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GRAPPA 2020 Research Award Recipients

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Abstract

At the 2021 Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) annual meeting, a summary of the research conducted by the recipients of the 2020 GRAPPA Research Awards was presented by the awardees. The summary of the 4 presentations is provided here.

Keywords

GRAPPA; psoriasis; psoriatic arthritis

Award Presentations

At the 2021 annual meeting of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA), awardees who were granted GRAPPA research project grants for 2020 were provided with an opportunity to present progress made on their respective research projects. GRAPPA takes great pride in nurturing trainees and early-career researchers interested in conducting research in psoriatic disease. Rochelle Castillo and Di Yan (collaborative dermatology–rheumatology project), Anneliese Ashhurst, Ashley Elliott, and Maria Maddalena Angioni presented their work, which was followed by a panel discussion involving the presenters and Profs. Kristina Callis Duffin and Oliver FitzGerald. The presentations are summarized here.

"Harnessing Spatially Resolved Gene Expression to Characterize the Transcriptional Landscape of Psoriatic Skin," by Rochelle Castillo and Di Yan, mentored by Jose Scher, Shruti Naik, and Andrea Neimann. The skin is a window into the immunopathogenic mechanisms in the joints of patients with psoriatic arthritis (PsA). Skin disease precedes joint involvement in ~90% of patients with PsA; thus, the study of the psoriatic skin transcriptome may yield insights into the immunopathogenesis of PsA. Spatial transcriptomics (ST) is a groundbreaking technology, allowing for mRNA sequencing from histologically intact tissue sections and facilitating precise localization of the site of gene expression. To date, we have accrued samples from 3 controls, 6 patients with PsA, and 6 patients with psoriasis (PsO). We found that gene expression is strikingly greater in the cell-dense epidermis and in appendageal structures than in the dermis in psoriatic lesional skin when compared to samples from nonlesional and control skin. Importantly, accuracy of spatial localization of gene expression and biological consistency of unbiased clustering was observed, with concordance of histopathologically annotated regions with gene expression–based clustering. Thus, we achieved successful optimization of both healthy and psoriatic human skin tissue for ST, with all samples meeting quality-control metrics. The expected biological variance in transcriptional activity across tissue regions and disease states was noted; the quantity, quality, and location of reads were biologically consistent; and there was no technical variation between samples. Thus, we can now perform spatial profiling of gene expression in psoriatic skin through ST.

"Self-derived Immunomodulatory Peptide RPpep as a Novel Therapeutic for Psoriasis," by Anneliese Ashhurst. Current therapies for PsO are not consistently efficacious for all patients, can be costly, and carry a risk of substantial adverse effects. New therapies that provide cost-effective and targeted suppression of inappropriate inflammation are needed. Immunomodulatory peptides offer potential for targeting specific immune pathways and have previously been identified from several natural sources. We have uncovered a novel role for a human peptide (termed *RPpep*) in modulating and suppressing inflammation, in particular myeloid cell function. A nonnative version of this peptide was produced by chemical synthesis with modifications to enhance ease of production and allow tagging to track the peptide in immunological studies. Culture of primary human or murine macrophages with RPpep led to reduced interleukin (IL)-12/23(p40), IL-6, and monocyte chemoattractant protein-1 release after Toll-like receptor stimulation. When injected intradermally into human skin explants, RPpep reduced spontaneous activation of dermal dendritic cells. In a mouse model of contact dermatitis, a single subcutaneous injection of RPpep prior to sensitization significantly suppressed elicitation of inflammation, as measured by a reduction in ear thickness and myeloid infiltrate. Further, in a murine model of imiquimod-induced PsO, subcutaneous injection of RPpep reduced erythema, skin thickness, scaling, and T cell influx into psoriatic skin, and increased the proportion of FoxP3+ CD4+ T cells in local skin-draining lymph nodes. Upon application in a topical formulation, RPpep penetrated the stratum corneum and colocalized with cells in the epidermis and dermis of murine and human skin explants. Reductions in disease were isolated to the local area in which RPpep was delivered, unlike topical glucocorticoid or injected monoclonal antibody therapy, which caused systemic immune suppression. RPpep therefore offers potential as a novel, locally acting, peptide-based therapy for management of inflammatory skin disease.

"Predicting Response to Treatment in Those Receiving Biologic Therapy in Psoriatic Arthritis: Linking Clinical, Imaging and Molecular Markers to Better Stratify Patients," by Ashley Elliott, mentored by Madeleine Rooney, Oliver FitzGerald, and Stephen Pennington. There are currently no biomarkers predicting response to treatment in PsA. Our aim is to integrate clinical assessment and imaging to better define disease, and then complement this by proteomics to develop and validate a predictive panel. This prospective observational study included patients aged ≥ 18 years who fulfill the classification criteria for PsA and were due to commence their first biologic therapy. The primary outcome was the change in MAdrid Sonographic Enthesitis Index (MASEI) scores at 16 weeks of biologic treatment.[1] The MASEI score was also modified to assess the active elementary lesions (Active MASEI) and then only include power Doppler signal that was within 2 mm of the enthesis insertion (Active mMASEI). All patients had serum samples stored for proteomic analysis, which is ongoing. Eighty patients with PsA were enrolled, with 24 patients commenced on secukinumab (150 mg, n = 18; 300 mg, n = 6) and 56 treated with tumor necrosis factor inhibitors (TNFi; adalimumab n = 50, certolizumab pegol n = 4, and etanercept n = 2). The mean reduction in MASEI score after 16 weeks of treatment was 3.42 with TNFi vs 1.74 with secukinumab ($P = 0.10$). There was a significant difference in the change in the Active MASEI score for TNFi vs secukinumab (4.37 vs 2.26, $P = 0.03$). The Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index correlated with the baseline

Active MASEI score (r_S = 0.23, P = 0.04) and a change in SPARCC significantly correlated with a change in Active MASEI (r_S = 0.30, P = 0.01). In this study we have, for the first time, compared the effects of different forms of biologic therapy on ultrasound-confirmed enthesitis in PsA. We have demonstrated the superiority of TNFi over secukinumab with regard to active entheseal disease. The SPARCC Enthesitis Index correlated with baseline active entheseal disease and with change in response to treatment, highlighting its ability to capture active entheseal disease.

"Pharmacogenetics of Treatment Response in Psoriatic Arthritis Toward Personalized Medicine (3PMedicine)," by Maria Maddalena Angioni, mentored by Alberto Cauli. Response to treatment of PsA is highly variable. Next-generation sequencing (NGS) has revolutionized genomics and can identify novel, rare, and low-frequency risk variants. Careful evaluation of patients integrated with NGS may facilitate a precision medicine approach. The primary objective of this study is to identify possible genetic markers of primary response to TNFi as defined by low disease activity at 6 months using the Disease Activity Index for PsA (DAPSA). Secondary objectives include identifying possible markers of primary response to other disease-modifying antirheumatic drugs (methotrexate, IL-17, and IL-12/23 inhibitors and apremilast). Clinical data (demographics, family history, medical history, findings on musculoskeletal and skin examination, and treatment response) and DNA were collected from 835 patients with PsA satisfying ClASsification for Psoriatic ARthritis criteria from 7 sites in Italy set up by the spondyloarthritis study group from the Italian Society of Rheumatology. A genome-wide association study (GWAS) will be done to find any associations with treatment response. To date, in this cohort we have identified genetic variants associated with PsA vs controls.[2] Due to the coronavirus disease 2019 pandemic, further progress on the project has been delayed. A GWAS for finding single-nucleotide polymorphisms associated with treatment response will then be completed, followed by NGS to identify variants and haplotypes associated with treatment response.

REFERENCES

1. De Miguel E, Cobo T, Muñoz-Fernández S, et al. Validity of enthesis ultrasound assessment in spondyloarthropathy. Ann Rheum Dis 2009;68:169–74.
2. Catanoso M, Macchioni P, D'Angelo S, et al. A genome-wide association study of psoriatic arthritis in Italian population [abstract]. Arthritis Rheumatol 2016;68 Suppl 10.