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TITLE

NEW MOLECULAR PATHWAYS FOR OVARIAN RESERVE PRESERVATION

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ABSTRACT

Advancements in early diagnoses and new treatments have greatly increased the survival rate of young cancer female patients. However, chemo- and radiotherapies can cause long term side effects, such as reduction of ovarian reserve, premature menopause and infertility. The effects of early menopause may be more important at younger biologic ages, with rapid and substantial effects not only on withdrawal of sex hormones but also on adrenal and pituitary functions and on lipid and carbohydrate metabolism.

Nowadays, several studies have focused on the identification of substances that, given before or together with the chemotherapeutic drugs, prevent their gonadotoxicity. These include the ceramide-pathway inhibitor sphingosine-1-phosphate, the antimitotic agent dexrazoxane and the immonomodulator AS101. Our laboratories have showed that Imatinib, an inhibition of c-ABL, has a protective effect on the ovarian reserve damaged by cisplatin (Cs).

Administration of gonadotropin-releasing hormone agonists during chemotherapy has been reported to be beneficial for fertility preservation, opening the exiting possibility of using biological molecules with targeted action. However the effectiveness and mechanisms of action of GnRHa, in protecting the ovarian reserve is still debated. In our recent paper we focused on the possibility to use gonadotropins with targeted action on the ovary as "fertoprotective agents" against Cs. We demonstrated that LH given together to Cs, preserved most of the primordial follicles and fertility of female mice against Cs-induced apoptosis. These findings establish a novel ovoprotective role for LH and further support the very attracting prospective to use physiological "fertoprotective" approaches for preventing premature infertility and risks linked to precocious menopause in young patients survived cancer after chemotherapy.

INSTITUTE