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Effects of synthetic glucocorticoids on breast cancer progression

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Glucocorticoids (GCs) are widely prescribed as adjuvant therapy for breast cancer patients. Unlike other steroid hormone receptors, the GC receptor is not considered an oncogene. Research in the past few years has revealed the complexity of GC-mediated signaling, but it remains puzzling whether GCs promote or inhibit tumor progression in different cancer types. Here we evaluated the potential of using a synthetic GC, dexamethasone (DEX), in the treatment of breast cancer. We found that the administration of low-dose DEX suppressed tumor growth and distant metastasis in the MCF-7 and MDA-MB-231 xenograft mouse model, whereas treatment with high-dose DEX enhanced tumor growth and metastasis, respectively. Treatment of breast cancer cells with DEX inhibited cell adhesion, migration, and invasion in a dose-dependent manner. The DEX-mediated inhibition of cell adhesion, migration, and invasion is partly through induction of microRNA-708 and subsequent Rap1B-mediated signaling in MDA-MB-231 cells. On the other hand, in MCF-7 cells, DEX-suppressed cell migration is independent from microRNA-708 mediated signaling. Overall, our data reveal that DEX acts as a double-edged sword during breast-cancer progression and metastasis: Lower concentrations inhibit breast cancer tumor growth and metastasis, whereas higher concentrations may play an undesired role to promote breast cancer progression.

Author contributions in this study
J-M Pang, Y-C Huang, S-P Sun, Y-R Pan, C-Y Shen, M-C Kao, R-H Wang, and K-T Lin carried out the experimental work. L-H Wang provided reagents, ideas, and suggestions. K-T Lin designed experiments, wrote the manuscript, directed the research, and approved the manuscript.

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