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The unknown predisposition can lie deep in the family tree

San Ming Wang
University of Nebraska Medical Center, USA

Genetic predisposition is the primary risk factor for hereditary breast cancer. For the majority of familial breast cancer, however, the genetic predispositions remain unknown. Currently, detection of the unknown predispositions is largely through screening large numbers of pooled individual cases, and the newly identified predispositions occur in disease population. Considering that family unit is the basic structure of genetics and hereditary breast cancer is an autosomal dominant disease, the disease family must carry the same genetic predisposition across generations. Therefore, focusing on the cases in lineages of familial breast cancer, rather than pooled, genetically-unrelated cases in disease population, is expected to provide high probability to identify the genetic predisposition for each family. We tested this concept by studying the family-specific variants in hereditary breast cancer families. We used exome sequencing to analyze three disease families and 22 probands with *BRCAx* (*BRCA*-negative) hereditary breast cancer. We observed the presence of family-specific, novel, deleterious germline variants in each family. Certain variants are putative deleterious genetic predispositions damaging functionally important genes involved in DNA replication and damaging repair, tumor suppression, signal transduction, and phosphorylation. Our study demonstrates that the unknown predispositions for many *BRCAx* hereditary breast cancer families can lie in each disease family. The application of a family-focused approach has the potential to detect those unknown predispositions.

Biography

San Ming Wang completed his graduate training from Swiss Institute for Experimental Cancer Research, and Postdoctoral studies from Northwestern University and University of Chicago. He is an Associate Professor in UNMC, specializing in cancer genetics and genomics. He has published over 60 papers in reputed journals.

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