

Genetic disposition

Environment (e.g. smoking, infections)

Citrullination of proteins

Polymorphisms associated with ACPA+ RA

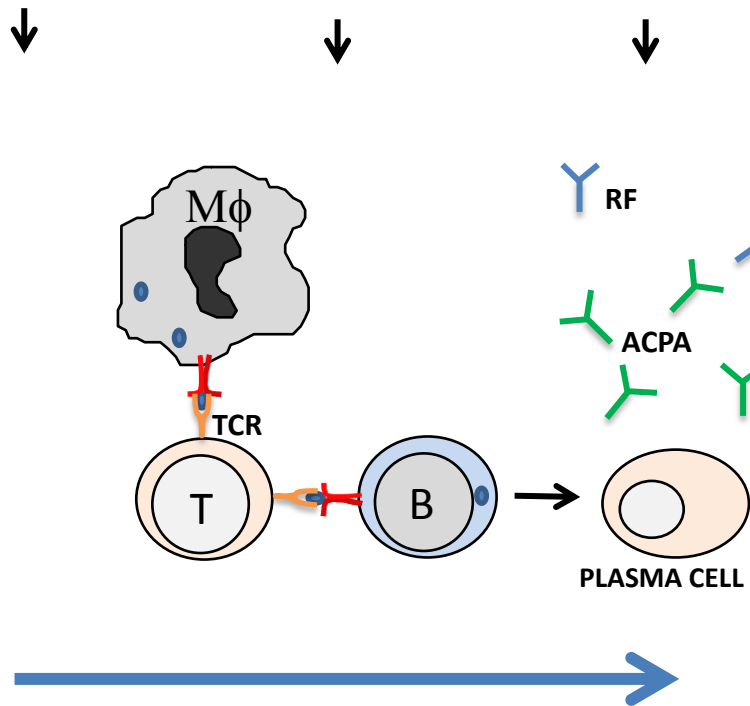
T and B cell activation Cytokines NF-κB pathway Other pathways

- HLA
- PTPN22
- CD2
- CD58
- PTPRC (CD45)
- AFF3
- STAT4
- CD28
- CTLA-4
- TAGAP
- CCR6
- IL2RA
- PRKCQ
- RAG1
- CD40

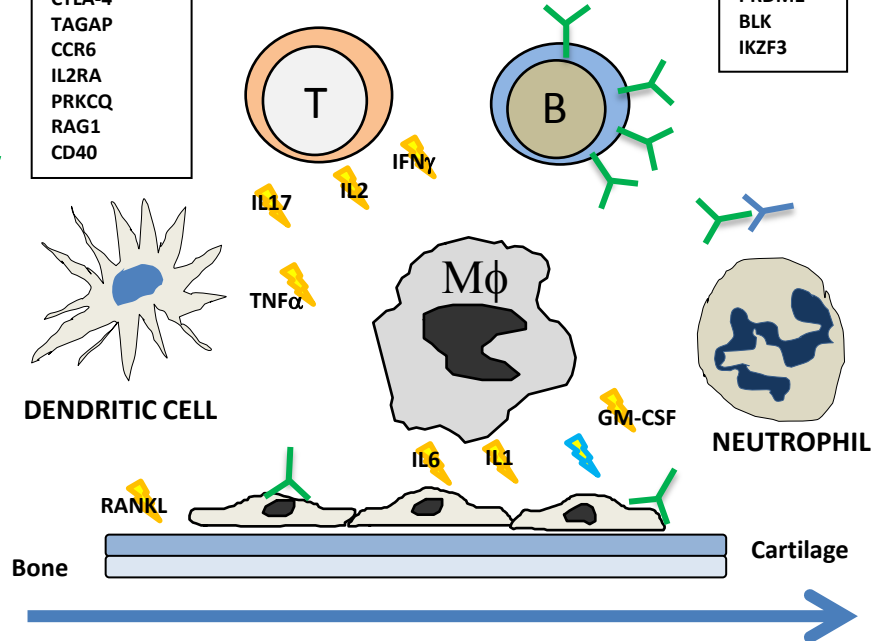
- IL2
- IL21
- AIF-1
- CCL21

- REL
- TNFAIP3
- IRF5
- TRAF1
- TRAF6

- TNFRSF14
- PADI4
- FCGR
- SPRED2
- PXK
- RBPJ
- IL6ST
- ADBR2
- PRDM1
- BLK
- IKZF3



Initiation of immune response to citrullinated peptides and proteins



Inflammatory phase of autoimmune response with destruction of synoviocytes and other cells of the joint