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Abstract

The Nerve-Growth Factor Signaling in Gender-Related Cancers †

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Abstract: The nerve-growth factor (NGF) was initially identified as a promoter of neuronal survival and differentiation. As such, it has captured the interest of neurobiologists for a long time. Nowadays, NGF is considered a multifaceted molecule with pleiotropic effects in quite divergent cell types, including hormone-dependent cancer cells. Many tumors exhibit derangements of nerve-growth factor and its receptors, including the tropomyosin receptor kinase A (TrkA). This receptor is frequently expressed in triple-negative breast cancers (TNBC), as well as prostate cancers (PC), although its role in the pathogenesis and aggressiveness of these diseases is still under investigation. We now report that the treatment of TNBC as well as PC-derived cells with NGF triggers the proliferation and survival of these cells. Simultaneously, NGF fosters cell motility and induces invasiveness in these cells by acting on the release of metalloproteases-9 (MMP-9). The somatic knockdown of TrkA or its pharmacologic inhibition by the specific inhibitor GW441756 impair these effects. A strong reduction in TNBC or PC-derived spheroid size is observed upon GW441756 treatment. The relevance of our studies is based on the novelty that further exploration of NGF pathway derangements in gender-related cancers will likely offer innovative targets and treatment opportunities in the clinical management of TNBC as well as PC patients.

Keywords: prostate cancer; triple-negative breast cancer; NGF/TrkA signaling

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