**THE INVOLVEMENT OF T- AND B-LYMPHOCYTES IN THE PATHOGENESIS AND PROGRESSION OF OSTEOMYELITIS AND OSTEOARTHRITIS.**

**COURSE CODE: ANA 404**

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**MATRIC NUMBER: 17/MHS03/032**

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**APRIL, 2020.**

**T LYMPHOCYTES**

T lymphocytes originate from precursor stem cells in fetal liver and bone marrow and differentiate into mature cell types after migration to the thymus (Yang *et al.,* 2010). T lymphocytes may be categorized based on their distinct function into cytotoxic T lymphocytes (expressing the surface protein cluster of differentiation (CD) 8 and responsible mainly for immune defense against intracellular pathogens and for tumour surveillance) and helper T lymphocytes (expressing the surface protein CD4) (Abbas *et al.,* 1996).

**B LYMPHOCYTES**

B lymphocytes develop from hematopoietic stem cells. Maturation of B cells takes place in bone marrow, whereas their activation occurs in the secondary lymphoid organs such as lymph nodes and the spleen (Kondo *et al.,* 2010). B cells represent mainly the humoral immunity. Nevertheless, their role as a cell itself is equally relevant.

**THE INVOLVEMENT OF T- LYMPHOCYTES IN THE PATHOGENESIS AND PROGRESSION OF OSTEOARTHRITIS**

 Macrophage is an exclusive source of inflammation in Osteoarthritis (OA) (Pelletier *et al.,* 2001). However, the role of T cells in the inflammatory process has not been considered, T cell infiltrates are frequently detected in the synovial membrane (SM) of patients with OA (Koch *et al.,* 1993, Smith *et al.,* 1997, Sakkas *et al.,* 1998, Koussidis *et al.,* 1999, Scanzello *et al.,* 2000, Johanson *et al.,* 2001). These infiltrates are often angiocentric (Sakkas *et al.,* 2000) and are associated with activation of local vascular endothelial cells, as suggested by the increase in expression of E-selectin (Koch *et al.,* 1993). In patients with advanced OA, T cell infiltrates in the SM exhibit a nodular pattern in 37% to 65% (Sakkas *et al.,* 1998) of the patients and express early (CD69), intermediate (CD25), and late (CD45RO, HLA–DR) activation antigens (Sakkas *et al.,* 1998). Additionally, T cell cytokine transcripts of the Th1 type interferon- (IFN) and interleukin-2 (IL-2) and IL-10 were found in the SM of patients with OA, whereas IL-4 and IL-5 were not detected (Sakkas *et al.,* 1998). There were no statistical differences in the levels of IFN and IL-2 transcripts in the SM between patients with rheumatoid arthritis (RA) and OA, when normalized for T cell number equivalents (Sakkas *et al.,* 1998). However, when the levels of IFN transcripts were normalized for total cell number equivalents, they were lower in OA than in RA. The presence of substantial proportions of T cells expressing early, intermediate, and late activation antigens and of the Th1 cytokine pattern (Sakkas *et al.,* 1998) in chronic SM lesions of patients with OA strongly suggests that T cells at least contribute to chronic inflammation in these patients. This Th1 response may be driven by macrophages. Macrophages and synovial lining cells express IL-12, a cytokine that drives the Th1 immune response (Sakkas *et al.,* 1998). OA synovial fluid exhibits increased levels of macrophage inflammatory protein1 (Koch *et al.,* 1995), a ligand for the chemokine receptor CCR5, present on Th1 cells (Loetscher *et al.,* 1998). Although these findings may be explained by a nonspecific activation of T cells, we have demonstrated (Scanzello *et al.,* 1999, Sakkas *et al.,* 2001) the presence of oligoclonal populations of T cells in the SM of advanced OA. Amplification of T-chain cell receptor (TCR) transcripts from the SM of patients with OA by either nonpalindromic adaptor polymerase chain reaction (PCR) or V-specific PCR (Slachta *et al.,* 2000), followed by cloning and sequencing of the amplified transcripts, revealed substantial proportions of identical-chain TCR transcripts, suggesting the presence of oligoclonal populations of T cells. These results strongly suggest that T cells have undergone antigen-driven proliferation and clonal expansion in situ in the SM of patients with OA, in response to as-yet-unidentified antigens. These antigen(s) are not known, but one study suggested a self-reactive immune response to chondrocyte membrane components (Alsalameh *et al.,* 1990). Like other conditions of chronic T cell activation (Krishnan *et al.,* 2001), such as RA (Matsuda *et al.,*1998), systemic lupus erythematosus (Liossis *et al.,*1998), and tumor-infiltrating lymphocytes (Finke *et al.,* 1993), T cells in the SM of patients with OA show decreased expression of CD3- chain transcripts and protein (Sakkas *et al.,* 1999). The inflammation in OA may not be confined within the joints. One study described perivascular lymphocytic infiltrates in muscle biopsies of 18% of patients with OA (Voskuyl *et al.,* 1998). Activated T cells, through cell contact– dependent interaction or through soluble mediators (Aarvak *et al.,* 1999), can stimulate monocytes to produce cytokines (Sebbag *et al.,* 1997). In rheumatoid synovitis, T cells were found to be largely responsible for the production of metalloproteinase (Klimiuk *et al.,* 1999). All these results taken together strongly suggest that a T cell immune response occurs in OA (Scanzello *et al.,* 1999). Substantial evidence has been accumulated suggesting that OA is an inflammatory disease. The traditional view that OA is a noninflammatory disease must be revised. We believe that it is difficult to explain the chronic inflammation that is observed in the SM of patients with OA without a role for T cells and a role for putative antigen(s) in the initiation and propagation of the disease.

B cells, although present in low numbers, B cells and plasma cells were detected in OA (Saito *et al.,* 2002, Pessler *et al.,* 2012). However, their relative abundance is lower than in RA44. OA with increased inflammatory infiltrate contained relatively more B cells. Moreover, infiltrated B cells in patients with OA were shown to be oligoclonal, suggesting an antigen-driven expansion (Shiokawa *et al.,* 2001). Supporting this observation sequencing of the complementarily determing region (CDR) regions of these cells indicated that B cells have been clonally expanded. Therefore, a role for these cells during the course of OA cannot be excluded.

**THE INVOLVEMENT OF T- AND B-LYMPHOCYTES IN THE PATHOGENESIS AND PROGRESSION OF OSTEOMYELITIS**

The innate immune response is critical in the early phase of bacterial colonisation. It is triggered at the site of bacterial infection by the production of cytokines like interleukin-1 (IL-1), IL-6 and tumour necrosis factor (TNF) (Marais *et al.,* 2013). These cytokines recruit and activate phagocytic cells such as polymorphonuclear (PMN) leukocytes and macrophages to produce bacteriolytic free radicals (Boyce *et al.,* 2011). Neutrophils, which engulf bacteria, die at the site of infection and comprise much of the material we see as pus draining from a sinus. Macrophages are critical for the phagocytosis of planktonic bacteria and necrotic material (Marais *et al.,* 2013). This process is facilitated by opsonisation (the binding of an antibody to a bacterial antigen), which anchors the bacteria to the Fc-receptors on phagocytic cells and activates intracellular signaling pathways to produce free radicals like superoxide and nitrous oxide (Marais *et al.,* 2013). Acquired or adaptive immunity is responsible for the eradication of chronic or persistent infections and also plays an important role in the prevention of recurrence. The first component of the adaptive immune response is the cellular response in which cytotoxic CD8+ T cells lyse infected host cells. The second component is the humoral response involving the production of antibodies by B lymphocytes. Centrally positioned within the adaptive immune response are macrophages which produce Th1 lymphokines (IL-12 and interferon-γ) which drive cell-mediated immunity, as well as Th2 lymphokines (IL-3 and -4) regulating the humoral response. Most cases of chronic osteomyelitis involve extracellular organisms and therefore the humeral immune response, incorporating antibody opsonisation and phagocytosis of bacteria, plays a central role (Marais *et al.,* 2013). Animal studies have identified several bacterial antigenic proteins in antibody-mediated immunity in *Staphylococcus aureus* biofilm-based infections, including cell-surface-associated beta-lactamase, lipoprotein, lipase, autolysin and ABC transporter lipoprotein (Brady *et al.,* 2006). Some of these antigens are currently being investigated as possible targets for vaccination (Heilmann *et al.,* 1997). Anti-autolysin monoclonal antibodies (mAbs), for example, may have a protective effect through the inhibition of adhesion and growth of *Staphylococcus sp.*

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