

sCD206 as a biomarker for classification and early diagnosis of Juvenile Idiopathic Arthritis Subtypes

Ludwig Fuhrmann¹, Anja Grahnert², Sunna Hauschildt³, Maik Friedrich², Nadine Fischer⁴, Johannes-Peter Haas⁴, Christian Klemann¹

¹Department of Pediatric Immunology, Rheumatology and Infectiology, University Hospital Leipzig, Germany; ²Institute of Clinical Immunology, Medical Faculty Leipzig, Germany; ³Faculty of Life Sciences, Institute of Biology, Leipzig, Germany; ⁴German Centre for Pediatric and Adolescent Rheumatology, Garmisch-Partenkirchen, Germany

Abstract

In patients with Juvenile Idiopathic Arthritis (JIA) early diagnosis and introduction of appropriate therapy are crucial for improving patient outcomes. Especially in the oligoarticular arthritis accurate subtype classification is often delayed. Soluble mannose receptor (sCD206), a macrophage activation marker, has shown promise as a biomarker in inflammatory diseases. In rheumatoid arthritis, sCD206 levels correlate with disease activity and reflect macrophage-driven inflammation. They decrease with effective treatment. Synovial macrophages expressing CD206 are

implicated in sustaining joint inflammation. **In this study, we analyzed the potential of sCD206 as a biomarker for early JIA subtype classification.**

Serum sCD206 levels were measured using an enzyme-linked immunosorbent assay (ELISA) in 289 patients aged 1-18 years suffering from four different JIA subtypes. Mean rank comparisons were performed to assess differences in sCD206 levels across the JIA subtypes. Higher mean ranks correspond to higher sCD206 levels.

We could demonstrate significant ($p < 0.0019$) differences in serum sCD206 levels among JIA subtypes, though the observed differences do not consistently reflect disease severity.

Classification of Juvenile Idiopathic Arthritis

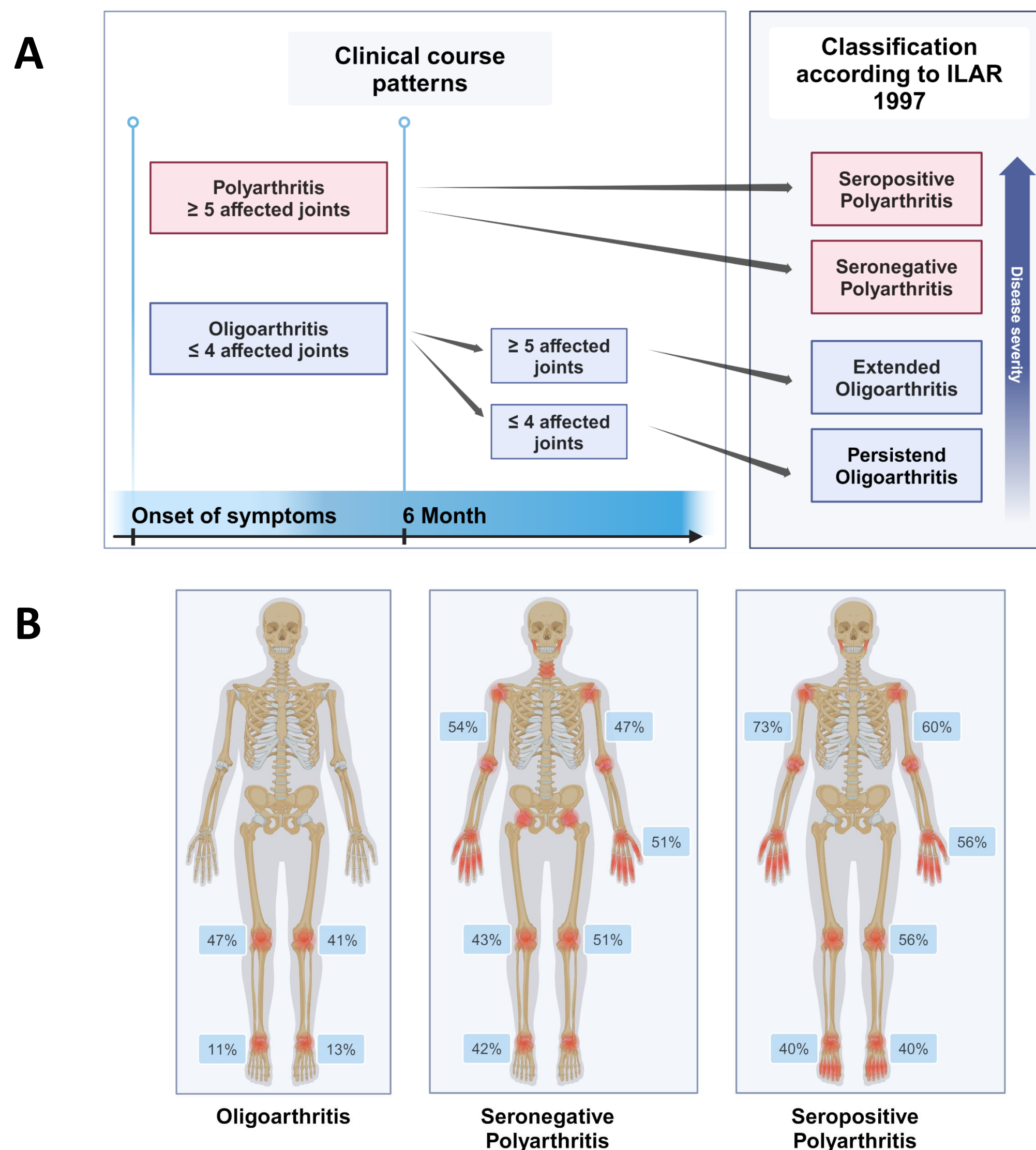


Fig. 1: Classification of Juvenile Idiopathic Arthritis, ILAR: International League of Associations of Rheumatology (A); Joint involvement patterns across JIA subgroups within the first 12 months of disease onset, based on core documentation data from 2005 (n=714, mean disease duration 6 months) [Minden, K., Niewerth, M. Klinische Formen der juvenilen idiopathischen Arthritis und ihre Klassifikation. Z. Rheumatol. 67, S.106] (B)

sCD206 levels in JIA subtypes

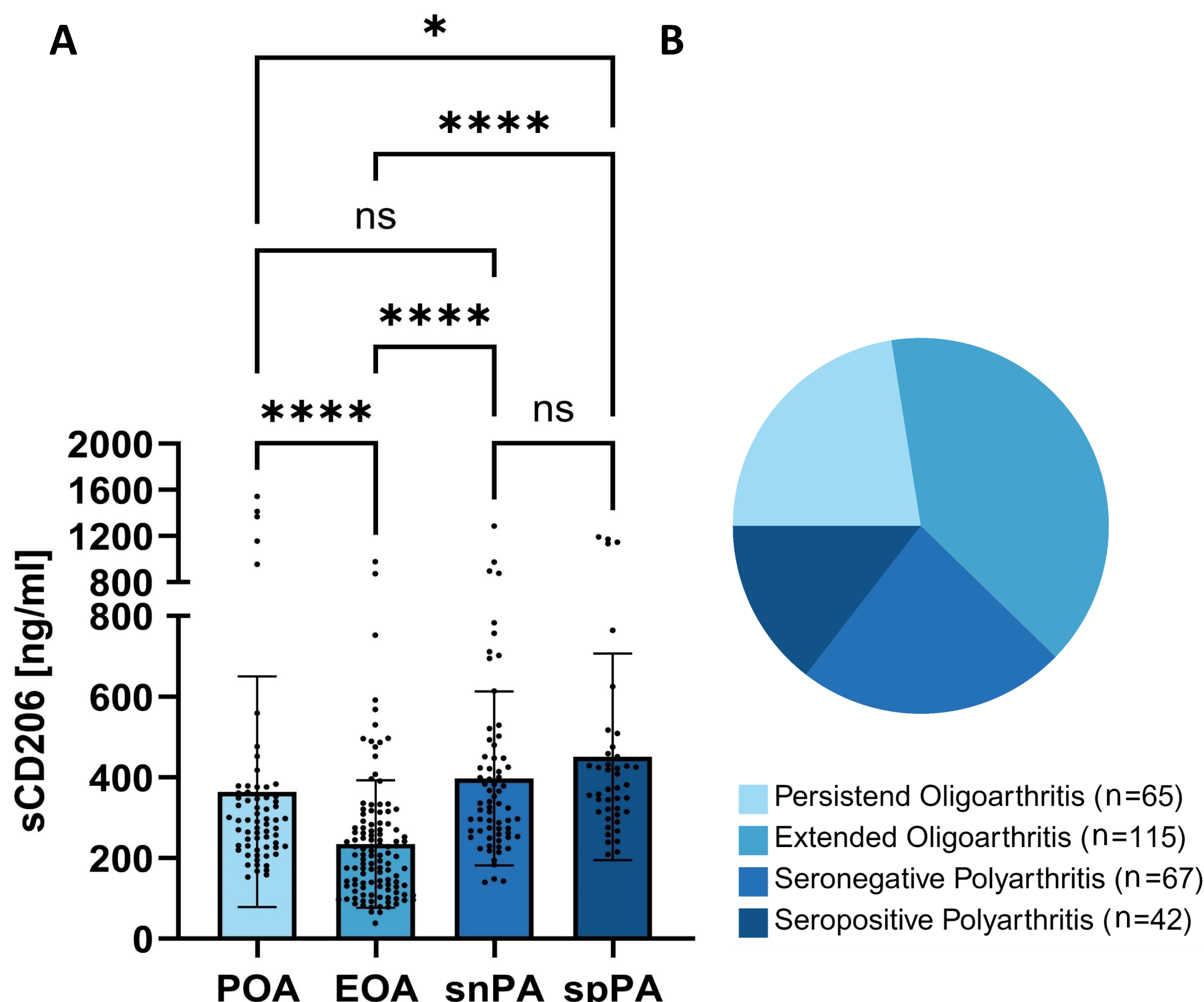


Fig. 4: sCD206 levels in ng/ml in JIA subtypes, POA: Persisted Oligoarthritis, EOA: Extended Oligoarthritis, snPA: Seronegative Polyarthritis, spPA: Seropositive Polyarthritis (A); Cohort size per subtype, total n=289 (B)

ns=not significant; * $p < 0.05$; **** $p < 0.0001$

Macrophage Differentiation and Function of CD206

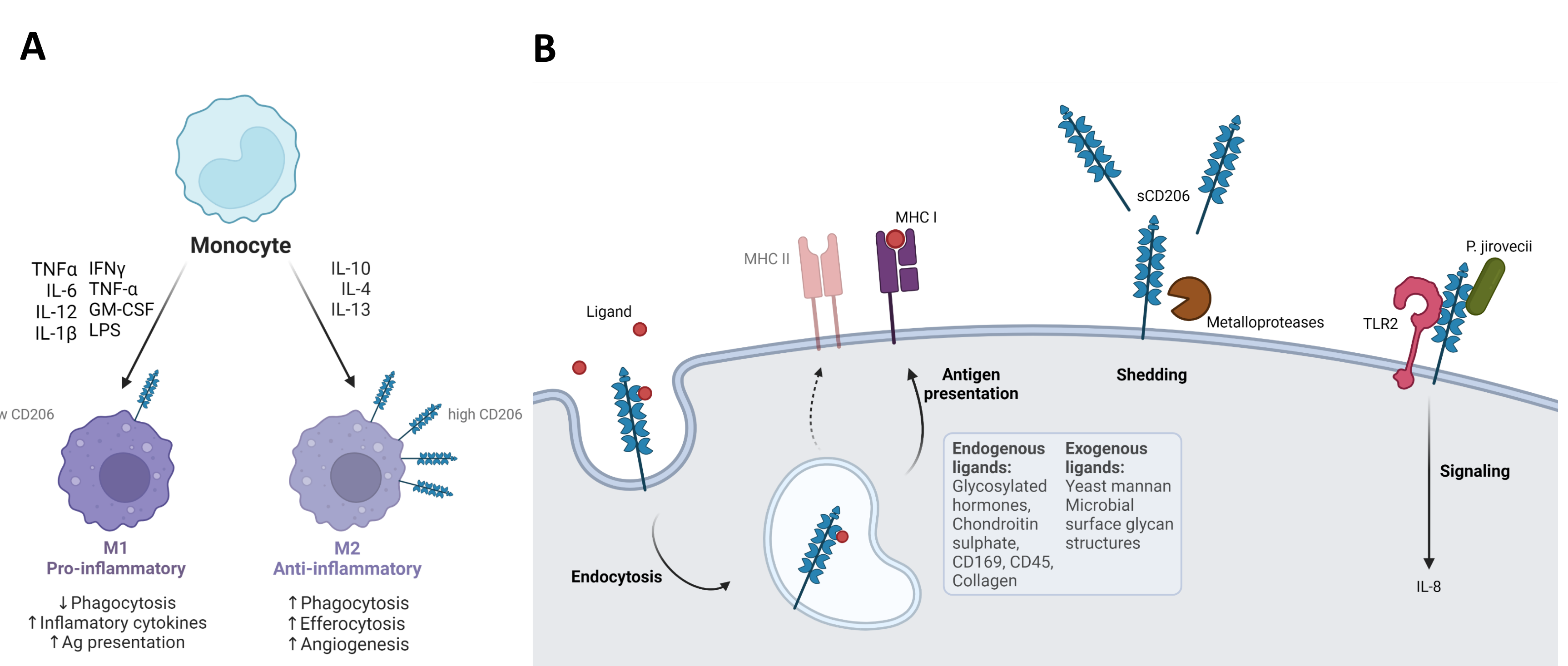


Fig. 2: Macrophage Differentiation: M1 vs M2 Phenotypes, modified from PMID: 15482253 (A); Function of CD206: CD206 enables extracellular ligand recognition and internalization. Endocytosed antigens are processed for cross-presentation onto MHC I molecules, activating CD8+ T cells. CD206 also enhances TLR2 signaling (e.g., during *P. jirovecii* recognition) and can be shed by metalloproteases into a soluble form, modified from PMID: 34721436 (B)

sCD206: Structure and Detection by ELISA

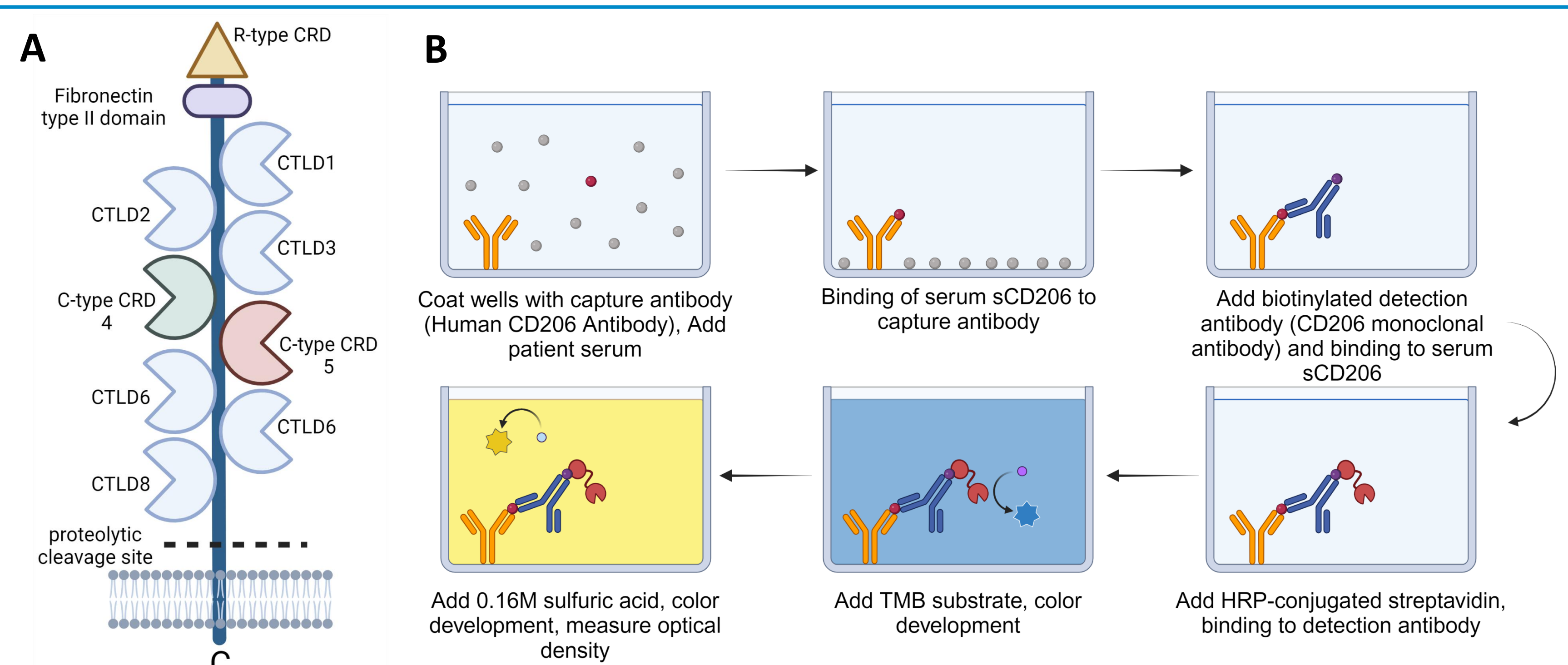


Fig. 3: Schematic of CD206 Receptor Domain Structure, CRD: Carbohydrate-recognition domain, CTLD: C-type lectin-like domain, modified from PMID: 33545173 (A); sCD206 enzyme-linked immunosorbent assay (ELISA) Workflow; HRP: Horseradish Peroxidase; TMB: 3,3',5,5'-tetramethylbenzidine (B)

Conclusion

sCD206 levels vary significantly across JIA subtypes ($p < 0.05$), with highest levels in seropositive polyarthritis and lowest in extended oligoarthritis. While promising for distinguishing between oligoarthritis and polyarthritis groups, its utility as a standalone biomarker is limited by overlap between seronegative and seropositive polyarthritis subtypes. Integration with additional biomarkers may enhance its diagnostic value.

Current work of research

- Retrospective analysis of therapeutic interventions in our JIA cohort (n=289) in relation to their sCD206 levels
- Establishment of reference ranges through measurement of sCD206 levels in healthy pediatric controls