Allergic Contact Dermatitis: characterising the relationship between T cells and skin sensitising potency

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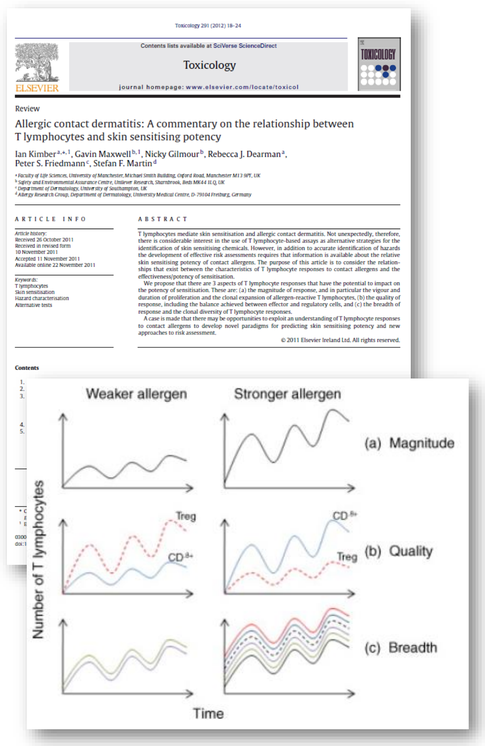
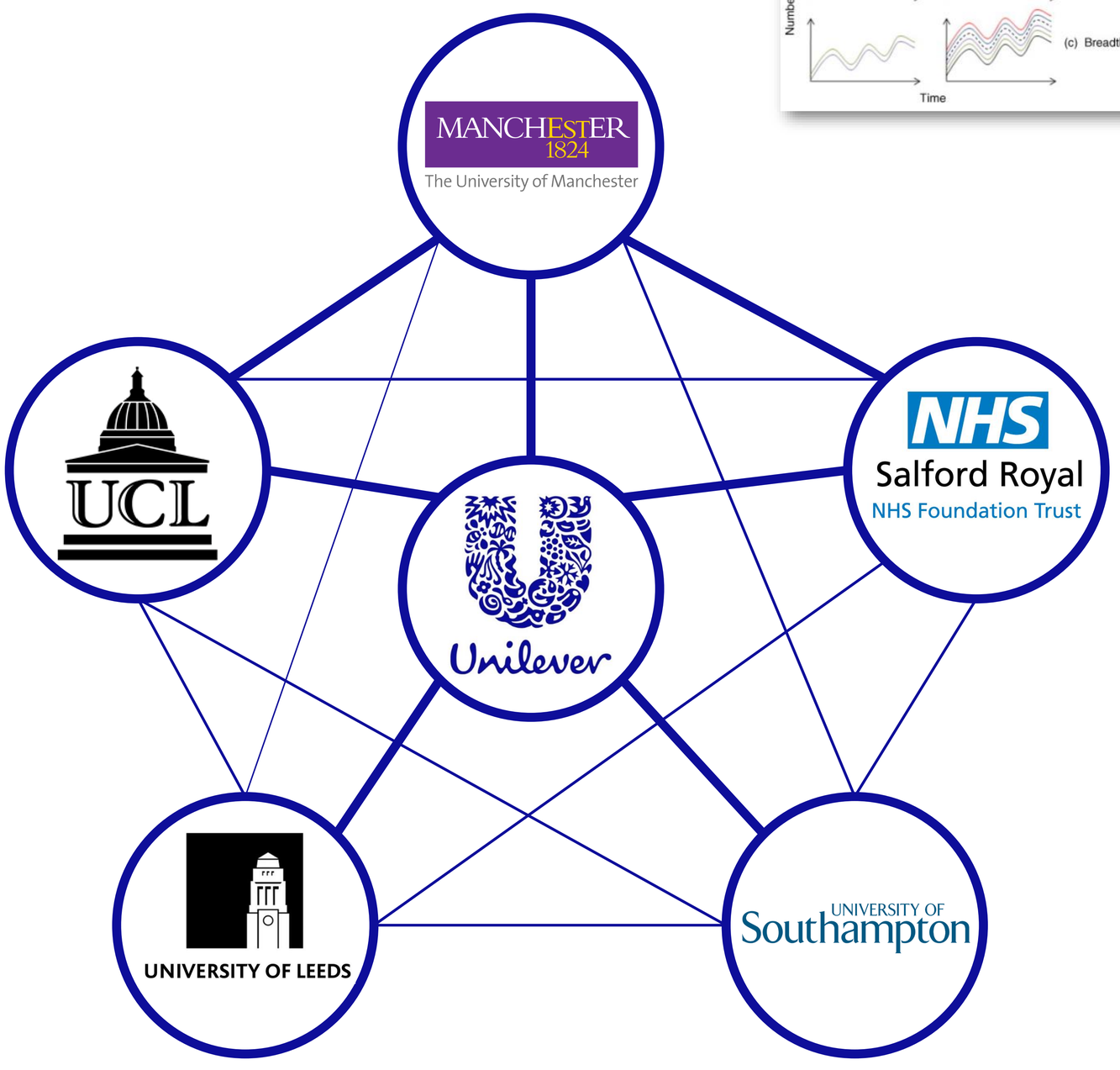
Introduction

A workshop entitled 'T Lymphocytes: Orchestrators of Skin Sensitisation' was held in London in 2010 to identify opportunities to exploit an improved understanding of T cell responses to contact allergens in developing novel paradigms for estimating skin sensitising potency and risk assessment. The conclusions of that workshop were translated into a multi-centre, inter-disciplinary research programme (termed the 'T Cell Forum') to characterise and mathematically model skin sensitiser-induced T cell responses to chemical allergens in patients with allergic contact dermatitis (ACD).





Materials and Methods

Over the last six years, approx. 200 patients with ACD to methylisothiazolinone (MI), 5-chloro-2-methylisothiazol-3-one (MCI)/MI, nickel or paraphenylenediamine (PPD) have had their blood T cell populations characterised to understand how their T cell phenotype relates to their sensitisation status [study approved by North West REC – Greater Manchester East (12/NW/0602)].

In addition, a cohort of 30 alopecia patients undergoing treatment with diphenylcyclopropenone (DPC) have been similarly characterised to monitor the initiation and maturation of the DPC-induced T cell response resulting from repeated, controlled exposure to a contact allergen [study approved by NRES Ethics Committee East of England – Norfolk [14/EE/1067]].

This research was conducted in parallel with a quantitative analysis of protein haptenation following incubation with selected chemical allergens (cinnamaldehyde, dinitrochlorobenzene, MCI and 6-methyl coumarin), as well as with the development of mathematical and statistical models of $CD8^+$ T cell-mediated immune responses based on several differentiation hypotheses.

Results

The results of these multi-disciplinary studies provide a comprehensive characterisation of human T cell-mediated immune responses to several skin sensitising chemicals (including analyses of T cell phenotype; proliferation; and T cell receptor (TCR) repertoire) presented in the context of diagnostic patch test information on skin sensitisation status. To find out more please attend the following presentations:

- 15.30-15.50; Thursday, 18th Oct, Parallel Hall 2; **Determination of protein haptenation by chemical sensitisers within the complexity of skin proteome** – Maja Aleksic
- 17.10-17.20; Thursday 18th Oct, Plenary Hall; **Characterisation of T lymphocyte responses in nickel and phenylenediamine allergic patients** – Kate Wicks
- Poster; **Immune Responses to repeated application of the contact allergen diphenylcyclopropenone (DPC) in humans: evidence of down-regulatory mechanisms** – Kate Wicks

References

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Conclusions and Next Steps

By bringing together basic research and clinical expertise, the T Cell Forum has extended our mechanistic understanding of skin sensitisation and ACD from both perspectives. Overall conclusions will be discussed in the context of opportunities to apply these mechanistic and clinical insights to improve skin allergy risk assessment during '**Improving skin sensitisation: opportunities to reduce uncertainty through research**' symposium at 12.30-13.30, Thursday 18th Oct in the Plenary Hall.

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