

Rheumatoid Arthritis Patients Display Genetically Disparate DNA in Lesions

November 14, 2011

JR Schoenborn

During pregnancy, bidirectional exchange of fetal and maternal cells across the placenta can lead to establishment of 'foreign' cell lineages that persist for decades in both mother and child, referred to as naturally acquired microchimerism (Mc). Mc of fetal origin is a frequent finding in mothers, with 50-75% displaying Mc. Maternal Mc is detected less often, but is also common. The health consequences of Mc are unclear, but it has been postulated to play a role in autoimmunity, including rheumatoid arthritis (RA). RA is a chronic autoimmune disorder resulting in inflammation, destruction and pain in joints and other body organs. A prominent clinical feature of RA that is commonly associated with more severe disease is the rheumatoid nodule (RN). RNs are necrotic and fibrotic lesions often present at areas prone to mechanical trauma or pressure, such as near joints. While the cause and pathogenesis of RA are incompletely understood, Mc has been observed in the blood of patients with RA.

Dr. William Chan and Dr. J. Lee Nelson in the Clinical Research Division, and colleagues from the University of Victoria, Canada, hypothesized that maternal Mc drives the development of RNs. To address this hypothesis, Chan *et al.* used quantitative real-time PCR to detect male Y-chromosome DNA in nodules isolated from female RA patients as a test for Mc of presumed fetal origin. To provide more definitive evidence for naturally acquired Mc, they examined RNs for foreign HLA sequences that could only be acquired from a fetal or maternal source. The authors report that nearly half of all RNs tested contained microchimeric DNA. Results further supported pregnancy exchange as the likely source for most patients. Nodules from three patients contained microchimeric DNA that was neither fetal nor maternal in origin, suggesting other possible sources including previous miscarriages or blood transfusions. The authors conclude that microchimeric DNA is present in nodules of RA patients, frequently attributable to placental exchange during pregnancy. Future studies are planned to define what role the disparate cells and/or DNA may have in immune activation at sites of tissue damage. Specifically, classifying the types of microchimeric cells present in nodules and defining the exact immune stimuli of the intact cells and/or their DNA could lead to greater understanding of the initiation and progression of RA.

[Chan WFN, Atkins CJ, Naysmith D, van der Westhuizen N, Woo J, Nelson JL](#). 2011. Microchimerism in the rheumatoid nodules of rheumatoid arthritis patients. *Arthritis & Rheumatism*, Epub ahead of print, doi: 10.1002/art.33358