Felix Fernandez Madrid

Wayne State University, USA

Autoimmunity in breast carcinogenesis: Implications for vaccination in solid tumors

Our findings of anti-mitochondrial and anti-centrosome antibodies as well as autoantibodies targeting, RNA and RNA-protein complexes, histones, idiotypes and molecules involved in remodeling of the microenvironment in breast cancer [BC] sera, support our proposal that autoimmunity to tumor associated [TAA] and stromal associated antigens [SAA] is involved in breast carcinogenesis. Autoimmunity is mechanistically involved in the pathogenesis of rheumatic autoimmune and organ-specific autoimmune diseases by triggering chronic inflammation with consequent end-organ tissue damage. It is generally accepted that chronic inflammation may lead to the development of cancer. The most effective anti-tumor immune responses in animal models as well as in humans have relied on the efficient generation of TH1-cell immunity that promotes CTL responses that would favor tumor regression, while TH2 responses, i.e., autoantibodies and cytokines have failed to provide a vigorous anti-tumor effect. In this context, efforts to prevent and/or eradicate solid tumors with the use of vaccination, although promising have been largely disappointing. We have proposed that autoimmunity to TAAs and SAAs is responsible for autoimmune breast tissue damage, fueling chronic inflammation with generation of tumorigenic signals providing the rationale for the reported paradoxical association of B-cell hyperactivity and BC progression. The proposed model of cancer progression based on mitochondrial autoimmunity implies a vicious cycle of mitochondria/ER stress, immune recognition of accumulated unfolded or misfolded mitochondrial, centrosome and other proteins by auto-reactive immune cells, autoimmune damage of the target organ and chronic inflammation with generation of tumorigenic signals. Autoantibodies in BC do identify autoantigens participating in breast carcinogenesis. Some autoantibodies and cytokines involved in immune surveillance may have anti-tumor effects while others may be tumorigenic and promote cancer progression. This model has the potential ability of identifying protective and tumorigenic responses as well as new candidate biomarkers for targeted immunotherapy and for cancer vaccination in solid tumors.

Speaker Biography

Félix Fernández Madrid is a Professor of Internal Medicine at Wayne State University in Detroit Michigan. His affiliations are Department of Internal Medicine, Center for Molecular Medicine and Genetics, Karmanos Cancer Institute. Based on the established role of autoantibodies as diagnostic and prognostic biomarkers in the rheumatic autoimmune diseases [RADs] and on their involvement in disease pathogenesis he became interested on a novel biomarker discovery approach which may contribute to the diagnosis of BC and other solid tumors. Along with his team, they demonstrated that autoantibodies in BC are not epiphenomena and that anti-mitochondrial antibodies targeting subunits of mitochondrial electron transfer chain complexes I, IV and V encoded by mtDNA are BC autoantigens, suggesting that these autoantibodies are the expression of mitochondrial autoimmunity in BC. A major goal of his research program is to establish the role of tissue damage produced by autoimmunity to breast antigens as contributors to creating a chronic inflammatory milieu promoting the progression of BC, and other solid tumors.

e: fmadrid@med.wayne.edu

Notes: