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EDITORIAL

# Infographic: Osteoimmunology mechanism of osteonecrosis of the femoral head

**Keywords:** Osteoimmunology, Osteonecrosis of the femoral head.

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Osteonecrosis of the femoral head (ONFH) is a common and refractory disease.[1] Increasing evidence suggests inflammatory osteoimmunology plays an indispensable role in the pathogenesis of ONFH.

M1 macrophages produce pro-inflammatory cytokines, whereas M2 macrophages produce anti-inflammatory cytokines.[2] A disbalance in favour of the M1 phenotype can result in chronic inflammation, which then contributes to ONFH. The shift from M1 to M2 phenotype effectively decreases inflammatory cytokines and alleviates the symptoms of ONFH.[3]

The cytokines of interleukin (IL)-23/IL-33 produced by T cells may predict risk for ONFH.[4] The elevated levels of T helper cell (Th)17 and IL-17 in both synovium and peripheral blood in ONFH patients indicated a correlation between inflammation and ONFH.[5] Th9/Th17 cells secrete IL-9 to upregulate inflammatory cytokines that degrade cartilage matrix.[6] Regulator T (Treg) cells secrete anti-inflammatory cytokines to inhibit osteoclast activity, thereby preventing bone damage. Inhibitory T cells can also suppress osteoclast activity by binding to osteoclast precursors, and the reduction in its number may be associated with ONFH progression.[7] B cells induce humoral responses and inflammation that contributes to ONFH.[8]

Activated neutrophils release so-called "neutrophil extracellular traps" (NETs). The NET-forming neutrophils appear to disturb local blood flow, and stimulate thrombus formation and coagulation in the small vessels surrounding the femoral head, contributing to ONFH.[9]

Signalling moleculars associated with osteoimmunology of ONFH may include several pathways such as Janus kinase (JAK)-signal transducer and activator of transcription (STAT), c-Jun N-terminal kinase (JNK), and Toll-like receptor (TLR)4/nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB).[2,6,10] Future research should clarify the inflammatory signalling mechanisms, as well as interactions between immune cells and other cell types that contribute to ONFH. Relevant clinical studies shoud also be conducted to fill the gap from theory to practice.

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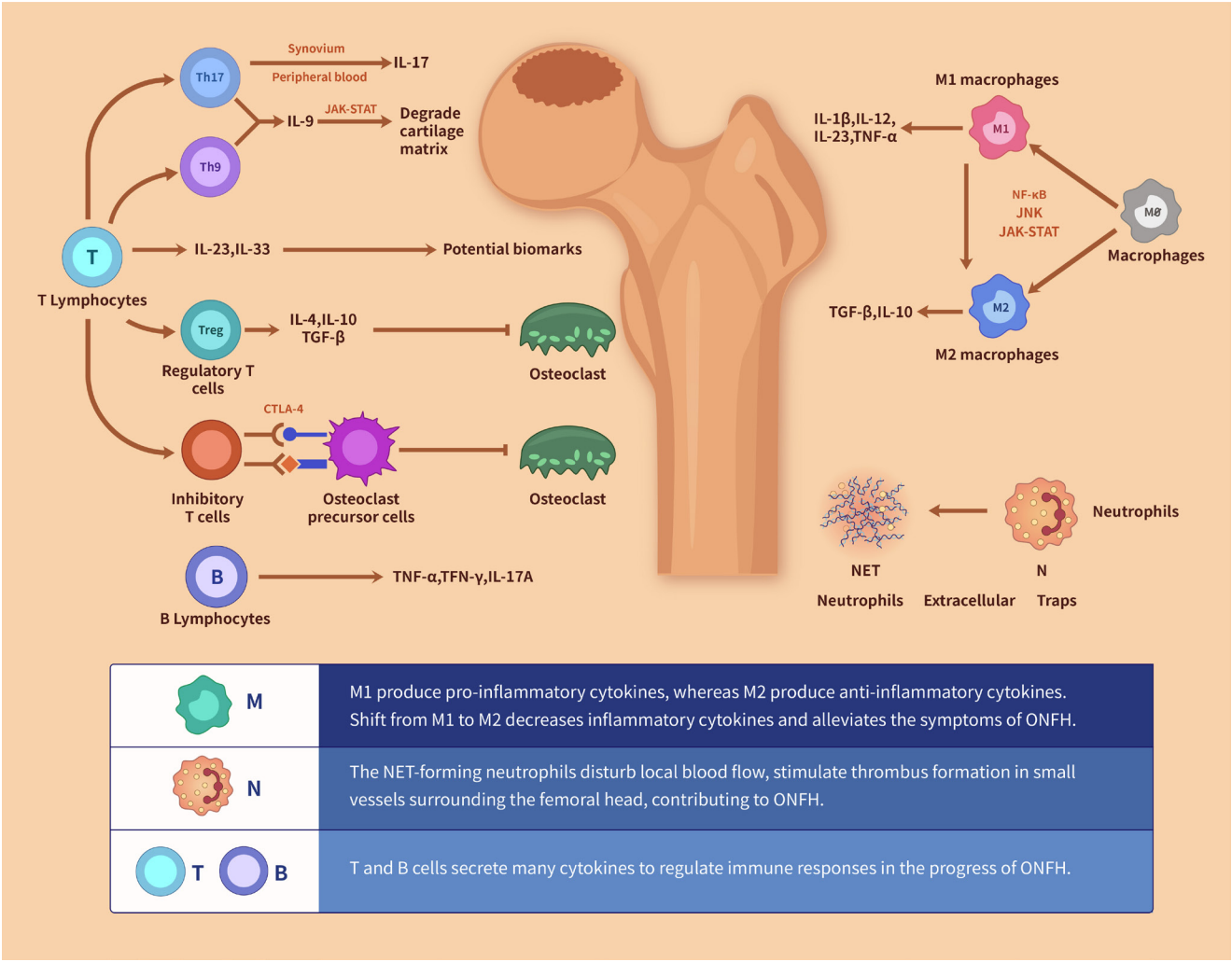
Th17
Synovium
Peripheral blood
IL-17
IL-9
JAK-STAT
Degrade cartilage matrix
Th9
T
T Lymphocytes
IL-23,IL-33
Potential biomarks
Treg
Regulatory T cells
IL-4,IL-10 TGF-β
Osteoclast
CTLA-4
Inhibitory T cells
Osteoclast precursor cells
Osteoclast
B
B Lymphocytes
TNF-α,TFN-γ,IL-17A
M1 macrophages
IL-1β,IL-12, IL-23,TNF-α
M1
NF-κB
JNK
JAK-STAT
MØ
Macrophages
TGF-β,IL-10
M2
M2 macrophages
NET
Neutrophils
Extracellular
N
Traps
Neutrophils
M
M1 produce pro-inflammatory cytokines, whereas M2 produce anti-inflammatory cytokines. Shift from M1 to M2 decreases inflammatory cytokines and alleviates the symptoms of ONFH.
N
The NET-forming neutrophils disturb local blood flow, stimulate thrombus formation in small vessels surrounding the femoral head, contributing to ONFH.
T
B
T and B cells secrete many cytokines to regulate immune responses in the progress of ONFH.