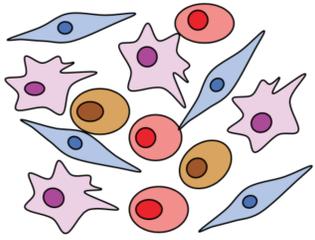


# Laboratory of Human Immune Disease Genetics

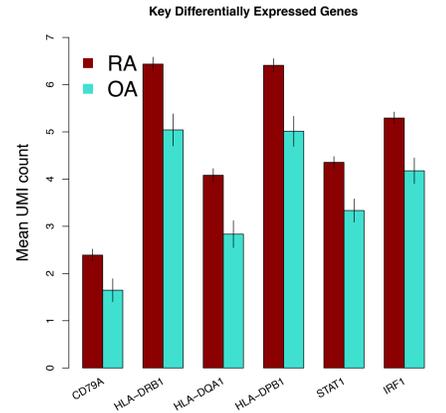
Students: Oleg Demianchenko, Daria Kirillova, Anastasia Kolos, Julia Panova, Valentina Sjenic, Rauf Verdiev, Amir Kuanishbaev  
 Lab Staff: Yaroslav Lozinsky, Angelika Branwen  
 PI: Tiffany Amariuta



## Background and Goals

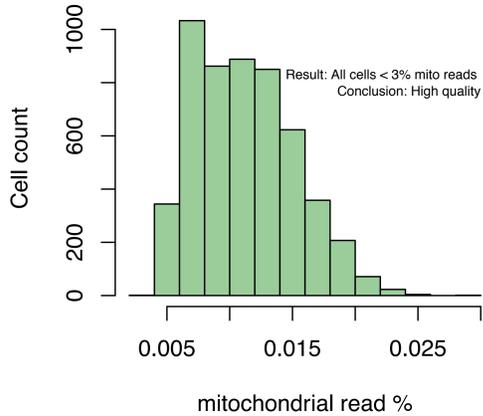


We aimed to study transcriptional signatures of rheumatoid arthritis (RA) to better understand this complex disease. Synovial tissue biopsies from affected knee joints of patients with RA (N=18) or osteoarthritis (OA) (N=3) were subjected to single cell RNA sequencing, where gene expression of peripheral blood mononuclear cells (PBMCs) was measured, resulting in a gene expression matrix of 32,391 genes and 5,265 cells.



Zhang, Slowikowski, Fonseka, Rao, Wei et al, Nature Immunology 2019

## Cell quality assessment

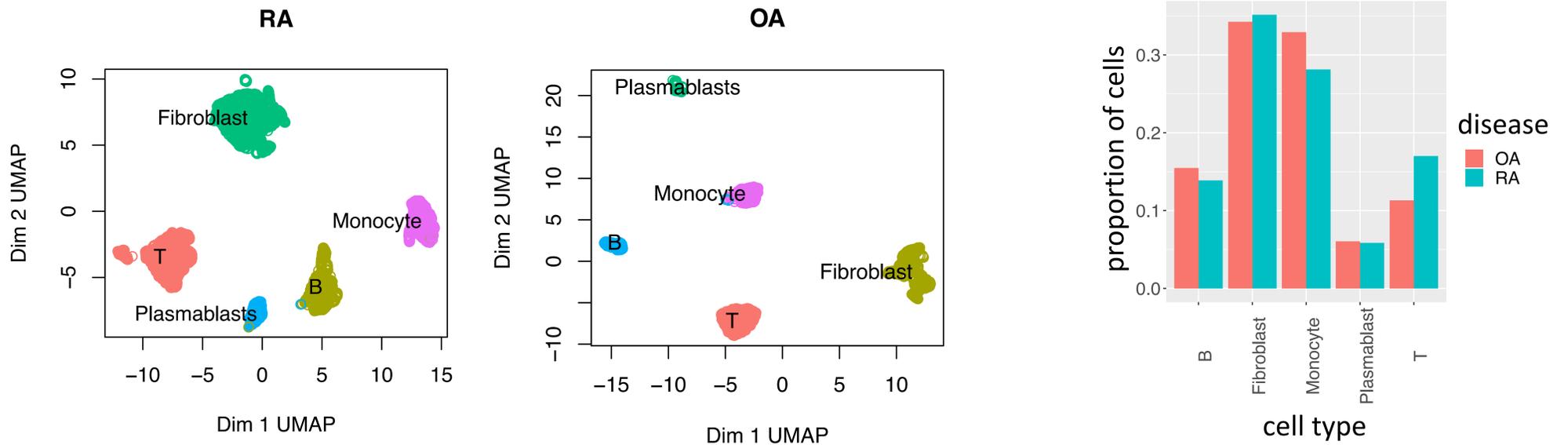


## Gene selection quality outperforms state-of-the-art method Seurat

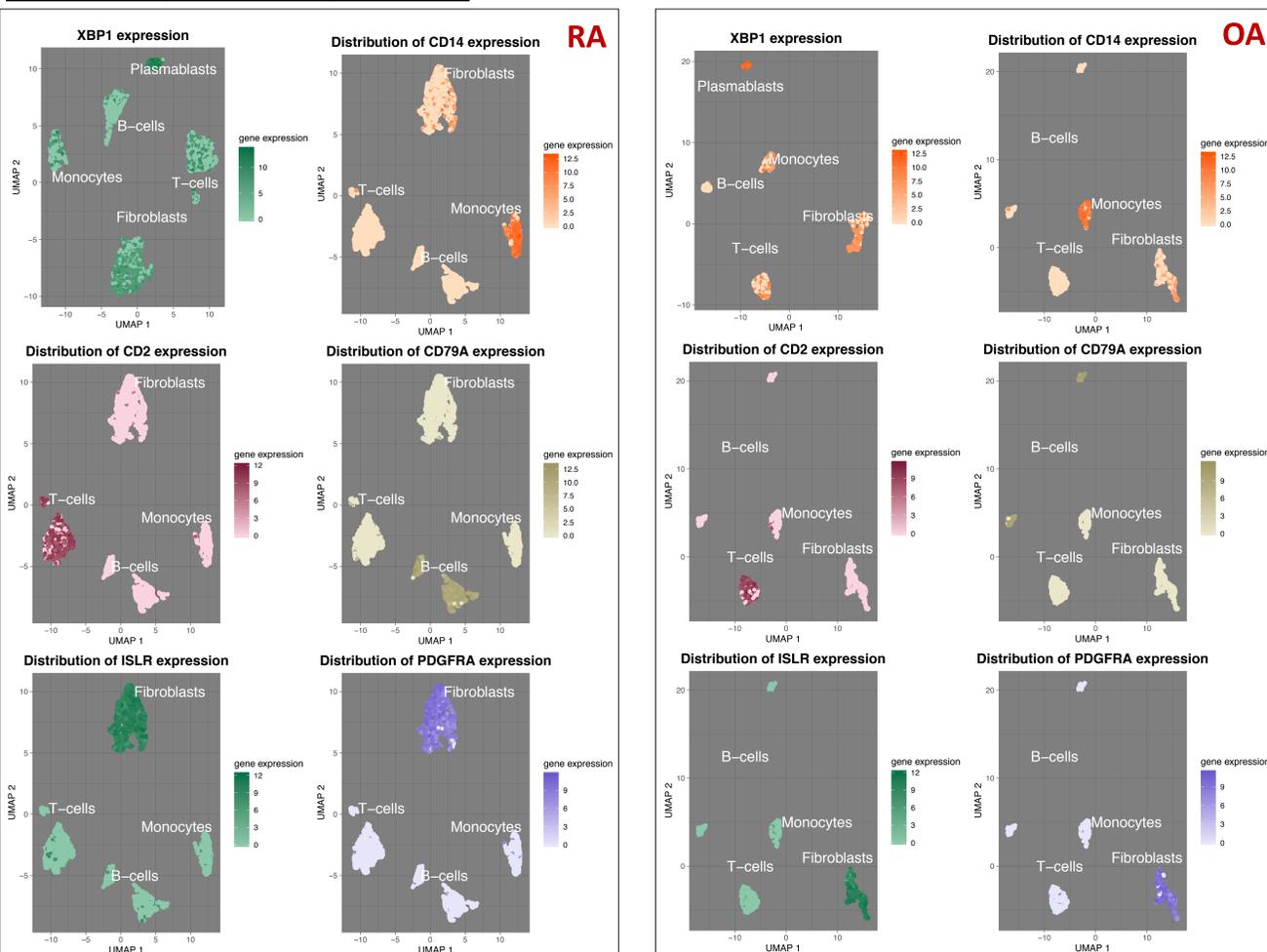
marker_gene	Comparison of vst-like methods for choosing variable genes								Comparison of variance measures for choosing variable genes				
	2e	2em	2enzm	2nzm	4em	4pow	myo	seur	16med	2mean	4mean	jenny	nzm2
PDGFRA(fib)	17	130	909	1825	707	718	136	245	190	134	208	26996	5117
CD2(Tc)	2505	84	2289	13344	174	189	94	213	186	325	120	25290	1086
CD79A(Bc)	2257	21	397	12250	61	66	39	115	90	196	37	24770	123
CD14(monoc.)	2918	77	1565	15037	76	86	90	198	81	899	63	24243	1219
30 score	52.89%	67.35%	48.39%	49.67%	60.01%	59.71%	65.77%	62.42%	66.13%	61.82%	67.24%	37.95%	52.78%

Legend (per-gene metrics)  
 2,4: indicates ^nth; e: # cells expressing; em: mean expression; enz: mean non-zero expression; pow: sd ^nth; original: (mean exp)^2; seur: Seurat's (mean exp)^2; med: median expression; jenny: economic disparity measure; 30 score indicates the proportion of variance captured by the top 30 PCs using each metric.

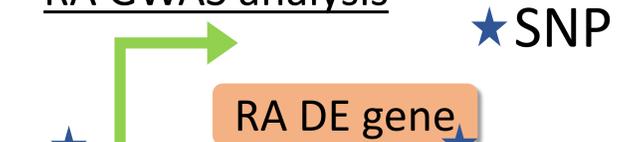
## Cell type annotation (dimensionality reduction and unsupervised clustering)



## Gene expression profiles



## RA GWAS analysis



*hypothesis:* SNPs in/near to differentially expressed genes in RA compared to OA should have greater disease association based on GWAS. SNPs in regulatory regions may impact transcription factor binding, next resulting in gene expression changes.

## Disease associations in RA specific genes

