

## Lecture 19. MHC Class I-associated Diseases: Spondyloarthritis and Reactive Arthritis

### LEARNING OBJECTIVES:

1. Appreciate the different clinical entities in this group of class I associated disease, their common clinical, mechanistic and genetic features and the elements that distinguish them from each other and from other forms of inflammatory arthritis.
2. Understand the host-pathogen-immune response relationships of these diseases, how they involve CD8 T cells in their pathogenesis and that for some they are triggered by infection with certain intracellular bacteria.

### SUMMARY:

1. Spondylitis diseases are a group of individually distinct diseases with common, unifying features that include Ankylosing spondylitis (ASp), Psoriatic arthritis (PsA), Reiter's syndrome (RS), reactive arthritis (ReA), undifferentiated spondyloarthritis (USpA), and enteropathic arthritis (ulcerative colitis, regional enteritis).
2. There are three main target sites of inflammation: entheses, spine and SI joint and synovium, plus variable involvement of skin, eye, heart, etc.
3. Inflammatory back pain is an important diagnostic feature.
4. Genetic features are striking with high familial aggregation and variable association of susceptibility with HLA-B27. Ankylosing spondylitis is a male predominant disease of young adults that has an intense association with HLA-B27.
5. Pathogenesis is incompletely understood but seems to be at the interface of triggering CD8 T cell clones of the adaptive immune system by receptors recognizing innate immune system ligands.
6. Psoriatic arthritis is a clinically distinctive complex of spondyloarthritis occurring in the setting of psoriasis. It may involve the spine or peripheral joints in a variety of patterns. DIP arthritis with heterotopic new bone formation plus erosions and nail matrix inflammation are characteristic. It appears to be genetically heterogeneous with one subset associated with HLA-B alleles, including HLA-B27 and another with the HLA Cw\*0602 allele strongly associated with the risk of developing psoriasis.
7. Reiter's syndrome/reactive arthritis was the first example of a MHC allele controlling an immune response in humans to infection with bacteria that cause intracellular infection. It is distinguished by the classical triad of urethritis, arthritis and conjunctivitis and is characterized by interesting host pathogen relationships.
8. In advanced HIV infection in the absence of a functional CD4 T cell system, an intense syndrome with features of Reiter's syndrome and psoriatic arthritis can develop, an experiment of nature pointing to the role of memory effector CD8 T cells in its pathogenesis.