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Estrogen-signaling pathway: a link between breast cancer and melatonin oncostatic actions.

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Abstract

BACKGROUND: Melatonin exerts oncostatic effects on different kinds of tumors, especially on endocrine-responsive breast cancer. The most common conclusion is that melatonin reduces the incidence and growth of chemically induced mammary tumors, in vivo, and inhibits the proliferation and metastatic behavior of human breast cancer cells, in vitro. Both studies support the hypothesis that melatonin oncostatic actions on hormone-dependent mammary tumors are mainly based on its anti-estrogenic actions.

METHODS AND RESULTS: Two different mechanisms have been proposed to explain how melatonin reduces the development of breast cancer throughout its interactions with the estrogen-signaling pathways: (a) the indirect neuroendocrine mechanism which includes the melatonin down-regulation of the hypothalamic-pituitary reproductive axis and the consequent reduction of circulating levels of gonadal estrogens and (b) direct melatonin actions at tumor cell level. Melatonin's direct effect on mammary tumor cells is that it interferes with the activation of the estrogen receptor, thus behaving as a selective estrogen receptor modulator. Melatonin also regulates the activity of the aromatases, the enzymes responsible for the local synthesis of estrogens, thus behaving as a selective estrogen enzyme modulator.

CONCLUSIONS: The same molecule has both properties to selectively neutralize the effects of estrogens on the breast and the local biosynthesis of estrogens from androgens, one of the main objectives of recent antitumor pharmacological therapeutic strategies. It is these action mechanisms that collectively make melatonin an interesting anticancer drug in the prevention and treatment of estrogen-dependent tumors, since it has the advantage of acting at different levels of the estrogen-signaling pathways.

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