

Characterisation of T-cell responses in nickel- and paraphenylenediamine- allergic patients

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Gavin Maxwell, Clare Stretton, Rebecca J Dearman, Ian Kimber

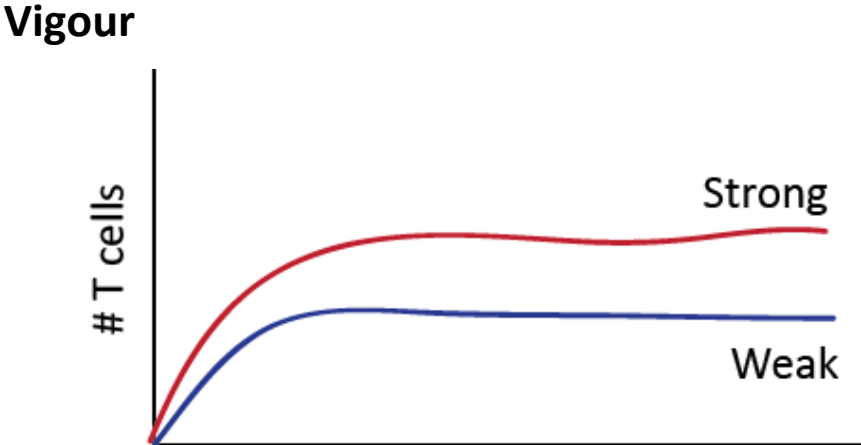


Unilever

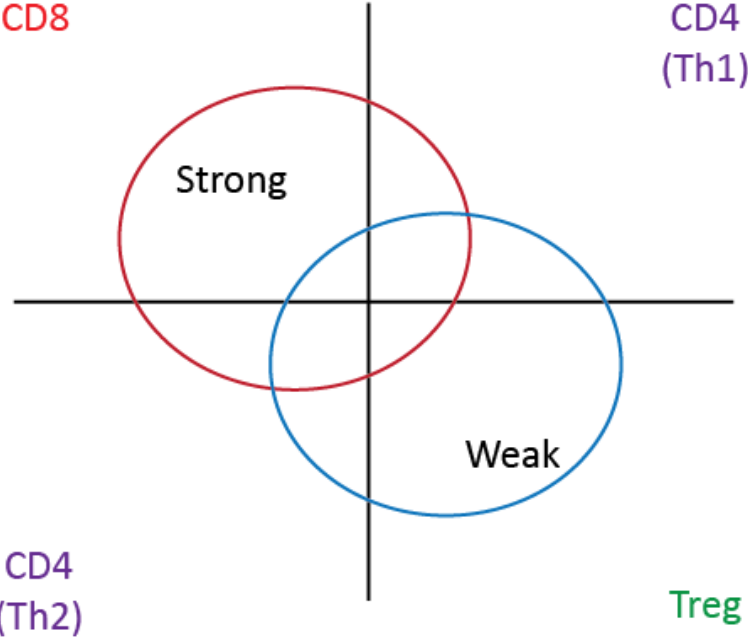
Aims & Objectives

- Understand why chemical allergens differ in sensitisation potency
- Determine the features of contact allergens that influence sensitisation potency
- Apply to development of *in vitro* predictive tests for identification of contact allergens
- Part of broader project investigating correlation between characteristics of T-cell responses to chemical allergen and potency of skin sensitisation

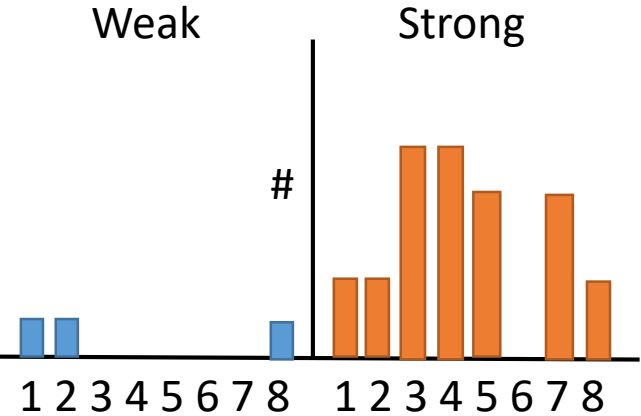
What T-cell response characteristics potentially influence potency?



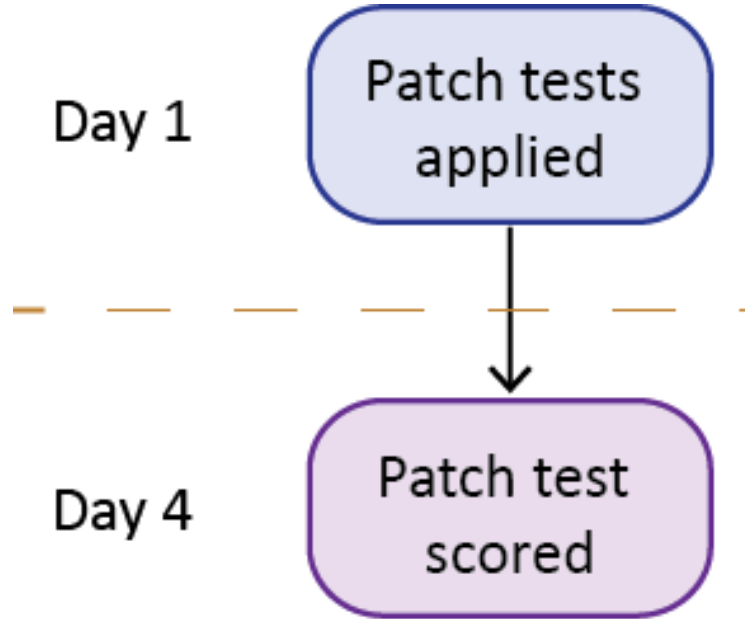
Quality



Breadth

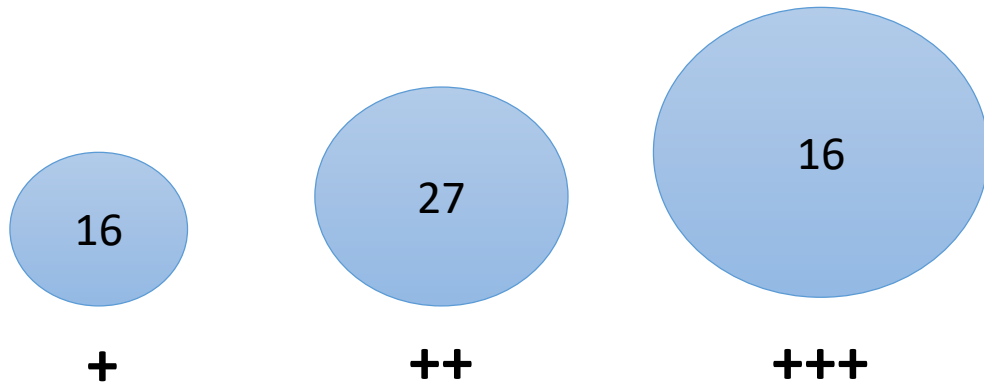


Study design



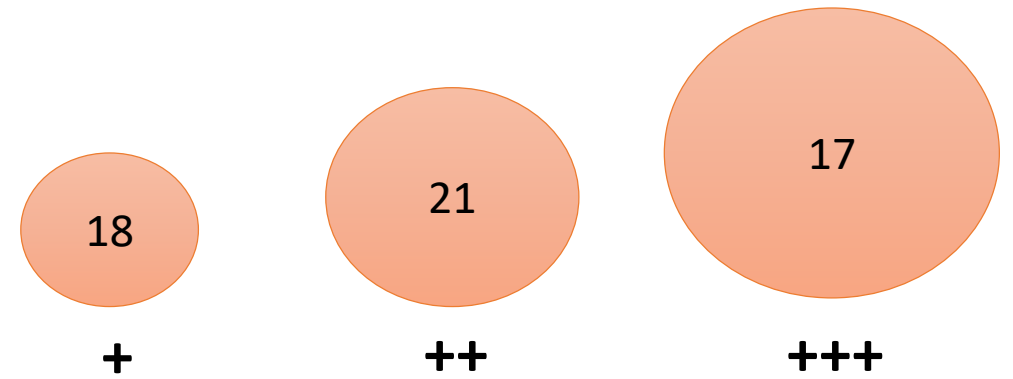
Nickel-allergic patients

N=59



PPD-allergic patients

N=56

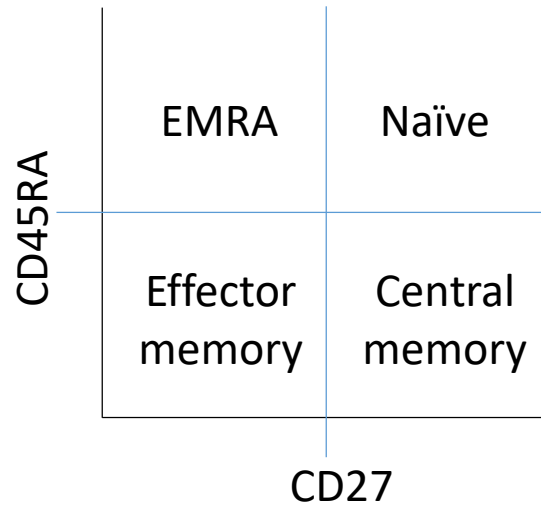


Controls

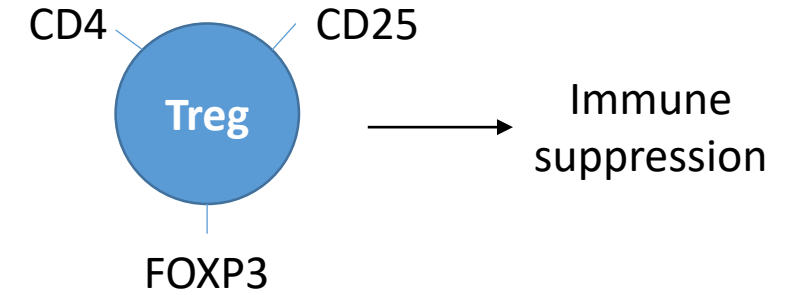
N=14

Assaying T-cell quality in ACD by flow cytometry

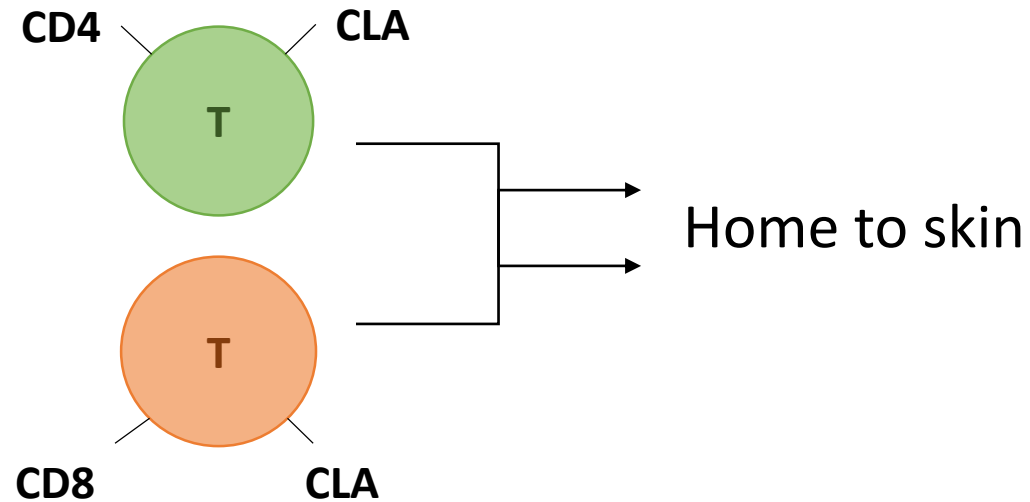
Quantifying T-cell subsets



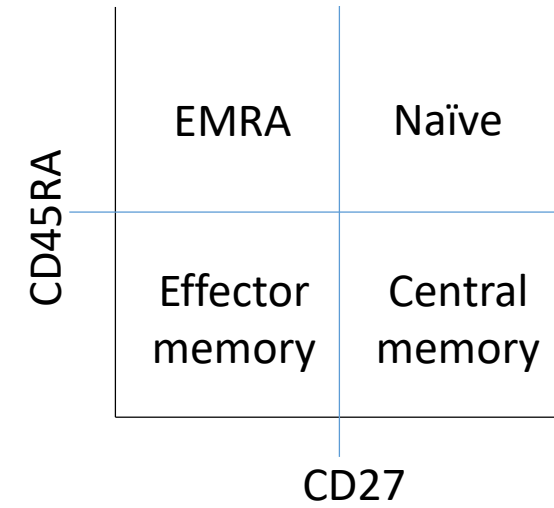
Assaying regulatory T-cell abundance



Measuring cutaneous lymphoid antigen expression

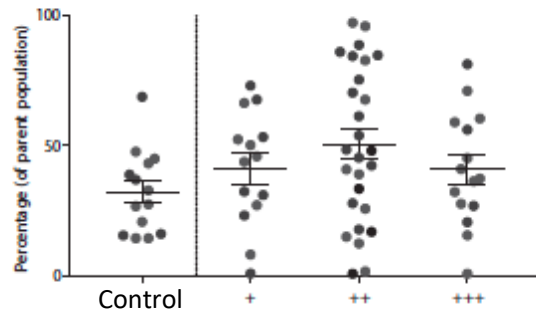


Does ACD perturb the phenotype of the CD4+ T-cell populations?

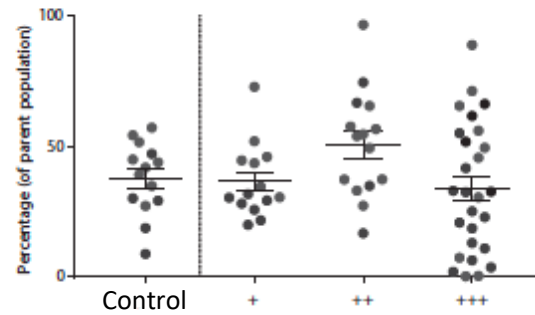


Nickel allergic

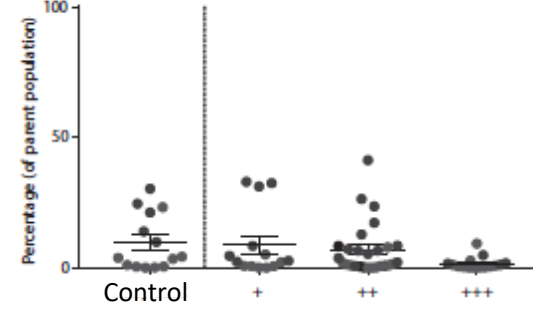
i) Naive



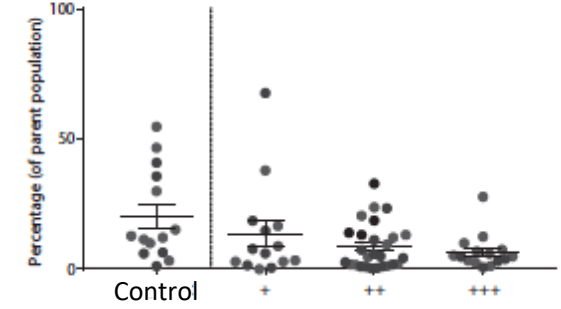
ii) Central memory



iii) EMRA

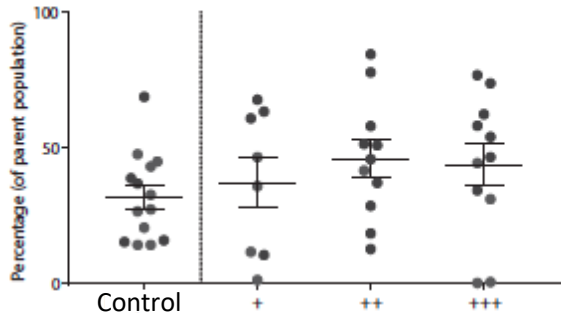


iv) Effector memory

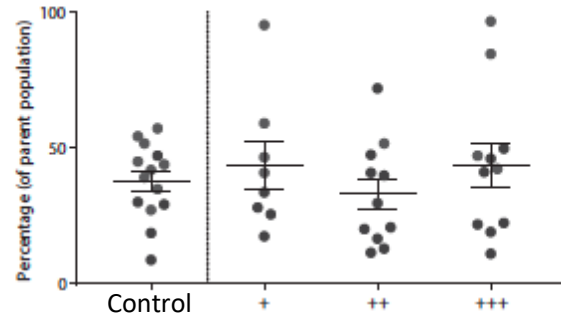


PPD allergic

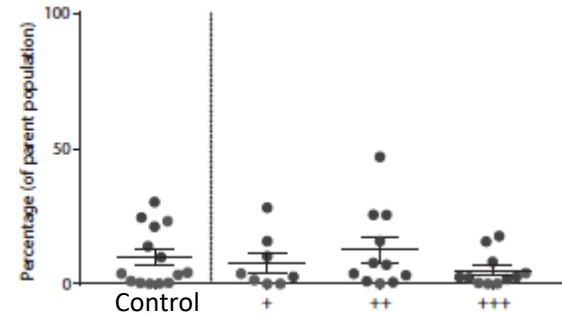
i) Naive



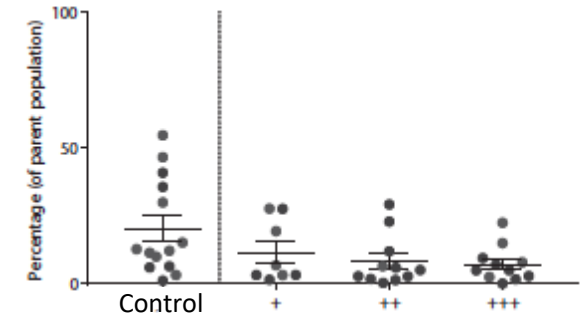
ii) Central memory



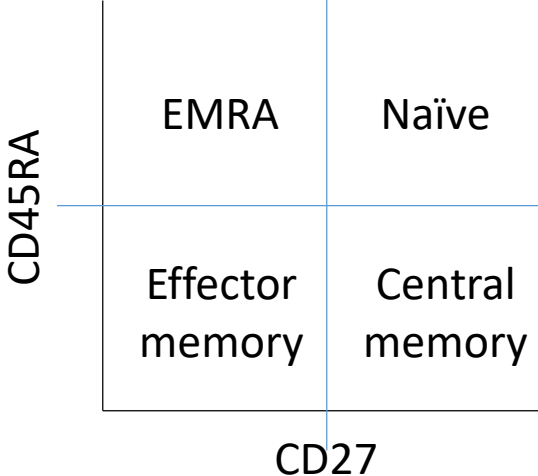
iii) EMRA



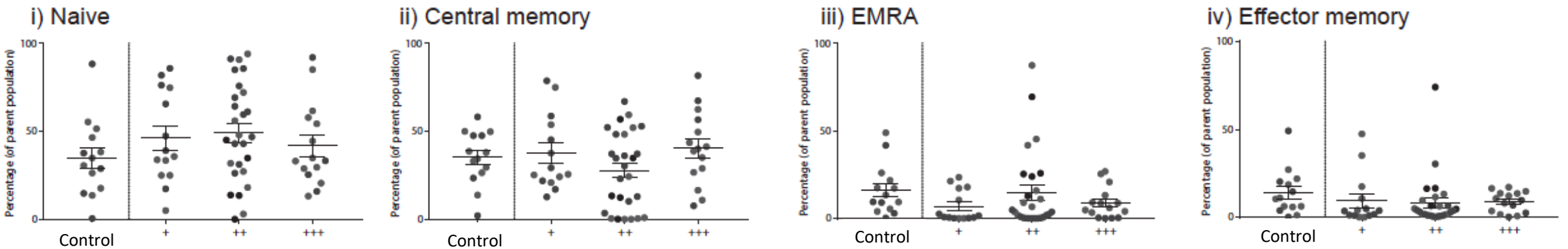
iv) Effector memory



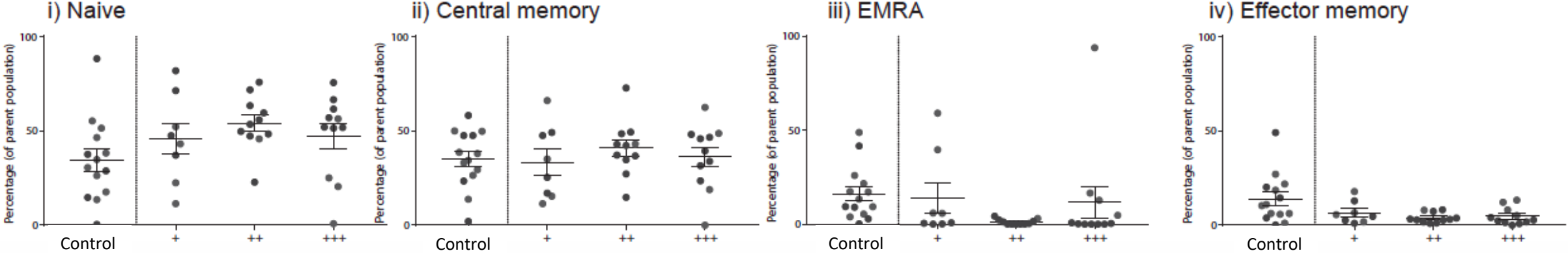
Does ACD perturb the phenotype of the CD8hi T-cell populations?



Nickel allergic

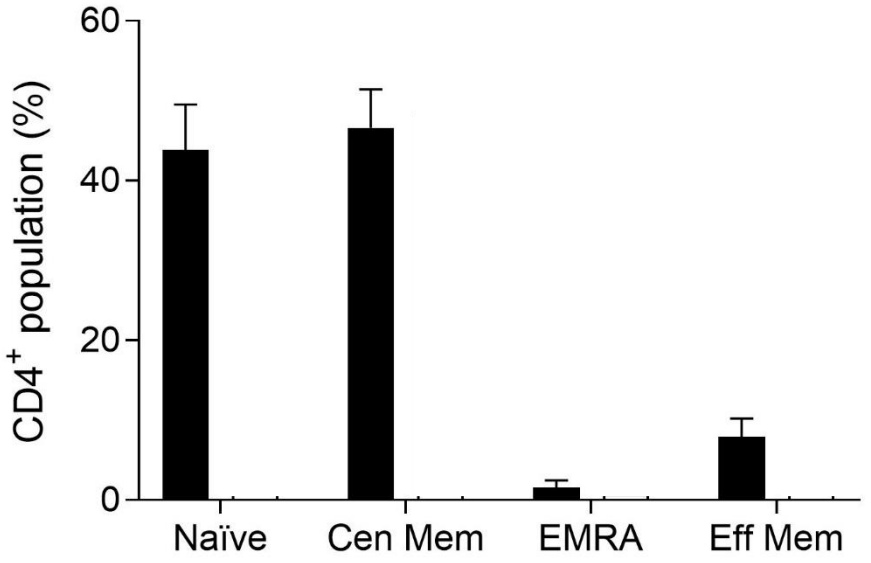


PPD allergic

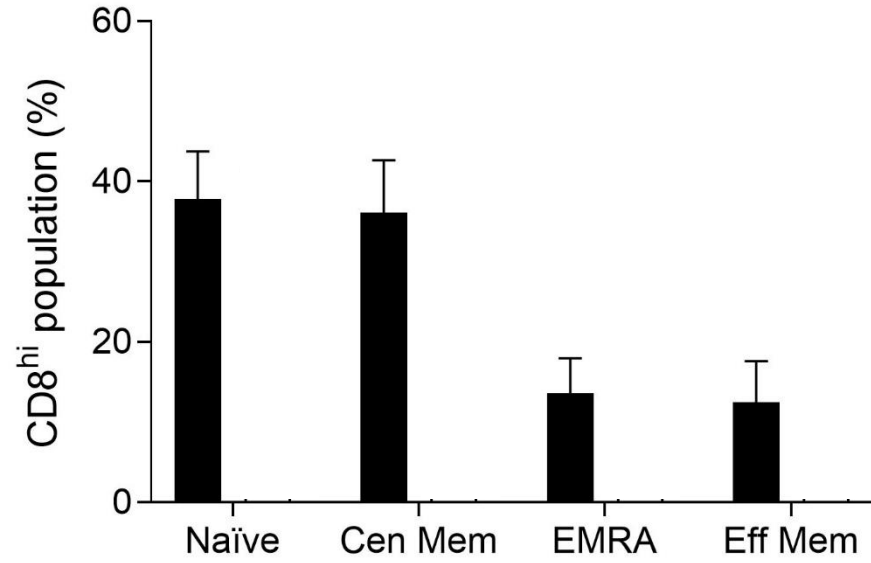


Does application of a patch test series perturb the phenotype of T cells?

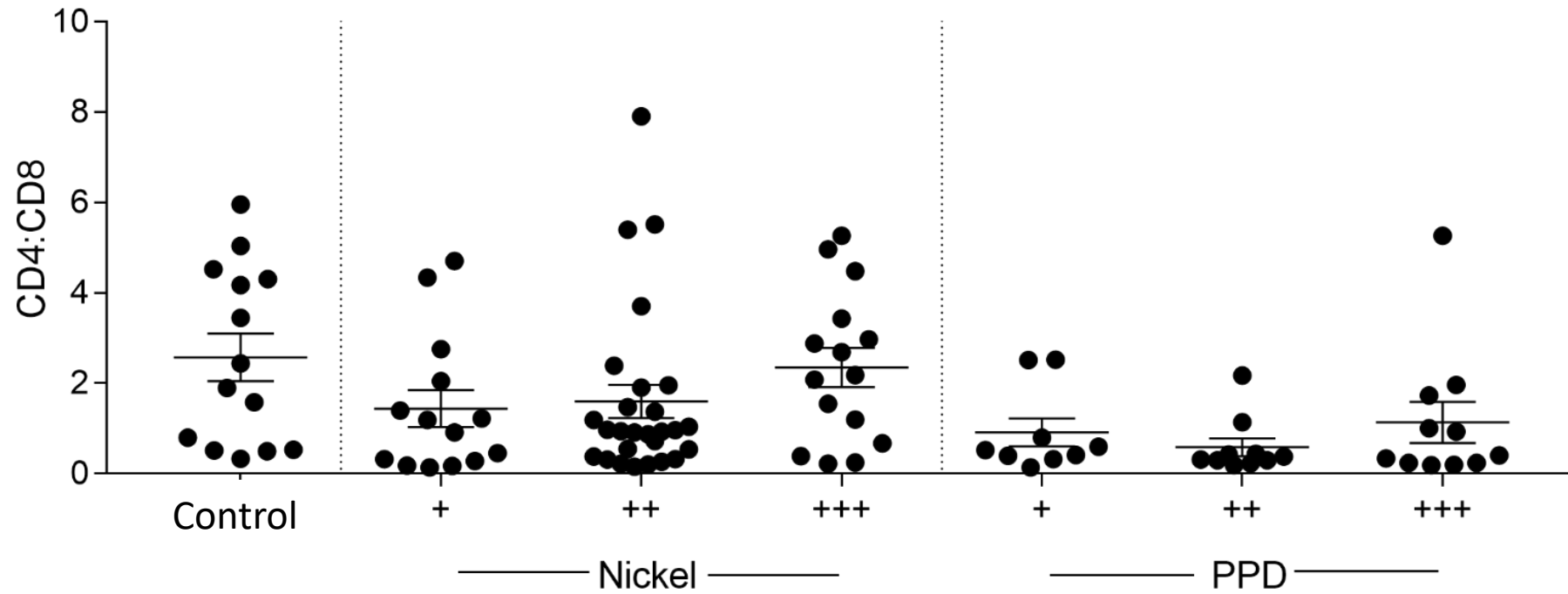
A



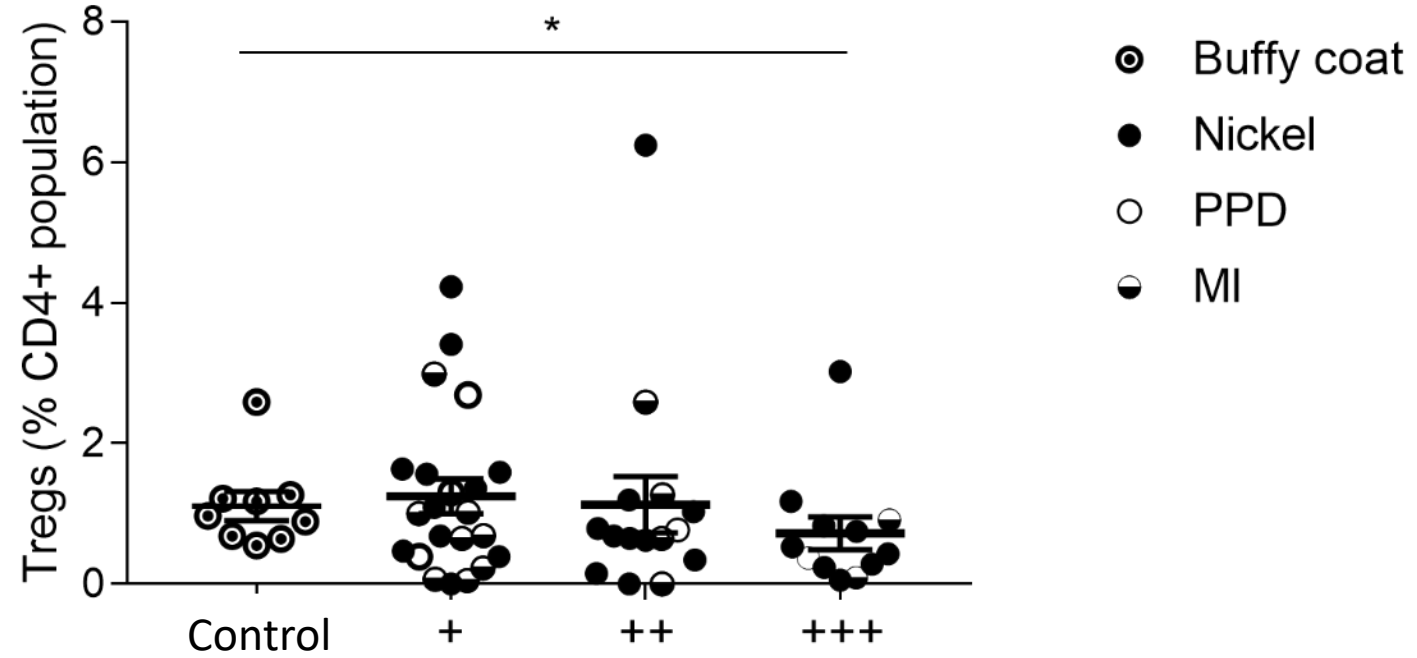
B



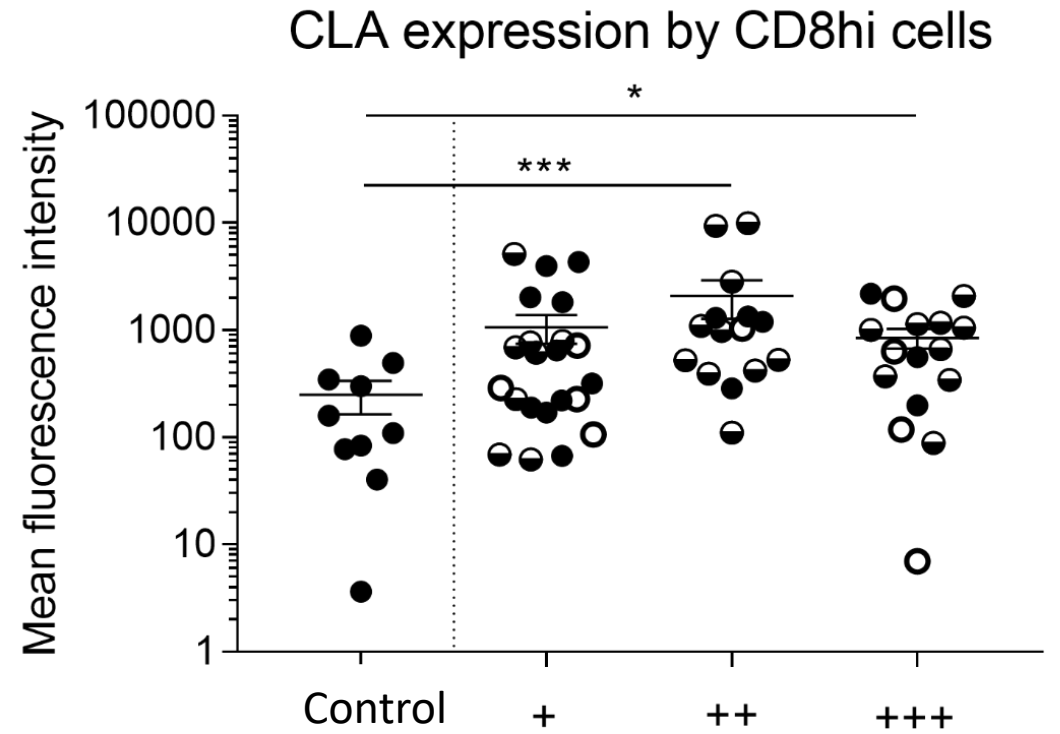
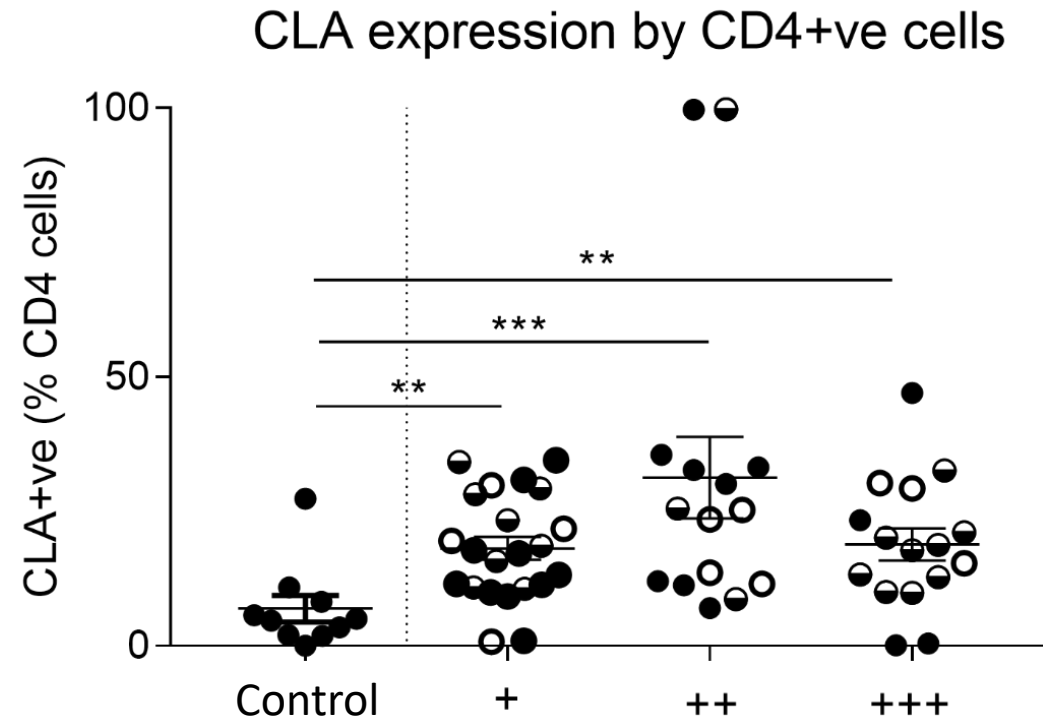
Is ACD associated with an altered CD4:CD8 ratio?



Is ACD associated with altered Treg abundance?



Is ACD associated with increased expression of CLA?



Conclusions

- Immunological study of T-cell characteristics can be used to understand sensitisation potency
- Quality can be assessed *ex vivo*
- Flow cytometric analyses of CD4+ and CD8hi T-cell populations from nickel and PPD allergic patients showed:
 - Increased naïve cells
 - Decreased EMRA & effector memory cells
 - Lower CD4:CD8 ratio
 - Increased CLA expression (skin homing)
 - Fewer Tregs (immune suppressors)
- Work is ongoing to characterise T-cell receptor diversity (breadth)
- Insights from nickel allergy may be applicable to contact allergy in general

Acknowledgements



- Participants and their families
- Members of the Kimber/Dearman lab