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Beta-adrenergic pathway: A promising therapeutic target in advanced breast cancer

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Stress is usually considered among the numerous factors involved in the complex process of cancer carcinogenesis. However, how stressors or stress response impact on the natural history of this disease is still unknown. The adrenergic pathway is involved in stress responses in daily life being epinephrine and norepinephrine its key mediators. These hormones have been previously described as potent mitogens in normal and malignant cells. The blockage of this pathway by beta-adrenergic antagonists (BBs) has proven to disrupt cell proliferation and migration in malignant cell models. In the clinical setting, BBs have also been linked to improved cancer control rates in patients with localized and advanced breast cancer. Inconsistent results from different retrospective studies have encouraged the conduction of distinct meta-analyses from which, as of today, no clear conclusions can be made. Recently, our team has shown significantly improved outcomes in patients with advanced triple negative breast cancer who received BBs for other comorbidities. We hypothesize that the discordance observed in the available evidence could be a consequence of methodological limitations and tumor heterogeneity. Consequently, we are now conducting a back-translational project to search consistent signals now in breast cancer pre-clinical models exposed to BBs, with the objective to improve the understanding of their mechanism of action. In addition to this, confirming the value of adding BB to standard therapies in a prospectively designed clinical trial is needed. Because BBs are inexpensive and well-established agents with an excellent safety profile, prospective controlled studies in this context are feasible.

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