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Beta protein 1 homeoprotein induces cell growth and estrogen-independent tumorigenesis by binding to the estrogen receptor in breast cancer

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ABSTRACT

Expression of *Beta Protein 1 (BP1)*, a homeotic transcription factor, increases during breast cancer progression and may be associated with tumor aggressiveness. In our present work, we investigate the influence of *BP1* on breast tumor formation and size *in vitro* and *in vivo*. Cells overexpressing BP1 showed higher viability when grown in the absence of serum ($p < 0.05$), greater invasive potential ($p < 0.05$) and formed larger colonies ($p < 0.004$) compared with the controls. To determine the influence of BP1 overexpression on tumor characteristics, MCF-7 cells transfected with either empty vector (V1) or overexpressor plasmids (O2 and O4) were injected into the fat pads of athymic nude mice. Tumors grew larger in mice receiving O2 or O4 cells than in mice receiving V1 cells. Moreover, *BP1* mRNA expression levels were positively correlated with tumor size in patients ($p = 0.01$). Interestingly, 20% of mice injected with O2 or O4 cells developed tumors in the absence of estrogen, while no mice receiving V1 cells developed tumors. Several mechanisms of estrogen independent tumor formation related to BP1 were established. These data are consistent with the fact that expression of breast cancer anti-estrogen resistance 1 (*BCAR1*) was increased in O2 compared to V1 cells ($p < 0.01$). Importantly, O2 cells exhibited increased proliferation when treated with tamoxifen, while V1 cells showed growth inhibition. Overall, *BP1* overexpresssion in MCF-7 breast cancer cells leads to increased cell growth, estrogen-independent tumor formation, and increased proliferation. These findings suggest that BP1 may be an important biomarker and therapeutic target in *ER* positive breast cancer.

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