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.

025

ALA-PDT inhibits skin squamous cell carcinoma (cSCC) via regulating formation of tertiary lymphoid structures

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Topical ALA-mediated PDT, ALA-PDT, is a novel therapeutic modality widely used to treat actinic keratosis, Bowen's Disease, superficial skin SCC, and other cancerous and precancerous skin diseases. Several studies have proved that ALA-PDT can inhibit SCC growth. Subsequent research suggested that ALA-PDT not only directly induced tumor cells apoptosis, but also improve tumor microenvironment through regulation of immune cells. However, the anti-tumor immune function of ALA-PDT is still need to be elucidated. Here, we found that tertiary lymphoid structures (TLSs), which are ectopic lymphoid organs that develop in non-lymphoid tissues at sites of chronic inflammation including tumors, play a pivotal role in anti-tumor immune function of ALA-PDT. We analyzed 77 samples of cSCC patient in our hospital. TLS was observed in 79% of the patient samples, and the density of TLS is negatively correlation with the Brodes classification of cSCC. Intriguingly, immunohistochemistry showed that ALA-PDT could promote the formation of TLS in vivo. We also found that promotion effect of ALA-PDT on TLS is mediated by M1 macrophage, which function as lymphoid tissue inducer cells in TLS formation and recruited by ALA-PDT. Further investigation substantiated that PDT-secreted exosomes were involved in M1 macrophage polarization. Our study elucidated a mechanism that ALA-PDT influence M1 macrophage polarization via PDT-secreted exosomes, which could facilitate the formation of TLS. Thus, our research may contribute to in-depth molecular understanding of the ALA-PDT on anti-tumor immune function.

026

CXCR4$^+$ skin-resident natural killer T cells participate in cutaneous allergic inflammation in atopic dermatitis

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Natural killer T (NKT) cells is an unconventional subset of lymphocytes that bridge innate and adaptive immunity. However, the role of NKT cells in the development of atopic dermatitis (AD) has not been well understood. So, we aimed to investigate the function of NKT cells in the cutaneous allergic inflammation in atopic dermatitis. In global transcriptomic and proteomic analyses, CXCR4 and CXCL12 were significantly upregulated in human AD skin and CXCR4$^+$ NKT cells were enriched in AD skin and were consistently elevated in AD mouse models. Skin-resident NKT cells uniquely expressed CXCR4, unlike NKT cells in liver, spleen and lymph nodes. Interestingly, skin fibroblasts were the main source of CXCL12. In addition, the adoptive transfer of allergen-induced NKT cells in Rag1$^{-/-}$ mice, which do not have conventional T cells, also developed significant cutaneous allergic inflammation. By using parabiosis technique and intravital imaging, CXCR4$^+$ NKT cells preferentially trafficked to CXCL12-rich areas, forming an enriched CXCR4$^+$ NKT/CXCL12$^+$ cell cluster, which developed in acute and chronic allergic inflammation in our AD mouse models. Taken together, CXCR4$^+$ skin-resident NKT cells may form a niche that contributes to atopic dermatitis, where CXCL12 is highly expressed.

027

Langerhans cells rely on good neighbors to overcome gene deficiencies

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We recently identified that epidermal resident Langerhans cells (LCs) acquire gene expression fingerprints from surrounding keratinocytes (KCs) in the form of mRNA and protein. In the present study, we aimed to determine whether this transfer can also overcome gene deficiencies. For this purpose, using the Cre/Lox system, we specifically deleted genes for connexin 43 (Cx43), MyD88, and MHC-II in LCs. While all three genes underwent recombination, reduced protein levels were only observed for MHC-II, whereas Cx43 and MyD88 protein levels remained unaltered. Considering that KCs lack MHC-II, but express Cx43 and MyD88 at high levels, we posit that LCs can acquire gene products from surrounding KCs to overcome their own deficiencies if those products are available. Preliminary experiments suggest that LCs can also provide, though to a lesser extent, to KCs in need. In summary, we present evidence that cells can compensate for gene deficiencies if the surrounding cells can provide. These findings highlight the limitations of cell-specific gene deletion and could provide an explanation as to why certain gene deletions do not lead to measurable deficiencies.

028

Use of systemic immunosuppressive treatment is not related to COVID-19 infection in a retrospective review of patients in Massachusetts

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Importance: It is unclear if systemic immunosuppression for chronic conditions modifies patients' risk of contracting COVID-19, leading to uncertainty among patients and dermatologists treating immune-mediated skin conditions during the pandemic. Methods: We partnered with the Massachusetts Department of Public Health to identify COVID-19 positivity and mortality for patients treated at the Mass General Brigham who were prescribed a systemic immunosuppressant from 07/01/19-02/29/20. We excluded biologics, steroids, and antirheumatic drugs from the analysis. Patients were compared with exact matched controls using a multivariable logistic regression for infection and multivariable Poisson regression for mortality, adjusting for demographics, comorbidity score, and local infection rate. Results: The most common medications identified were Methotrexate (23.5%), Mesalamine (19.2%), Paclitaxel (8.3%), Mycophenolate (7.8%), Hydroxyurea (6.0%), and Tacrolimus (5.3%). 218 of 14,865 (1.5%) patients prescribed systemic immunosuppressants and 1,368 of 80,318 (1.7%) controls were identified as COVID-19 positive. Of these, 26 (0.2%) patients prescribed immunosuppressants and 162 (0.2%) controls died after diagnosis. Patients prescribed immunosuppressants were not more likely to have a COVID-19 diagnosis (OR 0.91, 95% CI 0.79-1.05, p=0.22) or die after diagnosis (OR 0.95, 95% CI 0.62-1.44, p=0.80) after adjusting for demographics, comorbidity score, and local infection rate. Conclusions and Relevance: We found no evidence that systemic immunosuppression preceding the COVID-19 pandemic increased risk of contracting COVID-19 or risk of mortality among COVID-19 positive patients.

029

Topical xenobiotics promote oral food allergy

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Allergic disease is increasing in prevalence in industrialized nations. Children with atopic dermatitis are at an increased risk of developing food allergies. The prevailing theory to explain this relationship is termed epicutaneous sensitization, whereby chronically scratched skin comes into contact with food allergens like peanut and this leads to the development of an allergic reaction to the food when eaten. Our preliminary work has shown that certain chemicals, including food preservatives and over-the-counter drugs promote the development of oral food allergy. The ability for xenobiotics to promote allergic sensitization may in part explain the rise in prevalence in allergic disease in industrialized nations where these agents have become ubiquitous. We hypothesized that the immune system may be similarly shaped by exposure to substances within topicals frequently in contact with the skin (like soaps, emollients, detergents), such that upon ingestion of certain foods, primed individuals will develop an allergic response. To test this, mice were sensitized by intradermal injection of the xenobiotic, sulforaphane, concurrently with oral gavage of the model food antigen ovalbumin (Ova). We then assessed for Ova-specific IgE and IgG1 and tested whether mice would anaphylax to Ova re-exposure. We have found that topically applied xenobiotics can induce allergic sensitization to orally administered Ova which leads to an anaphylactic response upon re-challenge. This suggests that topical xenobiotics are sufficient to induce allergic sensitization to orally ingested allergens.

030

Defining adaptive and innate immune cell profiles in Hidradenitis Suppurativa at the single cell resolution

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Hidradenitis suppurativa (HS) is a severe chronic inflammatory skin disease lacking effective therapeutic options due to little understanding of the complex immune response within the lesional skin. Using single-cell transcriptomic analyses, we examined the signature changes in each immune cell types during HS progression, as well as *in silico* ligand-receptor predictions between different immune cell types to construct the interaction network that contribute to HS pathogenesis. Our results revealed a predominant Th17 response, as well as a distinct regulatory T cells existing in the lesional skin. We found that M1-polarized macrophages likely facilitate chemotaxis and IL1B responses in perilesional skin, while regulate lymphocyte activation and tissue remodeling in the lesional skin. In addition, we identified a significant increase of CCR7 expressing dendritic cells, as well as activated stromal fibroblasts expressing CCR7-ligand CCL19, which together support the organization of tertiary lymphoid organ (TLO)-like aggregates that contribute to persistent local inflammation. Importantly, we demonstrated a dense infiltration of plasma cells near sinus tracts, and that clonal expansion of the plasma cells frequently exists in HS patients. Together, our work provides a comprehensive understanding of immune responses and cytokine networks defining disease chronicity in HS, as well as significant implications for future therapeutics.