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Introduction

- Rheumatoid arthritis (RA)** is a systemic autoimmune disease characterised by persistent inflammation of synovial tissue, progressive joint destruction and extra-articular manifestation.
- About 3-10% of RA patients remain symptomatic and can be considered to have **'difficult-to-treat RA' (D2T RA)**
- microRNAs (miRNAs) are **small non-coding RNAs** regulating mRNA expression, including genes related to **RA**.

Objectives

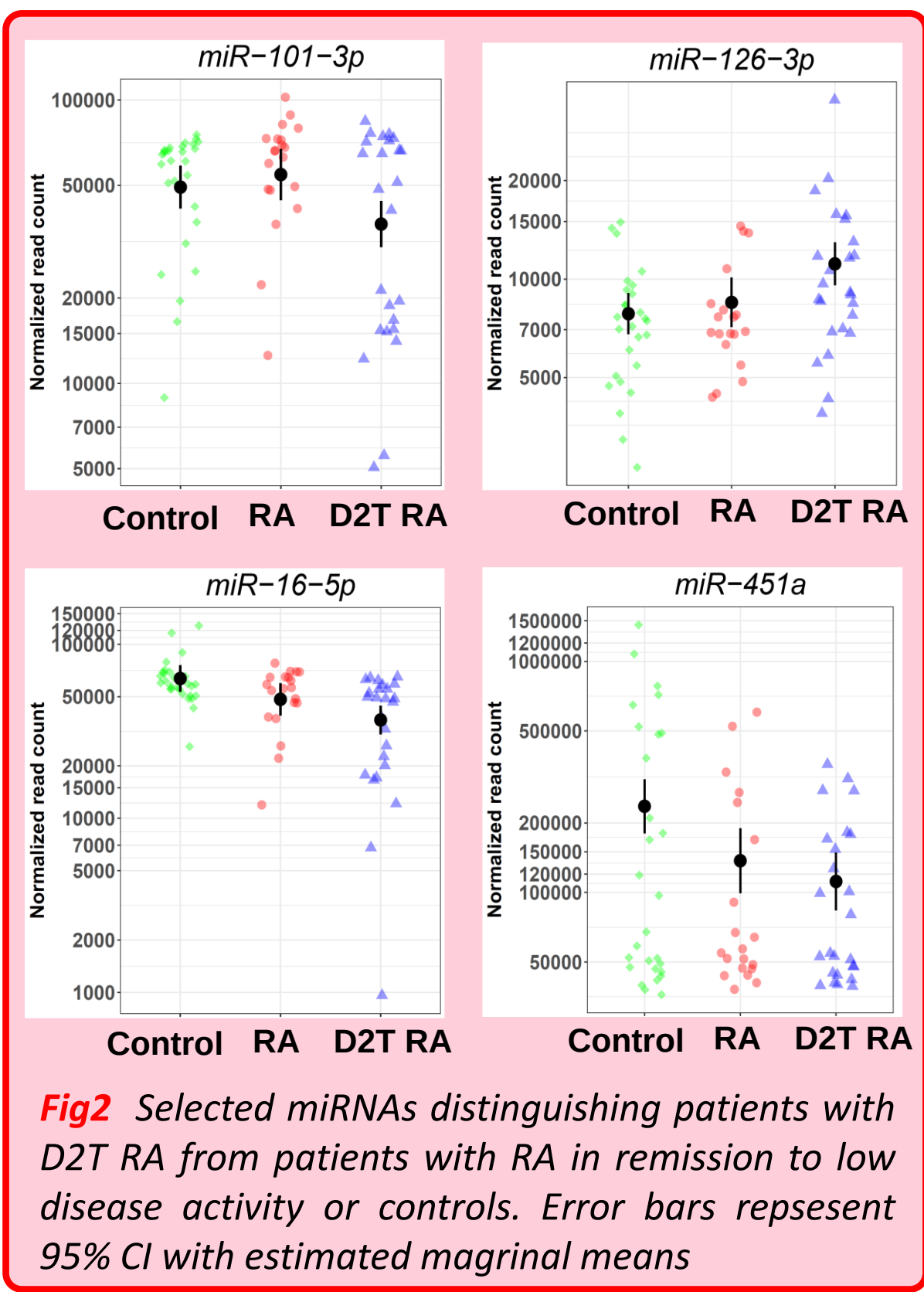
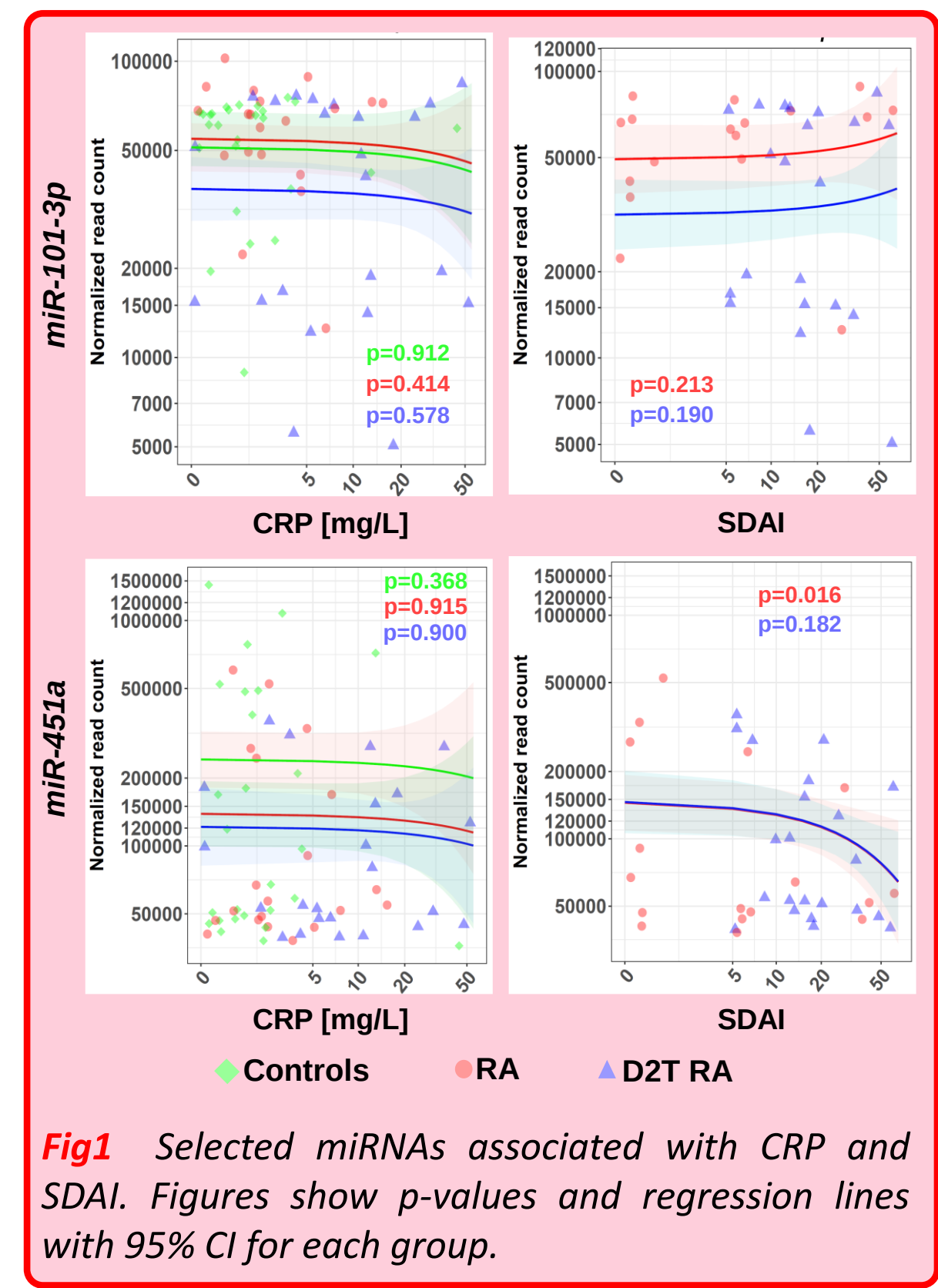
- In a retrospective study, we analyzed patients' blood samples prior to b-/ts-DMARD treatment and profiled circulating miRNAs to predict the development of D2T-RA.

Conclusion

- We discovered four miRNAs (miR-101-3p, miR-126-3p, miR-16-5p, miR-451a) that could differentiate D2T RA patients not only from healthy controls, but also from treatment responders.
- These miRNAs have been previously associated with RA pathogenesis or they are suggested candidate biomarkers for RA.
- miR-451a was significantly decreased and inversely associated with disease activity of D2T RA patients.

Characteristics		Controls n=36	RA-resp n=36	D2T RA n=36	p-value
Age	Mean (SD)	61.1 (7.7)	66.3 (9.6)	59.2 (10.9)	0.008
Gender	Female (%)	22 (61.1)	31 (88.6)	31 (88.6)	0.004
Duration of targeted treatment [months]	Median (IQR)		62.0 (41.5 - 101.0)	139.5 (83.5 - 212.8)	<0.001
FW [mm/1st h]	Median (IQR)		14.0 (9.0 - 21.5)	19.0 (10.5 - 31.0)	0.114
CRP [mg/L]	Median (IQR)	1.6 (1.1 - 3.2)	2.0 (1.2 - 5.7)	6.6 (3.0 - 12.9)	0.001
SJC [count]	Median (IQR)		0.0 (0.0 - 2.8)	2.0 (0.2 - 4.8)	0.011
TJC [count]	Median (IQR)		0.0 (0.0 - 3.0)	3.0 (1.5 - 6.0)	0.001
MDGAS	Median (IQR)		5.0 (0.0 - 17.0)	28.5 (10.5 - 48.0)	<0.001
VAS	Mean (SD)		21.0 (25.1)	43.6 (21.7)	<0.001
DAS28-ESR	Mean (SD)		2.8 (1.6)	4.1 (1.4)	0.001
DAS28-CRP	Mean (SD)		2.5 (1.5)	3.8 (1.3)	0.001
SDAI	Median (IQR)		3.3 (0.5 - 9.9)	14.4 (9.2 - 23.1)	<0.001
Glucocorticoids [count]	n (%)		19 (54.3)	31 (88.6)	<0.001
csDMARD [count]	n (%)		31 (88.6)	27 (77.1)	<0.001
tsDMARD [count]	n (%)			3 (8.6)	0.044
bDMARD [count]	n (%)			32 (91.4)	<0.001
Number of failed ts/bDMARDs	Median (IQR)			3 (1-3)	

Tab1 Demographic and clinical characteristics of subjects included in the screening cohort.



miRNA	Clinical parameter	Incidence Rate Ratio	2.5% CI	97.5% CI	p-value
miR-101-3p	CRP	0.00	-0.01	0.01	0.535
	SDAI	0.00	-0.01	0.01	0.482
	SJC	0.01	-0.02	0.03	0.618
miR-126-3p	CRP	0.01	0.00	0.02	0.127
	SDAI	0.00	-0.01	0.01	0.853
	SJC	-0.01	-0.03	0.01	0.537
miR-16-5p	CRP	0.00	-0.01	0.01	0.889
	SDAI	0.00	-0.01	0.01	0.848
	SJC	0.01	-0.02	0.03	0.661
miR-451a	CRP	0.00	-0.02	0.01	0.700
	SDAI	-0.01	-0.02	0.00	0.015
	SJC	-0.02	-0.05	0.01	0.116

Tab2 The association of selected miRNAs with CRP, simplified disease activity index (SDAI), and swollen joint count (SJC)

References:

- de Hair MJH, Jacobs JWG, Schoneveld JLM, van Laar JM. Difficult-to-treat rheumatoid arthritis: an area of unmet clinical need. *Rheumatology* 2018;57:1135-44.
- Nagy G, Roodenrijs NMT, Welsing PMJ et al. EULAR definition of difficult-to-treat rheumatoid arthritis. *Ann Rheum Dis* 2021;80:31-5