chemoresistance with either biomarker and/or screening potential will have a significant impact for the treatment of this disease.

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