

Supplementary Table S1. Overview of RA cohorts and their analytical role in the study.

Cohort	b/tsDMARD status	<i>In vivo</i> treatment	N (patients)	Samples/assays	Main analytical purpose
Cohort 1	Naïve	<i>Ex vivo</i> only	48	PBMCs, neutrophils to <i>ex vivo</i> JAKi-TNFi; Functional assays; Olink	Define drug-specific <i>ex vivo</i> functional and proteomic signatures in immune cells
Cohort 2	Non-naïve	JAKi	32	Pretreatment baseline serum; Olink	Evaluate <i>ex vivo</i> JAKi signature in non-naïve patients; clustering; ML validation
Cohort 3	Naïve	JAKi	36	Pretreatment baseline serum; paired baseline/6-month serum in remission subset; Olink; 3D model	Evaluate <i>ex vivo</i> JAKi signature <i>in vivo</i> ; clustering; longitudinal response; ML training; 3D synovium (JAKi)
Cohort 4	Non-naïve	TNFi	30	Pretreatment baseline serum; Olink	Evaluate <i>ex vivo</i> TNFi signature in non-naïve patients; clustering; ML validation
Cohort 5	Naïve	TNFi	125	Pretreatment baseline serum; paired baseline/6-month serum in remission subset; Olink; 3D model	Evaluate <i>ex vivo</i> TNFi signature <i>in vivo</i> ; clustering; longitudinal response; ML training; 3D synovium (TNFi)
ML dataset	Naïve + Non-naïve	JAKi vs TNFi	223	Pretreatment baseline serum; 7 protein panel	Train (naïve) and validate (non-naïve) dual-therapy ML model (remission with JAKi vs TNFi)