Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Selective inhibition of tyrosine kinase 2 prevents and restores interleukin-12-induced hair follicle immune privilege collapse: a novel approach to alopecia areata therapy?

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Alopecia areata (AA) is an immune-mediated hair loss disorder characterized by elevated levels of IFNγ and Th1-driven inflammatory responses toward the hair follicle (HF) bulb. This results in immune privilege (IP) collapse, premature catagen development, and HF dystrophy. Given the critical role of interleukin (IL)-12 in priming Th1 responses, we investigated whether IL-12 could be directly involved in inducing HF-IP collapse and whether the selective tyrosine kinase 2 (TYK2) inhibitor, BMS-986202, could prevent or reverse the process. By quantitative immunohistomorphometry, we showed that *ex vivo* treatment of microdissected HFs with IL-12 (3 ng/mL) + IL-18 (20 ng/mL) upregulated MHC-I and II as well as MICA/B expression in the hair bulb (cardinal features of IP collapse), increased the numbers of $CD3^+$ or $CD56^+$ cells in HF epithelium and mesenchyme, and selectively enriched IFNγ-inducible genes. In addition, more peribulbar IL-12RB2+ cells were found in acute lesional scalp skin samples of AA patients than healthy controls. We further confirmed the role of IL-12 in the HF-IP collapse by selectively blocking IL-12 receptor signaling. BMS-986202 (300 nM), when administered to microdissected HFs before or after IL-12 + IL-18 stimulation, prevented or attenuated the expression of MHC-I and II as well as secretion of IFNγ. Therefore, our data demonstrate that local IL-12 directly promotes perifollicular immune cell expansion, IFNγ secretion, and HF-IP collapse. These findings support a potential role of IL-12 signaling in AA pathogenesis and highlight IL-12 as a potential new target for pharmacologic AA therapy.

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Classification of atopic dermatitis patients based on skin properties

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Atopic dermatitis (AD) is a multifactorial inflammatory skin disorder, suggesting that individual approach due to pathological condition is crucial. Although skin barrier research has revealed importance in the pathology of AD, the diversity of skin properties in AD patients is not fully understood. Herein, we evaluate and classify AD patients using multiple skin parameters, such as TEWL, hydration, pH, elasticity, frictional resistance and sebum, and to assess the relationship between skin properties and clinical multimodal data. In this study, 39 AD patients and 40 healthy subjects were enrolled and 17 parameters reflecting 6 skin properties were measured with Cutometer DUAL MPA580. Simultaneously, medical examination by dermatologist, blood tests and skin microbiome analysis were performed. Dimensionality reduction was performed for the 17 skin parameters using Non-negative Matrix Factorization. Then, the stratification was performed using Uniform Manifold Approximation and Projection and k-means clustering based on the reduced factors. Interestingly, the stratification based on the skin parameters revealed three clusters associated with the Eczema Area and Severity Index (EASI). In the first cluster including patients with mild to moderate AD, S. aureus were well correlated with EASI score, whereas in the second cluster, which included patients with moderate to severe AD, S. aureus did not show significant correlation, but inflammatory cytokines were correlated with EASI score. Both S.aureus and inflammatory cytokines were associated with EASI score in the third cluster, which included healthy subjects in addition to AD patients. These results revealed the diversity of skin barrier conditions in patients with AD, suggesting that the pathogenic factors involved in inflammation differ depending on the skin condition. This study demonstrates the importance of stratifying AD patients according to skin barrier properties in order to understand complexed pathophysiology of AD and enable precision medicine.

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A new case series of Olmsted syndrome subjects confirms EGFR activation and shows remarkable efficacy of targeted systemic EGFR inhibition with acceptable side effects

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Olmsted syndrome (OS) is a rare, painful, and severe form of palmoplantar keratoderma (PPK). It is most often caused by dominant mutations in the transient receptor potential vanilloid-3 (*TRPV3*) gene, resulting in the constitutive activation of this thermosensitive calcium channel. TRPV3 signaling leads to epidermal growth factor receptor (EGFR) activation and subsequent abnormal proliferation and differentiation of keratinocytes in mice and cell lines. We previously reported that blocking EGFR transactivation with oral Erlotinib treatment resulted in remarkable improvement in 4 young patients. Here, we aimed to decipher the pathogenic role of EGFR signaling in OS and evaluated the clinical response to oral Erlotinib among 5 new patients treated for at least 1 year. *In situ* EGFR activation was directly assessed using proximity ligation assay, which revealed a significant increase in EGFR homodimer formation in lesional skin. All patients also presented strong activation of the kinase mTOR, the central mediator of Akt signaling, as measured by phosphorylation of ribosomal protein S6. In contrast, pErk1 and pSTAT3 were not increased. Oral Erlotinib treatment led to a drastic reduction of PPK, pruritus, and pain with improved quality of life after a few months of treatment in the 5 new patients, as observed in the previous cases. Adverse effects were acceptable. Together, our results suggest that EGFR activation contributes to OS pathogenesis through Akt-mTOR activity and provide further evidence that the pharmacological inhibition of EGFR is a powerful treatment strategy in OS.

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Short-term intravenous clindamycin accelerates the benefit of oral clindamycin-rifampicin treatment in hidradenitis suppurativa (HS)

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A 10-to-12-week course of combined clindamycin/rifampicin or tetracyclines are the first-line medical treatment for moderate-to-severe HS. A recent multicenter European study revealed significant efficacy of oral clindamycin/rifampicin and tetracyclines without differences between them, independently of baseline HS severity. Our study explored the efficacy of a treatment induction with a 5-day loading dose of i.v. clindamycin (3x600 mg/d) prior to the oral clindamycin/ rifampicin combination, in 95 consecutive, previous treatment-naive adult HS patients. The patients were assessed for severity using the IHS4 and the DLQI before (T0) and immediately after the 5-day treatment with i.v. clindamycin (T1), as well as after a 10-12-week period of oral clindamycin/ rifampicin treatment (T2). Data groups (T1 vs. T0 and T2 vs. T1) were evaluated using Wilcoxon's signed rank test. $p<0.05$. After a Bonferroni correction, the results were considered significant at $p<0.008$. The IHS4 median value (interquartile range [IQR]) was reduced from 10 (5-20) at T0, to 7 (3-14) at T1 ($p<0.001$), and 4 (1−12) at T2 ($p<0.001$ in comparison to T0; n.s. in comparison to T1). DLQI median value (IQR) decreased from 17 (7-21) at T0, to 8 (5-19) at T1 ($p=0.002$), without further reduction at T2: 8 (2-16; $p<0.001$ in comparison to T0, n.s. in comparison to T1). In conclusion, a significant improvement of HS severity and quality of life was demonstrated after a 5-day i.v. clindamycin treatment, which was maintained during the S1-European guideline-recommended oral clindamycin/rifampicin course. These data indicate that the overall antiinflammatory effect of antibiotics can be accelerated, achieved through a 5-day i.v. clindamycin course, so more effective treatments can be initiated thereafter.

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Application of teledermatology during the first wave of the COVID-19 pandemic in Hungary

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During the first wave of the COVID-19 pandemic, outpatient care was limited and it resulted in developing an asynchronous teledermatology system. The aim of our retrospective study was to provide quantitative data the first time about use of teledermatology in the Hungarian healthcare system between March 25 and July 13, 2020. The number of cases, regional distribution and type of diagnoses were analyzed. We also followed up patients who were referred to in-person dermoscopic examination. A total of 10.287 teledermatology consultations were completed at our department. 5.967 (58%) patients were female and 4.320 (42%) patients were male with a mean age of 32.7±22.5 years. 5.967 (58%) cases were from the capital city and its metropolitan area and 32% was from other regions of Hungary. The most common diagnosis was dermatitis, followed by skin infections and pigmented skin lesions. In 1.440 cases, the patient was referred to a dermoscopic examination. Teledermatological examination raised also the diagnosis of malignant skin cancer in 190 patients. Later it was confirmed in 111 cases based on dermoscopic examination. Melanoma was confirmed in 14%, squamous cell carcinoma in 15%, basal cell carcinoma in 63% and other malignancies in 8%. We compared the presumed diagnosis given during the teledermatology consultation with the personal examination. The sensitivity of our system proved to be 87% with a specificity of 86% for diagnosing malignant skin lesions. In addition to the large number of general skin conditions, life-threatening diseases were screened, using teledermatology under the first wave of the COVID- 19 pandemic. The correct diagnosis and treatment of most diseases is a significant achievement. Overall, use of asynchronous teledermatology was an outstanding method during the pandemic period and it has the potential to become an important part of patient care in the future.

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Single nucleotide polymorphisms in aldo-keto reductase 1C3 associate with early-onset psoriasis in female patients

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Psoriasis is a multifactorial disease associated with both genetic and non-genetic factors. We hypothesized that single nucleotide polymorphisms (SNPs) in aldo-keto reductase (AKR) 1C3, which regulates keratinocyte differentiation and loricrin expression in human epidermis, confer a genetic susceptibility to psoriasis. In 232 psoriasis patients, including 171 males and 61 females, a TaqMan SNP genotyping assay revealed that the rs12529 genotype distribution in our cohort was G/G: 75.0%, G/C: 22.8%, and C/C: 2.2%, and the rs12387 genotype distribution was A/A: 75.0%, A/G: 22.8%, and G/G: 2.2%. Surprisingly, these 2 SNPs were always observed in the same patients. The proportion of patients with both the rs12529 G/C, C/C and rs12387 A/G, A/A variants was 2-fold higher than that in 2 cohorts of healthy Japanese individuals in the NCBI database (rs12529, p=0.0088 [vs. ss69068306], p=0.024 [vs. ss71643788]; rs12387, p=0.037 [vs. ss2827707], p=0.024 [vs. ss66361131] Fisher's exact test). The number of female patients with disease onset %22 years of age having both the rs12529 G/C, C/C and rs12387 A/G, G/G variants was significantly higher than that having the rs12529 G/G and rs12387 A/A variants (p=0.0213, Fisher's exact test). Immunohistochemical staining of lesional psoriasis skin samples obtained from patients with the rs12529 G/C, C/C and rs12387 A/G, G/G variants revealed significantly lower expression of AKR1C3 in the epidermis compared to patients with the rs12529 G/G and rs12387 A/A variants (p=0.0434, Student's t test). AKR1C3 downregulation in the epidermis induces abnormal terminal differentiation and skin barrier dysfunction. This may contribute to exposure to environmental factors such as tobacco smoke or environmental pollution, which may increase disease susceptibility of psoriasis in young females.