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**Status:** Professor

**Title :** From menopause hormone treatments to resistance to endocrine therapy: ERalpha, a key player

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Currently, women live a third to a half of their lives in menopause. Menopause is associated with several symptoms, such as hot flashes, vulvovaginal atrophy, and osteoporosis, that lead to a massive decrease in the quality of life. To alleviate these symptoms, menopause hormone treatments (MHT) based on estrogen-only or estrogen combined with a progestogen can be used. However, these treatments are associated with side effects, such as an increased risk of breast cancer. Several MHT formulations exist, but the ideal MHT is still missing.

For several years, we have been working to open new strategies to develop MHT with an optimized benefit/risk ratio. We focused on the nature of the estrogen used for MHT and on the route of administration, evaluating their impact on breast cancer growth. Our results clearly evidence that the fine-tuning of the estrogen receptor alpha (ER $\alpha$ ) activity and signaling in several estrogen-sensitive tissues is central to alleviate menopause symptoms and prevent side effects.

This regulation of ER $\alpha$  activity and expression by specific estrogen treatments leads us to evaluate the relevance of using this strategy to improve the efficacy of endocrine therapy in breast cancer and overcome resistance.