Editor’s Choice – John Ingram – January 2024

The role of enhancers in psoriasis and atopic dermatitis

Enhancers are regulatory DNA sequences that activate gene expression. They can be affected by epigenetic modifications, interactions with transcription factors or changes to the enhancer DNA sequence itself. Disease-mapping studies show that alterations to enhancer activity contribute to common inflammatory skin diseases including psoriasis and atopic dermatitis (AD). In this review article, the authors discuss the definition and function of enhancers, their roles in psoriasis and AD susceptibility and progression, and how enhancers may present an opportunity for new therapeutic approaches for these conditions.

Self-care treatment for lymphoedema of lymphatic filariasis using integrative medicine

Lymphatic filariasis (LF) is a neglected tropical disease presenting mainly as lymphoedema (elephantiasis). At present, LF is not effectively treated. Integrative medicine (IM) treatment for lymphoedema uses a combination of Indian traditional medicine known as Ayurveda, alongside yoga exercises, compression therapy, antibiotics and antifungal treatments, designed for resource-limited settings. The current study assessed the effectiveness of the IM intervention in lower limb lymphoedema management, to determine whether treatment outcomes aligned with World Health

Figure: Alterations to enhancers and their associated histones and proteins (red X) contribute to psoriasis and atopic dermatitis
Organization (WHO) goals for LF management. Data for all 1698 community patients with LF in India who received the intervention from 2010 to 2019 were analysed. Limb volume reduced by 24.5% (95% confidence interval 22.47–26.61; n = 1660) following an intensive supervised care period (mean 15 days). Regarding bacterial entry points, there was a 78.4% reduction in excoriations and a 26.7% reduction in intertrigo by discharge. Health-related quality of life, measured using the disease-specific Lymphatic Filariasis Specific Quality of Life Questionnaire, showed an average score of 73.9 on admission, which improved by 17.8 points at the first follow-up (mean 81 days) and 18.6 at the second follow-up (mean 231 days). The authors concluded that the IM intervention aligns with WHO treatment goals for LF and is a low-cost, predominantly self-care management protocol with the potential to change care models and improve the lives of patients with lymphoedema.

### Retrospective pharmacogenetic study of psoriasis highlights the role of KLK7 in tumour necrosis factor signalling

The authors conducted a retrospective pharmacogenetic study using self-evaluated treatment response in 1942 genotyped patients with psoriasis, to explore the potential genetic pathways associated with drug response. They examined 6.5 million genetic markers to model their associations with response to six treatment options, adjusting for cohort variables and demographic features. Treatments included topical therapy, phototherapy, acitretin, methotrexate, other systemics such as apremilast, and anti-tumour necrosis factor (TNF) biologics. An integrative approach incorporating epigenomics, transcriptomics and a longitudinal clinical cohort was used to provide biological implications for the topmost signals associated with drug response. A novel marker associated with anti-TNF response, rs1991820, was also associated with cutaneous mRNA expression levels of the known psoriasis-related gene KLK7. Furthermore, by inhibiting the expression of KLK7, the authors showed that keratinocytes have decreased proinflammatory responses to TNF. Hence, the results of the study implicate genetic regulation of cytokine responses in predicting clinical drug response, raising the possibility of personalizing psoriasis therapy in the future.

### Phase III randomized controlled trial of nemolizumab for atopic dermatitis in paediatric patients aged 6–12 years

Nemolizumab, a humanized monoclonal antibody against interleukin-31 receptor A, was recently approved in Japan for the treatment of itch associated with atopic dermatitis (AD) in children aged ≥13 years. The present phase III randomized controlled trial examined the impact of nemolizumab plus topical therapy in Japanese children aged 6–12 years with AD and moderate-to-severe pruritus inadequately controlled by topical therapy and antihistamines. Participants were randomized 1 : 1 to receive subcutaneous nemolizumab 30 mg or placebo every 4 weeks, the primary efficacy endpoint being change in the weekly mean five-level itch score from baseline to week 16. The mean age of the 89 participants was 9.1 years and there was a statistically significant difference in the primary outcome for the nemolizumab treatment group (−1.3) compared with placebo (−0.5; least squares mean difference −0.8, 95% confidence interval −1.1 to −0.5; P < 0.0001). Improvements with nemolizumab were observed from the second day of treatment administration. No adverse events resulted in discontinuation, and the overall safety profile in patients aged 6–12 years was comparable with that in older patients.