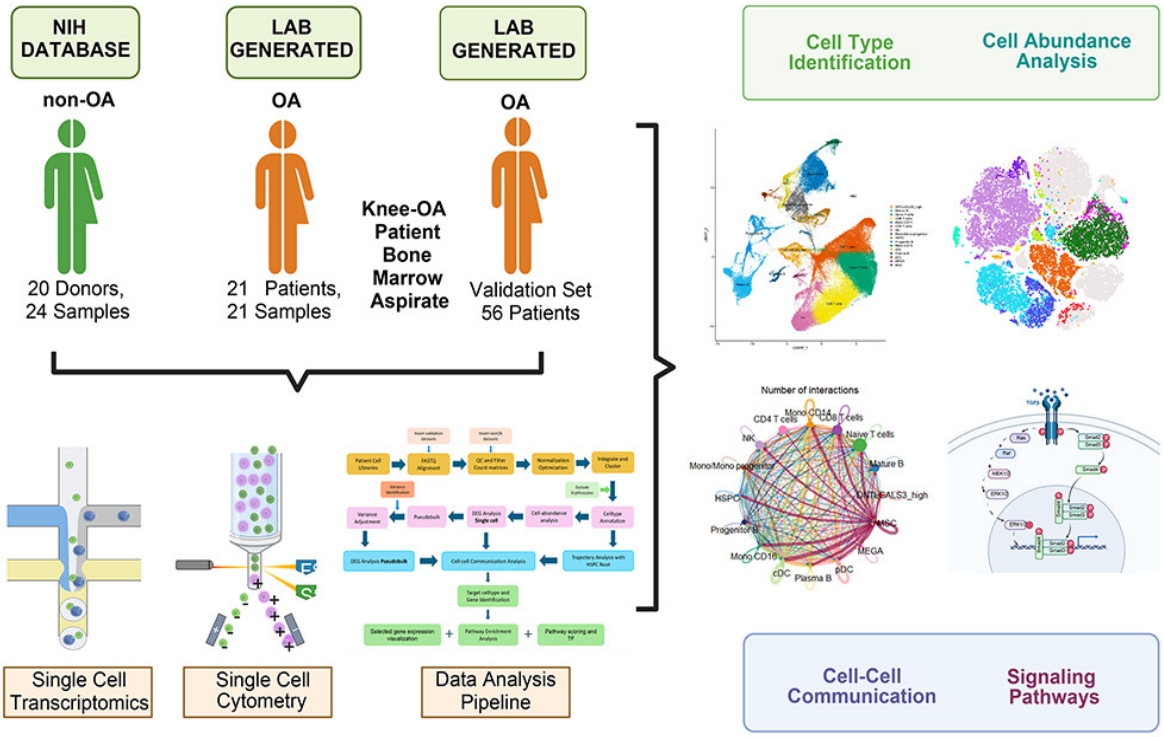
1. **Single-cell transcriptome and crosstalk analysis reveals immune alterations and key pathways in the bone marrow of knee OA patients**

Knee osteoarthritis (OA) is a significant medical and economic burden. To understand systemic immune effects, we performed deep exploration of bone marrow aspirate concentrates (BMACs) from knee-OA patients via single-cell RNA sequencing and proteomic analyses from a randomized clinical trial (MILES: NCT03818737). We found significant cellular and immune alterations in the bone marrow, specifically in MSCs, T cells and NK cells, along with changes in intra-tissue cellular crosstalk during OA progression. Unlike previous studies focusing on injury sites or peripheral blood, our probe into the bone marrow—an inflammation and immune regulation hub—highlights remote organ impact of OA, identifying cell types and pathways for potential therapeutic targeting.



Our findings highlight increased cellular senescence and inflammatory pathways, revealing key upstream genes, transcription factors, and ligands. Additionally, we identified significant enrichment in key biological pathways like PI3-AKT-mTOR signaling and IFN responses, showing their potentially crucial role in OA onset and progression.