Immunopathology

HARD-BOILED

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Mrs AR is a 37-year-old lady from Kenya who presented as a teenager with a history of recurrent abscesses in the axilla, breasts and groin, requiring antibiotic treatment and multiple drainages. A histological diagnosis of hidradenitis suppurativa was made, with initial good control using minocycline. Following the birth of her first child, the disease became refractory to anti-inflammatory antibiotics, anti-androgens (cyproterone acetate) and retinoic acid derivatives (roaccutane). Induction treatment with infliximab was commenced Jun–July 2014 with excellent clinical response, leading to maintenance treatment Oct 2014–Feb 2015. However, 2 months after completing the final infusion she developed new shoulder and breast lesions. Infliximab was recommenced, and she remains on 8 weekly infusions with an excellent clinical and biochemical improvement (falling CRP). Pathogenesis for this condition is unknown, but proinflammatory cytokines such as IL-1 β , IL-10 and TNF α are markedly increased in lesional and perilesional skin. Elevated serum levels of TNF α and IL-6 have also been measured in patients with stage 2 and 3 disease.

EXPLORING THE MECHANISMS OF LARGE LOCAL REACTIONS TO INSECT BITES IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKAEMIA

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Background: There is an increased prevalence of large local reactions to mosquito bites in patients with chronic lymphocytic leukaemia (CLL), the formation of which are primarily dependent on IgE-mediated mechanisms. We hypothesise that these patients may have circulating autoantibodies that bind to the FC ϵ RI receptor of mast cells and basophils, and are capable of triggering the IgE-mediated development of large local reactions.

Methods: Six patients with CLL and large local reactions to mosquito bites were included in the study. Basophils from one atopic and one non-atopic donor were incubated with basophil stimulation buffer and serum from all six patients. Upregulation of basophil CD63 surface expression was measured.

Results: In atopic donor basophils, significant CD63 upregulation was induced by the serum of 3 of 6 patients. In contrast, no significant CD63 upregulation was induced by serum in non-atopic donor basophils.

Conclusions: Upregulation of CD63 surface expression in atopic basophil donors was detected in a subset of patients with

large local reactions to mosquito bites and CLL. This supports the hypothesis that a subset of patients with CLL may have circulating autoantibodies that bind to the FC ϵ RI receptor of mast cells and basophils, which trigger large local reactions.

WHOLE EXOME SEQUENCING IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Systemic juvenile idiopathic arthritis (sJIA) shares clinical features with classic monogenic autoinflammatory diseases, and response to anakinra, canakinumab and tocilizumab suggests that cytokine dysregulation is a key pathophysiological mechanism. Whilst there have been HLA associations and polymorphisms noted on sJIA genome-wide association studies, in rare cases mutations have been found in genes encoding key components of the inflammatory response, which may contribute to disease pathogenesis. We aim to identify rare variants in innate immune genes that contribute to cytokine imbalance and lead to the inflammatory phenotype seen in sJIA patients by performing whole exome sequencing on probands with sJIA and their parents (trios). Recessive, compound heterozygous and *de novo* inheritance models were tested and variants evaluated for potential functional effect using a combination of SIFT, PolyPhen and MutationTaster. We confirmed candidate pathogenic variants by Sanger sequencing and cross-checked these variants with the Infevers database, known fHLH causing mutations and inflammatory pathways. We harnessed CRISPR-Cas9 gene editing technology to model mutations in appropriate cell lines, and investigate the pathogenic nature of identified novel variants. In total, there were 26 *de novo* variants (median=2, range 0–6 per trio), with 17 of these predicted to affect protein function (median=1, range 0–2 per trio). At least one *de novo* variant affects a known innate immune gene, and the pathogenic nature of this variant is being confirmed *in vitro*.

MDA-5 ASSOCIATED INTERSTITIAL LUNG DISEASE

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