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FOXK2: A novel oncogene that is amplified and over-expressed in breast cancer

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The chromosome 17 is a frequent site of cancer-associated genetic anomalies and is strongly associated with poor prognosis. Previous studies of breast cancer have revealed the amplification of several genomic regions on 17q. These amplifications are typically discontinuous and complex in structure, suggesting that multiple oncogenes in this chromosomal segment may be co-selected during breast carcinogenesis. By integrative analysis of public genomic datasets of breast cancers from The Cancer Genome Atlas (TCGA) including 910 tumor cases and 981 normal controls, we have found that FOXK2 in 17q25 displayed frequent genomic amplifications and correlated gene expression changes in all subtypes of breast cancer sclassified by PAM50 compared to normal controls. Its over-expression was associated with poor overall survival of breast cancer patients. FOXK2 knockdown using lentivirus mediated shRNAs inhibited breast cancer cell proliferation and anchorage-independent growth in four breast cancer cell lines with high FOXK2 expression status (MDA-MB-231, MCF-7, HCC1954 and MDA-MB-361). More importantly, over-expression of FOXK2 and oncogene RAS induced MCF10A cell colony formation, indicating that FOXK2 is an oncogene in breast cancer cells. Several pathways, including regulation of cell proliferation, regulation of cell division, cell adhesion and regulation of cell metabolism, were regulated by FOXK2 in breast cancer cells. Our data provide compelling evidence that FOXK2 is an oncogene in breast tumorigenesis and it might be a novel therapeutic target and a biomarker predicting poor outcome.

Biography

Hong (Amy) Zhang has completed her MD training in China and completed her PhD from University of Texas (UT)-Graduate School of Biomedical Science in 2000. She received residency training at UT-Medical School at Houston. She is a practicing surgical pathologist at UT-M D Anderson Cancer Center, majoring in breast pathology. She has published more than 38 papers in reputed journals and has been serving as an Editorial Board Member of several journals. Her research interest focuses on identifying new molecular markers and novel therapeutic targets for breast cancers using modern biotechnologies of cytogenetics, molecular biology, biochemistry and animal models.

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