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FOXK2 aberration in breast cancers

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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 cancers classified by PAM50 compared to normal controls. Its overexpression 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, overexpression of *FOXK2* and oncogene RAS induced MCF10A cell colony formation, indicating that *FOXK2* is an oncogene in breast cancer. The potential interacting molecules/pathways were explored using RNASeq technique on the *FOXK2* knockdown 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 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 cancers classified by PAM50 compared to normal controls. Its overexpression 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, overexpression of *FOXK2* and oncogene RAS induced MCF10A cell colony formation, indicating that *FOXK2* is an oncogene in breast cancer. The potential interacting molecules/pathways were explored using RNASeq technique on the *FOXK2* knockdown 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

Amy Hong Zhang is an Associate Professor in the Department of Pathology and Translational Molecular Pathology in University of Texas-MD, Anderson Cancer Center in Houston, TX she is an American Board certified practicing Pathologist since 2003. She has expertise in diagnosing breast cancers and the interpretation of the biomarkers relevant to breast cancers for patient care. She is also actively supervising research scientists and trainees on translational and laboratory research, focusing on the characterization of tumor markers significant for breast tumorigenesis and the development of small molecule inhibitors and potential novel molecular targets for breast cancer treatment.

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