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Amplification and over-expression of *MAP3K3* gene in human breast cancer promotes formation and survival of breast cancer cells

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Gene amplification in the 17q chromosomal region is observed frequently in breast cancers. An integrative bioinformatics analysis nominated *MAP3K3* gene, located in 17q23, as a potential therapeutic target in breast cancer. This gene encodes the mitogen-activated protein kinase kinase kinase 3 (MEKK3), but has not yet been associated with cancer-causal genetic aberrations. We found that *MAP3K3* was amplified in approximately 8-20% of breast carcinomas, and that its over-expression was an independent prognostic marker for poor outcome with respect to relapse-free and overall survival, especially among the estrogen receptor-positive breast cancer patients. shRNA- mediated knockdown of *MAP3K3* expression significantly inhibited cell proliferation and colony formation of *MAP3K3*-amplified breast cancer cell lines MCF7 and MDA-MB361, and promoted breast cancer cell apoptosis induced by TNFα, TRAIL, or a doxorubicin. In addition, ectopic expression of *MAP3K3*, in collaboration with Ras, induced colony formation in both primary mouse embryonic fibroblasts and immortalized mammary epithelial cells (MCF-10A). Together, these results suggest that *MAP3K3* is a potential biomarker indicating poor prognosis, contributes to resistance to therapy, and is an oncogene in breast carcinogenesis. Therefore, therapeutic targeting of *MAP3K3* may be attractive in breast cancer patients with *MAP3K3*-amplified breast cancer.

Biography

Amy Hong Zhang is currently an Associate Professor in the Department of Pathology and Translational Molecular Pathology in University of Texas-MD Anderson Cancer Center in Houston, TX, specializing on breast cancer pathology. 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 treatments in a different way of focusing.

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