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Antibodies to mitochondrial proteins in breast cancer

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Abstract

Breast cancer (BC) is the most frequent cause of death in women throughout the world. Using immunofluorescence on HEp-2 cells we demonstrated for the first time that antibodies to mitochondrial proteins [AMPs] are consistently present in the sera from patients with BC and in a group of healthy women with BI-RADS4 mammography assessment and benign breast disease. The mitochondrial specificity of these antibodies was confirmed by reactivity of BC sera with mitochondria on rodent sections of stomach and renal tubuli. Immunoscreening of cDNA libraries of BC proteins led to the identification of AMPs targeting subunits of mitochondrial complexes I, IV and V encoded by mtDNA and mitochondrial proteins encoded by nDNA. Further work using autoantigen microarray analysis led to the development of a classifier formed exclusively by AMPs which recognizes patients with BC with a sensitivity of 88% and a specificity of 68%. Selection of important AMPs was accomplished using random forests with ten-fold cross-validation. Antibodies that were identified as important in at least 5 of the ten folds were selected for simultaneous evaluation using logistic regression. The reactive epitopes targeted by AMPs bear conserved domains and are highly associated with BC. We propose the hypothesis that the panel of AMPs reported here is a potential promising diagnostic tool which could predict the aggressive behavior of BC. A mitochondrial-based non-invasive serologic test able to identify the aggressive behavior of BC may contribute to reduce the mortality and the cost of care due to BC.

Biography

Felix Fernandez Madrid, obtained an MD at the University of Buenos Aires, Argentina and a PhD in Physiology, Cellular and Molecular Biology at the University of Miami, Coral Gables, FLA, USA . He is Professor of Internal Medicine and Chief of the Rheumatology Division at Wayne State University. His research interests include the anti-cancer immune response, the parallel between the autoimmune phenomena in the systemic autoimmune diseases and the immune response in breast and other cancers and the relation between autoimmunity, inflammation and cancer progression.