Transcriptional regulation and role of S100P calcium-binding protein in cancer cells

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S100P is an EF-hand calcium-binding protein that was originally identified in placenta and subsequently linked to cancer. It is a member of S100 family of proteins functioning as extracellular and/or intracellular regulators of diverse cellular processes and contributing to various human pathologies. S100P expression was detected in a range of human tumor cell lines and tissues, particularly those derived from breast, prostate, pancreas and colon, where it was connected with malignant phenotype, hormone independence and resistance to chemotherapy. In line with these observations, forced overexpression of S100P was shown to promote tumorigenesis in prostate, breast and cervical cancer models. Functional studies of S100P indicate that it operates either via intracellular interaction with ezrin, leading to increased cell migration, or via extracellular signaling through RAGE receptor, resulting in increased proliferation and survival. Molecular mechanisms regulating expression of S100P in cancer cells are just starting to emerge. Besides earlier described DNA methylation, recent studies revealed involvement of bone morphogenic protein and non-steroidal anti-inflammatory drugs in control of S100P expression during tumor progression. We performed functional analysis of S100P promoter and identified SMAD, STAT/CREB and SP/KLF binding sites as key regulatory elements participating in transcriptional activation of S100P gene in cancer cells. Moreover, our latest data reveal that expression of S100P is up-regulated by activation of glucocorticoid receptor suggesting that S100P could play a role in therapy resistance mediated by glucocorticoids in solid tumors.