

## Antibodies and Infection in the Era of the Metagenome

Studies of autoimmune disease have focused on identifiable characteristics of antibodies. But as our knowledge of the genes associated with chronic disease expands, we are beginning to understand that humans must be viewed as superorganisms in which a plethora of bacterial genomes – a metagenome – exist in symbiosis with our own. The US NIH has estimated that 90% of the cells in *Homo sapiens* are microbial, and not human, in origin. DNA sequencing is revealing previously occult bacteria in and on the human body. For example, hydrothermal-vent eubacteria were found in studies of hip joints during revision arthroplasty. Recent DNA analysis of the salivary microbiome demonstrated the presence of over 100 bacterial genera in the mouth, including, *Neisseria*, *Treponema*, and *Yersinia*. These genomes can be transferred into the metagenome of individuals through close contact. Is it possible then that the chronic diseases of mankind result from the presence of persistent pathogens? We have previously shown that infectious agents seem to be at the root of various chronic illnesses. Antibodies associated with Hashimoto's thyroiditis, lupus, and rheumatoid arthritis cleared very quickly when patients were administered a novel VDR nuclear receptor agonist and subinhibitory antibiotics during a recent clinical trial. It follows that the antibodies observed in such diseases are almost certainly not autoantibodies but instead result from mutation of human genes, and gene products, by the bacterial metagenome. When the innate immune system is forced to respond to a chronic microbiota, the resulting cascade of cytokines and chemokines will stimulate an adaptive response. Fragments of bacterial DNA generated by phagocytosis or apoptosis of microbiota-infected cells trigger the adaptive immune system to generate antibodies. West China Hospital is currently collaborating to trial the VDR/antibiotic therapy in their autoimmune patients.

Proal, *Autoimmunity Reviews*, In press.

Proal, *Annals NY Acad Sciences*, In press.

Dempsey, *Arthritis Res Ther*, (2007).

Nasidze, *Genome Res*, (2009 Feb 27).