Functions of ZNF217, a Gene Amplified During Neoplastic Progression

Littlepage L.[1] and Werb Z.[1]
[1]University of California, San Francisco, San Francisco, CA, United States

The 20q13 region of the human genome is highly amplified in 20-30% of early stage human breast cancers, and this amplification correlates with poor prognosis. ZNF217, a candidate oncogene in 20q13.2, is a putative transcription factor that is a component of the corepressor of transcription associated with the human histone deacetylase complex (CoREST-HDAC), as well as in a complex with the transcriptional co-repressor C-terminal binding protein (CtBP). Overexpression of ZNF217 in human mammary epithelial cell lines leads to their immortalization. To investigate its effect on neoplastic progression in epithelial cells, we cloned mouse Znf217. We characterized the role of Znf217 as a putative transcription factor. Using Gal4-fusion constructs in transcription assays, we found that Znf217 is a strong transcriptional repressor. We then infected mouse epithelial SCp2 cells with vector or mouse Znf217 in a retroviral vector. Using an antibody raised against human ZNF217 that we found cross-reacts with mouse Znf217, we found that the cells expressed the Znf217 protein when induced, as determined by western blot analysis. Cells overexpressing Znf217 had altered cell and nuclear morphology and showed increased motility in scratch assays. Taken together, our data suggest that repression of a transcriptional target by ZNF217 may lead to increased motility of epithelial cells in culture. (Supported by Ruth L. Kirschstein National Research Service Award, American Cancer Society Postdoctoral Fellowship, NIEHS/NCI grant U01 ES012801, and grant CA058207 from NCI.)