selection and hyperparameter optimisation. The Sequential Model-Based Optimization procedure was used to automatically select the best model configuration amongst 10 feature selection filters, 2 class imbalance correction techniques, 3 data cleaning methods and 4 classification algorithms along with their respective hyperparameters. Model optimisation was performed using a 10-fold Cross Validation (CV) while a 10 times repeated 10-fold CV was used for the predictive performance evaluation. Receiver operating characteristic (ROC) and precision recall (PR) curves were used to directly compare the classification potential of molecular approaches.

Results: 12,035 gene expression features and 714,486 methylation features were available for classifier building after quality control in our early arthritis B-lymphocyte dataset. Performance estimation showed the expression profile of B-lymphocytes alone to have no significant discriminatory utility for RA in this setting (average area under [AU] ROC 0.48). Methylation profiles were significantly superior for discriminating RA (average AU ROC 0.71). Interestingly, when a combined transcriptome/methylome model was generated, further enhancement of discriminatory function was observed, although this was modest (AU ROC 0.74).

Conclusion: Methylation profiling of B-lymphocytes affords better discrimination for RA than does transcriptional profiling. This may differ in other cell types. Combining data from molecular platforms may be an optimal approach. Functional analyses of the resultant B-lymphocyte signatures may yield insight into molecular pathobiology.

Figure A. Table summarizing results of performance estimation of B cell gene expression and methylation profiles using 20 x 10-fold Cross Validation (200 paired training-testing samples). The performance of a combined model is also given. An ROC curve depicting discriminatory ability of the combined model is shown.

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FRI0010 TCR-CD3Z GENE EXPRESSION PROFILE IN A COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Advances in understanding the pathogenesis of RA support the contribution of T cells in the disease process through the recognition of the arthritogenic antigen (Ag) and maintenance of chronic inflammatory response [1].

Previous gene association studies have demonstrated that CD247 gene expressions are associated with a variety of autoimmune disease. As regard Rheumatoid Arthritis (RA), this relationship has not been fully clarified yet.

Objectives: We aimed to evaluate the T-cell receptor-CD3 zeta chain (TCR-CD3 ζ) gene expression profile in a cohort of patients with RA.

Methods: A case-control study on 150 consecutive RA patients diagnosed according to 2010 ACR/EULAR criteria and 150 matched healthy controls without family history of RA or other autoimmune diseases. RA patients with other autoimmune diseases, viral hepatitis B or C, malignancy or hematological disorders were excluded from the study.

All participants were subjected to history taking, clinical examination, assessment of disease activity (in RA patients) using DAS-28 and HAQ, routine laboratory investigations, inflammatory markers level, serological tests, as well as molecular analysis for TCR-CD3 ζ mRNA expression by quantitative real-time polymerase chain reaction.

Results: TCR-CD3 ζ gene expression was significantly lower in RA cases than in healthy controls ($p < 0.05$) (Table 1). Expression of TCR-CD3 ζ revealed a significant negative correlation with RA disease duration, RF, and ESR ($p < 0.05$) in RA cases. The level of TCR-CD3 ζ also showed a significant lower expression in +ve RF patients than in -ve RF patients ($p < 0.05$). The AUC of TCR-CD3 ζ level showed a moderate level of accuracy (AUC = 0.840, $p = 0.025$) (Figure 1), and the calculated cutoff value (≤ 0.077) can precisely discriminate subjects with RA from those without RA with 93.5% sensitivity and 75% specificity (Table 2).

Table 1. Comparison between RA cases and control group as regard CD247 (mRNA levels for TCR-CD3 ζ gene expression)

TCR-CD3 ζ	RA cases (n=150)	Healthy Controls (n=150)	Test of sig.	P
Min. – Max.	0.037– 12.467	0.034– 11.314	Z=3.047*	0.002*
Mean $\pm$ SD.	0.663 $\pm$ 1.90	0.816 $\pm$ 1.64		
Median (Q1-Q3)	0.178 (0.109-0.314)	0.315 (0.198-0.922)		

Z: Z-score of Mann-Whitney test

*: Statistically significant at $p \leq 0.05$

Table 2. Analysis of ROC curve for TCR-CD3 ζ level as a predictor of RA (high RF)

Variable	Cutoff point (ng/ml)	AUC	P	Sensitivity (%)	Specificity (%)	PPV	NPV	Accuracy (%)
TCR-CD3 ζ	≤ 0.077	0.840*	0.025**	93.5	75.0	78.9	92.0	84.3

AUC: Area under the curve

*AUC ≥ 0.5

** Statistically significant at $p \leq 0.05$

PPV: Positive Predictive Value

NPV: Negative Predictive Value

Figure 1. ROC curve for CD247 (TCR-CD3 ζ) level as a predictor of Rheumatoid arthritis

Conclusion: Our results demonstrated a lower expression of TCR-CD3 ζ in RA patients than in healthy controls. We suggested that CD247 gene down-regulation might contribute in the susceptibility to RA and help understanding the mechanisms responsible for deficient T-cell responses in RA patients.

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