The cAMP responsive element binding protein 1 transactivates epithelial membrane protein 2, a potential tumor suppressor in the urinary bladder urothelial carcinoma

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ABSTRACT

In this study, we report that *EMP2* plays a tumor suppressor role by inducing G_2/M cell cycle arrest, suppressing cell viability, proliferation, colony formation/anchorage-independent cell growth via regulation of G_2/M checkpoints in distinct urinary bladder urothelial carcinoma (UBUC)-derived cell lines. Genistein treatment or exogenous expression of the cAMP responsive element binding protein 1 (*CREB1*) gene in different UBUC-derived cell lines induced *EMP2* transcription and subsequent translation. Mutagenesis on either or both cAMP-responsive element(s) dramatically decreased the *EMP2* promoter activity with, without genistein treatment or exogenous CREB1 expression, respectively. Significantly correlation between the EMP2 immunointensity and primary tumor, nodal status, histological grade, vascular invasion and mitotic activity was identified. Multivariate analysis further demonstrated that low EMP2 immunoexpression is an independent prognostic factor for poor disease-specific survival. Genistein treatments, knockdown of *EMP2* gene and double knockdown of *CREB1* and *EMP2* genes significantly inhibited tumor growth and notably