AGING IN RHEUMATOID ARTHRITIS: A COMPARISON OF YOUNGER-ONSET RHEUMATOID ARTHRITIS AND LATE-ONSET RHEUMATOID ARTHRITIS

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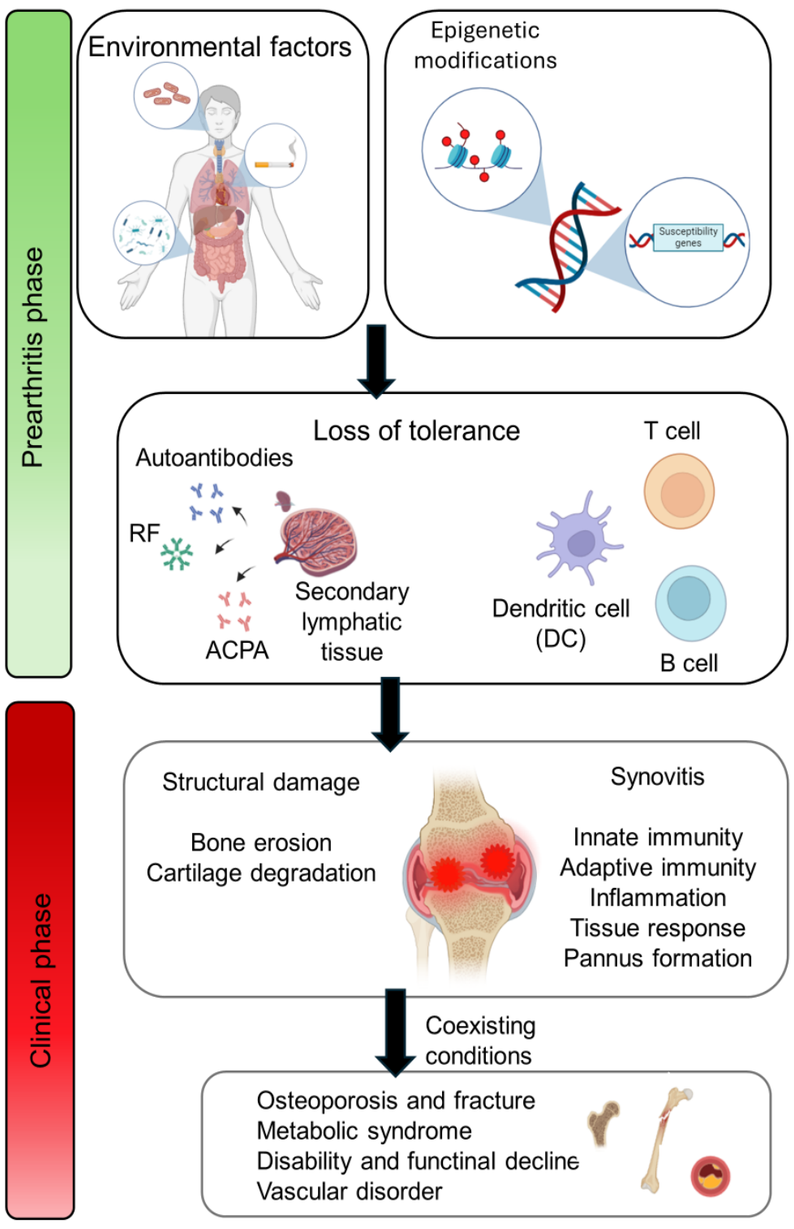
Background



- Rheumatoid Arthritis (RA) is a multifactorial autoimmune disorder characterized by a chronic inflammation mainly affecting synovial joints

→ It is characterized by synovial tissue proliferation, pannus formation, cartilage destruction, and systemic complications

- Prevalent in up to 1-2% of the global population, with women being two to three times more likely to develop RA than man
- Both genetic and epigenetic factors and environmental components play an important role in RA development
- Extra-articular manifestations (EAMs) in several organs and tissues
- RA phases: 1) **Prearthritis phase** → susceptibility genes, environmental and genetic factors, epigenetic modifications such as acetylation, methylation; 2) Altered post-transcriptional regulation → autoimmune response due to the loss of self-tolerance to autoantigens resulting in autoantibodies production. This condition allows the progression into the **clinical phase** of RA characterized by synovitis and bone erosion; 3)Other **coexisting conditions** such as cognitive impairment, osteoporosis, metabolic and vascular disorders can develop at this stage.

Aim of the study

We performed a literature search for reviews and original articles evaluating the characteristics, clinical features, pathogenesis and onset of RA. Furthermore, we searched the PubMed, Medline, and Cochrane libraries using the following search strategy: (Rheumatoid Arthritis OR younger onset rheumatoid arthritis OR late onset rheumatoid arthritis) AND (aging OR immunosenescence).

Results

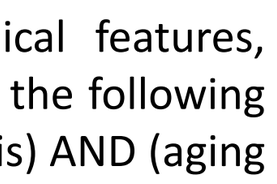
Differences

YOUNGER-ONSET RHEUMATOID ARTHRITIS (YORA)

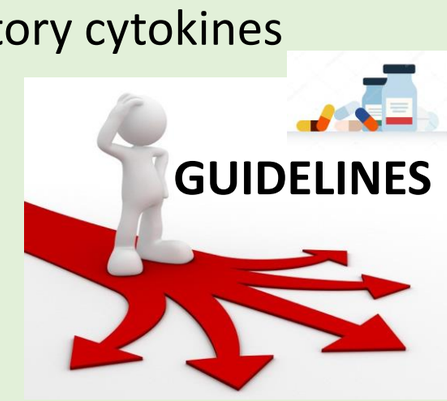
- diagnosed in individuals **under the age of 60**
- might be diagnosed with interstitial lung disease, typical rheumatoid hand deformities and Sjögren's syndrome (SS)
- Higher frequency of **autoantibodies** (rheumatoid factor (RF), anti-nuclear antibodies (ANA), anti-SSA/Ro and anti-SSB/La)
- Lower disease activity
- Allele variant **DRB1*04**
- **Clinical symptoms:** smaller joints inflammation

LATE-ONSET RHEUMATOID ARTHRITIS (LORA)

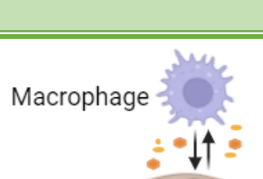
- diagnosed in individuals **greater or equal to 60**
- more **similar distribution** between male and female (ratio 1:1.4)



- **Clinical symptoms**: characterized by stronger synovitis and acute onset pattern, significant implication of the large joints and common structural damage due to the erosive changes
- might be diagnosed with uncommon manifestations such as polymyalgia rheumatica (PMR)-like syndrome, myalgia, weight loss, neuropathy and lymphadenopathy
- higher levels of pro-inflammatory cytokines →**inflammaging**
- Allele variant **DRB1*01**
- ↑ risk of depression
- ↑ incidence in comorbidities



Similarities



Significant interactions among macrophages, synovial fibroblasts, T and B lymphocytes as well as senescent B and T cells

Conclusions

These findings highlight that a better understanding of the pathogenetic molecular pathways and clinical differences involved in YORA and LORA groups will drive to novel and more defined guidelines and medical decision strategy in this age-related disease.