

Research Articles: Therapeutics, Targets, and Development

Cannabidiol as a novel inhibitor of Id-1 gene expression in aggressive breast cancer cells

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Abstract

Invasion and metastasis of aggressive breast cancer cells is the final and fatal step during cancer progression, and is the least understood genetically. Clinically, there are still limited therapeutic interventions for aggressive and metastatic breast cancers available. Clearly, effective and nontoxic therapies are urgently required. Id-1, an inhibitor of basic helix-loop-helix transcription factors, has recently been shown to be a key regulator of the metastatic potential of breast and additional cancers. Using a mouse model, we previously determined that metastatic breast cancer cells became significantly less invasive in vitro and less metastatic in vivo when Id-1 was down-regulated by stable transduction with antisense Id-1. It is not possible at this point, however, to use antisense technology to reduce Id-1 expression in patients with metastatic breast cancer. Here, we report that cannabidiol (CBD), a cannabinoid with a low-toxicity profile, could down-regulate Id-1 expression in aggressive human breast cancer cells. The CBD concentrations effective at inhibiting Id-1 expression correlated with those used to inhibit the proliferative and invasive phenotype of breast cancer cells. CBD was able to inhibit Id-1 expression at the mRNA and protein level in a concentration-dependent fashion. These effects seemed to occur as the result of an inhibition of the Id-1 gene at the promoter level. Importantly, CBD did not inhibit invasiveness in cells that ectopically expressed Id-1. In conclusion, CBD represents the first nontoxic exogenous agent that can significantly decrease Id-1 expression in metastatic breast cancer cells leading to the down-regulation of tumor aggressiveness. [Mol Cancer Ther 2007;6(11):2921-7]

Footnotes

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