2022 Best Research Poster Award

Barwon Health

DEAKIN UNIVERSITY

An epigenetic biomarker in *FOXP3*/*TIGIT* in cord blood correlates with the proportion of regulatory T cells and predicts food allergy at one year

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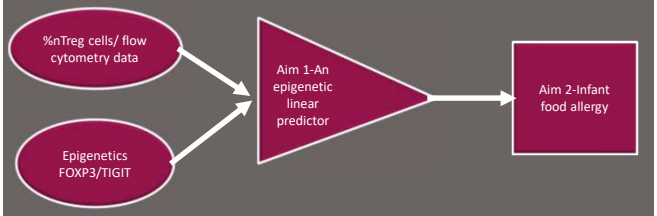
INTRODUCTION

Small studies have used flow cytometry to show that a higher proportion of naïve T regulatory (Treg) cells at birth is associated with decreased IgE-mediated food allergy during infancy[1,2,3].

OBJECTIVES

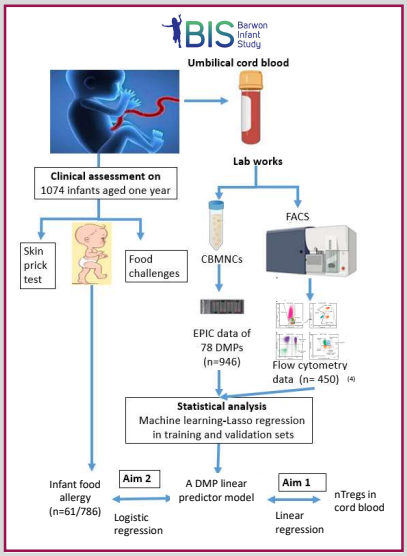
1. To develop an epigenetic biomarker in whole blood for the proportion of nTreg in cord blood mononuclear cells (CBMNCs)
2. To evaluate its association with infant food allergy



METHOD

The Barwon Infant Study (BIS) Cohort study

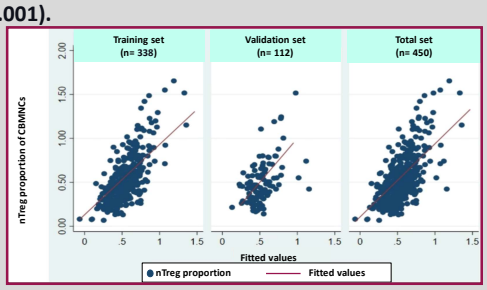
We measured Tregs in CBMNCs using flow cytometry in n=450, and cord blood DNA methylation was measured using the Illumina EPIC array in n=946. Food allergy was determined at 1 year. In a training set (n=338), we investigated if differential methylated probes (DMPs) in the *FOXP3* and *TIGIT* genes were associated with Treg:CBMNCs; and used LASSO regression to develop a DMP linear predictor. This predictor was evaluated in a validation set (n=112), and its association with food allergy was calculated in all participants with relevant data (n=786).



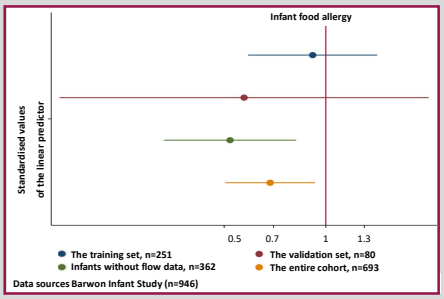
RESULTS

Lasso selected 21 of 78 DMPs strongly associated with the nTreg proportion in CBMNCs in the training set.

1. A linear predictor of nTreg derived via LASSO regression of these 21 DMPs correlated with nTreg in the validation set (R^2=0.2408, p<0.001).



Estimates of the odds ratio for infant food allergy per unit change in the DMP linear predictor in training, validation, the infants without nTreg flow cytometry data and entire datasets.



Subgroups	Odds ratio	*p*-values	95% Confidence Interval		Benjamini-Hochberg test
The training set	0.91	0.69	0.59	1.42	0.69
The validation set	0.57	0.39	0.16	2.02	0.53
Infants without flow cytometry data	**0.52**	**0.004**	**0.33**	**0.82**	**0.02**
The entire cohort	0.68	0.015	0.50	0.93	0.03

The DMP linear predictor was associated with subsequent food allergy in all participants with relevant data (n=786; *p*=0.015); as well as among the subgroup without nTreg flow cytometry data (n=445; *p*=0.004).

DISCUSSION

In this birth cohort study, the linear predictor model of the 21 Lasso-selected DMPs in these *FOXP3 and TIGIT* loci does not replace the role of flow cytometry in measuring the nTreg proportion in fresh cord blood. Instead, the linear predictor could be used as a proxy for estimating the proportion of functional nTreg cells in CBMNCs from the birth cohort without the flow cytometry data.

The linear predictor was associated with a reduced risk of IgE-mediated food allergy at one year of age. Low DNA methylation levels in these 21 DMPs, which may be associated with high gene expression of functional Treg markers against food allergy, may play a protective role in this association.

CONCLUSION

An epigenetic biomarker in whole blood collected at birth can be used to estimate the proportion of nTreg in CBMNCs, and is associated with decreased risk of subsequent food allergy.

REFERENCES

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