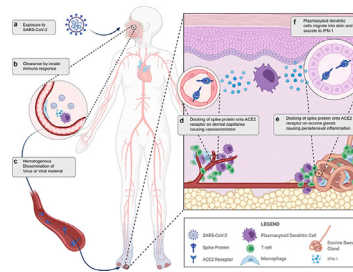
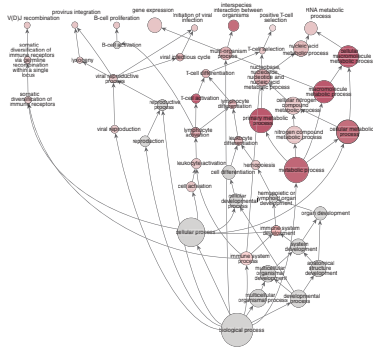


## COVID Toes May Be Linked to Excessive Innate Immune Response

Spatial and temporal association of pernio with the COVID-19 pandemic raised interest in the phenomenon, although patients with pernio most often were young, had close contact with COVID-19, and denied respiratory manifestations of the disease. Arkin et al. provided a thorough review of the recent literature describing this phenomenon. IFN-1 has proved critical in disease outcomes with robust responses in the absence of neutralizing antibodies involved in intrinsic resistance and defective responses leading to poor outcomes. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein and robust IFN-1 responses have been observed in the skin of patients with pernio, and these observations are consistent with the hypothesis that these manifestations stem from an excessive innate immune skin response to SARS-CoV-2. **See page 2791.**



## Romidepsin and Jak1/2 Combination Therapy Treats Cutaneous T-Cell Lymphoma



The histone deacetylase inhibitor romidepsin has proven to be effective for Sézary syndrome, an aggressive form of cutaneous T-cell lymphoma (CTCL) with an exceptionally poor prognosis. As a single agent, this drug provokes a response in only a fraction of patients, and the overall response is transient owing to development of resistance. Cortes et al. showed synergistic antilymphoma effects after *in vitro* treatment of CTCL cell lines and patient samples with romidepsin in combination with the alkylating agent mechlorethamine. These treatments

inhibited the Jak/signal transducer and activator of transcription signaling pathway, supporting pharmacological targeting of this signaling pathway in the treatment of CTCL and, possibly, prevention of romidepsin resistance. **See page 2908.**

## Genetic Characterization of a Rare Inflammatory Skin Disease

Because the molecular underpinnings of inflammatory linear verrucous epidermal nevus, a rare skin condition that is resistant to therapy, are unknown, Riachi et al. performed whole-exome sequencing of blood and affected skin from 15 pediatric patients and six healthy controls to identify somatic variants. Two of the patients harbored heterozygous missense variants, predicted to be pathogenic, in the *CARD14* gene. Characterization of one of the variants in cultured keratinocytes revealed increased expression of IL-12A and IL-23A, proliferation, and NF- $\kappa$ B p65 expression. Treatment of a patient, who was previously resistant to multiple therapies, with the IL-12A and IL-23A inhibitor ustekinumab led to considerable and sustained improvement, highlighting the clinical utility of genetic characterization of rare diseases. **See page 2979.**



## Proof of Concept of ALXN1830 for Pemphigus Treatment

Werth et al. reported clinically meaningful efficacy and tolerability of ALXN1830 for the treatment of chronic pemphigus, an autoimmune blistering disease caused by pathogenic IgG antibodies to desmosomal proteins, in eight patients who were refractory to available treatments. Treatment with this humanized IgG4 antibody that blocks interactions between Fc $\gamma$ Rn and IgG led to a reduction in IgG immune complex levels, pemphigus disease area index, and anti-desmogleins 1 and 3 titers in the majority of patients. Clinical responses were maintained after therapy ended in four of six responders despite normalization of serum IgG levels. This proof-of-concept study highlights the importance of the Fc $\gamma$ Rn in pemphigus and the utility of ALXN1830 in pemphigus treatment. **See pages 2777 and 2858.**

## Success of Golimumab in Hidradenitis Suppurativa Patients

In a retrospective cohort study, del Mar Melendez-Gonzalez et al. found that 6 of 13 patients with recalcitrant hidradenitis suppurativa (HS) experienced hidradenitis suppurativa clinical responses, which indicates a 50% reduction in abscess and nodule counts, after administration of the fully humanized TNF- $\alpha$  inhibitor golimumab. These patients, who had previously been treated with the approved TNF- $\alpha$  antibodies adalimumab and infliximab, also exhibited improvements in other disease scores without associated improvements in other clinical and laboratory assessments. Nevertheless, these findings indicate that golimumab is a promising potential immunotherapy for patients with treatment-resistant HS. **See page 2975.**