psoriatic cohort and using receiver operating characteristic curves. Results indicated the wGRS was a modest but better discriminator of cases and controls than the cGRS, which is consistent with other studies. Future efforts are aimed at updating each GRS with newly identified loci and comparing a PsA GRS plus screening questionnaires to screening questionnaires alone.

Peripheral Retinal Vascular Leakage in Moderate to Severe Psoriasis: A Pilot Study

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The impact of psoriatic inflammation on the eye is not fully understood. We investigated if peripheral vascular leakage (PVL), a feature of retinopathy, was evident in patients with psoriasis using ultra-wide field fluorescein angiography (UWFFA). We performed a cross-sectional, institutional review board-approved, prospective study comparing UWFFA in patients with psoriasis to healthy age-matched controls. Patients with active or history of moderate-to-severe plaque psoriasis underwent a complete ophthalmologic examination along with optical coherence tomography and UWFFA. Each examination was independently reviewed by 2 retinal physicians. Exclusion factors included other types of psoriasis, psoriatic arthritis, diabetes, history of retinal disease, uveitis, other autoimmune disorders, or recent intraocular surgery. Twenty-eight patients with psoriasis were enrolled. Average duration of psoriasis was 9.97 years, average body surface area of 4.96, average Psoriasis Area and Severity Index of 4.58, and average Physician Global Assessment of 1.93. Evidence of inflammation was detected in 6 (21.4%) patients with psoriasis compared to 1 (3.6%) in the controls ($P = .1012$). The pattern of inflammation in the psoriasis group was unique compared to that of the control group ($P = .0232$): UWFFA in the psoriasis group exhibited retinal PVL in the absence of other forms of inflammation in the remaining components of the eye examination. The ocular inflammation was not attributable to duration of disease, severity of psoriasis, treatment, nor comorbid disease. The study was limited by its small sample size. Further investigation into both the impact of psoriasis on the eye and the value of the ocular vasculature as a marker of comorbid disease is warranted.

miR-30a and miR-155 Target the Tripartite Complex CARD14-BCL10-MALT1 and Could Potentially Be Targeted to Downregulate a Psoriasiform Response

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We previously performed small RNA sequencing and identified 98 differentially expressed microRNAs (miRNAs) and a handful of novel small interfering RNAs in psoriatic versus healthy skin. We also discovered highly penetrant, gain-of-function, dominantly acting mutations within the human caspase recruitment domain family, member14 (*CARD14*) gene that led to the development of psoriatic (PS) and psoriatic arthritis. *CARD14* mutations lead to enhanced nuclear factor (NF)-κB signaling and activation of a subset of psoriasis-associated genes in keratinocytes. This enhanced NF-κB signaling is due to a tripartite complex formed between B-cell lymphoma 10 (BCL10) and mucosa-associated lymphoid tissue lymphoma translocation protein 1 (MALT1; CARD14-BCL10-MALT1). The introduction of the de novo p.E138A alteration into the *Card14* gene of mice leads to features of psoriatic skin including a thickened epidermal barrier and immune cell infiltration into lesions. Moreover, the altered transcriptomes of the skin of p.E138A versus WT mice are very similar to that of human psoriatic skin versus that of healthy controls. Guided by these preliminary data, we validated a set of psoriasis-specific differentially expressed miRNAs in the skin of human patients with PS and that of the p.E138A Card14 mouse knockin with qualitative real-time polymerase chain reaction. Two of these PS-specific miRNAs (miR-30e-5p and miR-155-5p) were predicted to target *BCL10* mRNA, one of the partners of CARD14 upon activation of NF-kB signaling. We confirmed the interaction of these 2 miRNAs with regions from the 3′UTR of *BCL10* messenger RNAs with luciferase assays ($P = .001$ and $P = .0002$, respectively) and hypothesize that miR-30a and miR-155 are regulators of CARD14 signaling that can be targeted to downregulate a psoriasiform response.

LL37 Antimicrobial Peptides Amplify Inflammation in Psoriasis by Assembling Into Protofibril Scaffolds That Present Ordered Nucleic Acids to TLR9 and TLR3

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LL37 is a cationic, amphipathic host–defense peptide (HDP) with dual antimicrobial and immunomodulatory properties essential to immune defense against microbial pathogens. However, LL37 has recently been identified as an autoantigen that breaks immune tolerance to self-nucleic acids via Toll-like receptors (TLRs) in psoriasis. At present, the mechanism by which LL37 interacts with self–double-strand DNA (dsDNA) or dsRNA to modulate TLRs is poorly understood. Here, we study the immunomodulatory behavior of LL37 from the perspective of "Janus" self-assembly, which can organize low-symmetry subunits into diverse nanostructures. We examined the supramolecular structures formed between prototypical helical HDPs and DNA using synchrotron small angle x-ray scattering and molecular modeling. We find that LL37 self assembles into cationic protofibrils with hydrophobic interiors, which in turn nucleate ordered complexes with spatially periodic DNA ligands. Interestingly, LL37-DNA complexes trigger strong immune responses in plasmacytoid dendritic cells by driving receptor clustering and multivalent binding of TLR9 to periodic DNA ligands within the nanocrystal, thereby amplifying TLR9-mediated inflammation. In cognate work, we find that this paradigm is general to other innate immune receptors. LL37 organizes dsRNA into spatially periodic nanocrystalline immune complexes to amplify TLR3-mediated inflammation in keratinocytes. LL37-dsRNA complexes have inter-RNA spacings well-matched with the steric size of TLR3, enabling multivalent binding of clustered TLR3 to periodic dsRNA ligands. These findings suggest that LL37–nucleic acid nanocrystals exacerbate inflammation in psoriasis through different parallel pathways in dendritic cells and keratinocytes. Our findings unveil potential therapeutic strategies to disrupt inflammation in psoriasis.

Psoriasis Incidence and Lifetime Prevalence: Suggestion for a Higher Mortality Rate in Older Age-Classes Among Psoriatic Patients Compared to the General Population in Italy

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Data on the psoriasis incidence and prevalence in the Italian population are limited. Such information is important in order to define the disease burden. Therefore, an accurate and timely understanding of the disease epidemiology is needed. This ad hoc study investigated psoriasis incidence and lifetime prevalence in a representative sample (n = 14 705) of the Italian adult population. Information on lifetime history of skin disorders with details about their onset, duration, and treatment was collected through a face-to-face interview. Psoriasis incidence showed a bimodal distribution pattern, with peaks in age classes, characteristic of early-onset (35-44 years) and late-onset (65-74 years) psoriasis. Late-onset psoriasis showed some variations according to the gender, with females being diagnosed earlier than males. Lifetime prevalence of psoriasis was 2.7% (95% confidence interval, 2.5-3.0): It increased to 3.5% at age 60 to 64 years, then decreased steadily after age 64, to 1.7% at age >74 years. This decrease, despite a peak in incidence rates, after age 64, may suggest a higher mortality rate among patients with psoriasis in older age classes, compared to the general population.

Pro-Inflammatory Cytokines Affect the Expression of T-Cell Regulating Molecules and can Disturb Tube Formation of Healthy Lymphatic Endothelial Cells

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Introduction: Most patients with psoriatic arthritis (PsA) develop psoriasis before their joint disease, providing an opportunity for prevention if we better understand the mechanisms underlying the transition from psoriasis to PsA. The lymphatic system, with the core component the lymphatic endothelial cell (LEC), has an important role in immune cell trafficking. Dysregulation of lymphatics in psoriasis may contribute to disseminating the disease from the skin to joint. This study aims to investigate to what extent LECs have the capacity to regulate T cell responses and homing under homeostatic and inflammatory conditions.

Methods: Human dermal LEC (hDLECs) were cell-sorted from skin discarded from healthy individuals undergoing elective skin surgery. We determined the messenger RNA expression of immunomodulatory molecules in hDLECs. Subsequently, we stimulated LECs for 24 hours with interleukin 17A (IL-17A), IL-22, and tumor necrosis factor-α (TNFα) and assessed changes in immunomodulatory molecule and cytokine expression, and tube formation.

Results: hDLECs express programmed death-ligand 1 (PD-L1), Delta-like ligand 4 (DLL4), and inducible T-cell costimulator ligand (ICOS-L). IL-17A increases chemokine (CCL5, CCL20, and CCL21) expression via canonical nuclear factor