

Clinical & Experimental Allergy

Inheritance and the sunshine vitamin

G. Roberts^{1,2,3}

¹Clinical and Experimental Sciences and Human Development and Health, Faculty of Medicine, University of Southampton, Southampton, UK, ²NIHR Southampton Respiratory Biomedical Research Unit, University Hospital Southampton NHS Foundation Trust, Southampton, UK and ³The David Hide Asthma and Allergy Research Centre, St Mary's Hospital, Isle of Wight, UK

In a recent publication in *Journal of Allergy and Clinical Immunology*, Jones et al. have described a study where they have assessed the efficacy of epicutaneous immunotherapy for peanut allergy.¹ Using a double-blind, randomized, placebo-controlled design, 74 children and young adults with peanut allergy were randomised to placebo, low dose (100 mg) or high dose (250 mg) therapy. They defined treatment success as safely consuming 5044 mg peanut protein or achieving a ≥ 10 -fold increase in the dose of safely consumed peanut from baseline. After a year of therapy, treatment success was seen in 3 (12%), 11 (46%) and 12 (48%) in the placebo, 100 and 250 mg groups respectively. Both active groups were statistically higher than placebo. But what does this mean in practice for patients? The medium change in peanut protein safely consumed from baseline were 0, 43, and 130 mg of protein in the placebo, 100 and 250 mg groups respectively. While the two active groups were again statistically significantly larger than the placebo one, such a small increase in threshold is unlikely to be clinically meaningful for

patients. More positively, while 14.4%, 79.8% and 79.8% of placebo, 100 mg and 250 mg doses respectively resulted in adverse reactions, these were mostly minor local reactions with no severe ones. So early promise given that there was a small, dose dependent clinical benefit with a relatively good safety profile. Might a higher dosage deliver a great clinical benefit while not compromising safety?

In this month's issue of *Clinical and Experimental Allergy*, Leung et al. assessed whether parental migration status impacted on the likelihood of children born in Hong Kong developing asthma and other childhood wheezing disorders.² This was a development of their earlier work.³ After adjusting for type of hospital at birth, parental allergy, parental age and highest parental education, they found that having both parents as migrants was associated with more hospitalization for asthma and other wheezing disorders (hazard ratio 1.30, 95% confidence interval (CI) 1.05–1.60). When the analysis was restricted to asthma, the hazard ratio was similar (1.33, 0.96–1.84). The interest here is that this was seen despite the migrate population being genetically very similar to the native one. The next question is, what is the mechanism?

Bertelsen et al. have examined whether parental clinical markers of asthma and IgE predict the development of asthma and hayfever in their offspring using the European Community Respiratory Health Survey (ECRHS).⁴ They found that offspring asthma with hay fever was more strongly



June Leung



Randi Bertelsen

Correspondence

G. Roberts, Paediatric Allergy and Respiratory Medicine (MP803), Clinical & Experimental Sciences & Human Development in Health Academic Units University of Southampton Faculty of Medicine & University Hospital Southampton, Southampton, UK.

Email: g.c.roberts@soton.ac.uk

Cite this as: Roberts G. *Clinical & Experimental Allergy*. 2017; (47)602–603.

Caption to cover illustration: IL-15-/- OVA-OVA mice demonstrated enhanced airway inflammation compared to OVA-OVA mice. [see figure 5a in C. B. Mathias et al. (pp. 639–655)].

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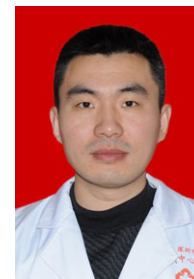
Marta Rava

associated with pre-natal rather than post-natal parental bronchial hyper-responsiveness (adjusted relative risk ratio 2.96, 95% CI: 1.92-4.57 and 1.40, 1.03-1.91 respective) and specific IgE (3.08, 2.13-4.45 and 1.83, 1.45-2.31 respectively). Such a pattern would be compatible with epigenetic inheritance with pre-natal disease activity impacting on epigenetic markers inherited by the offspring. Now we need to look to see whether results from murine epigenetic studies can be replicated in epidemiological studies.

Lastly in this issue of the journal, Liu et al. have examined whether the vitamin D receptor (VDR) regulates the dendritic cell (DC)-derived immunoglobulin domain molecule (TIM)4; this has an important

role in T helper (Th)2 responses.⁵

They found a number of associations: calcitriol (active form of vitamin D) levels were lower in participants with rhinitis than normal controls; peripheral DCs from rhinitis participants had higher levels of TIM4 and lower levels of VDR; VDR expression increased if DCs were exposed to calcitriol in culture; and VDR bound to the DC TIM4 promotor locus reduced gene transcription. These data provide a mechanism to explain why vitamin D deficiency might potentiate allergic disease.⁶



Zhi-Qiang Liu

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