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Proceedings of the 2021 GRAPPA-Collaborative Research Network (CRN) Meeting

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ABSTRACT. At the 2021 Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA)-Collaborative Research Network (CRN) annual meeting, the GRAPPA-CRN group presented a number of project updates, including a pilot investigator-initiated study to evaluate liquid and tissue biomarkers associated with axial involvement in psoriatic arthritis (PsA). The GRAPPA-CRN session updated progress made with 3 parallel international research initiatives based on 3 previously defined unmet needs in PsA. The Health Initiatives in Psoriasis and PsOriatic arthritis ConsoRTium European States (HIPPOCRATES) is a European research consortium formed to address unmet clinical needs in PsA. The Preventing Arthritis in a Multi-Center Psoriasis At-Risk Population (PAMPA) is a US-based organization that has defined consensus terminology for preclinical phases of PsA and is interested in the transition process from psoriasis to PsA. An overview of the Accelerating Medicines Partnership Autoimmune and Immune-Mediated Diseases (AMP AIM) program 2.0, a consortium including GRAPPA-CRN members that addressed these 3 unmet needs in PsA, was also presented.

Key Indexing Terms: biomarkers, GRAPPA, psoriasis, psoriatic arthritis

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Introduction

The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA)-Collaborative Research Network (CRN) held its fifth meeting at the 2021 GRAPPA annual meeting, which was presented virtually due to the coronavirus disease 2019 (COVID-19) pandemic. The CRN meeting was organized by a committee cochaired by Profs. Oliver FitzGerald and Christopher T. Ritchlin. Of 106 attendees, there were 66 rheumatologists, 18 representatives from the pharmaceutical industry, 6 dermatologists, 7 patient research partners (PRPs), and 9 others including nonclinical scientists and trainee physicians.

The GRAPPA-CRN meetings held in 2018 and 2019 led to the identification of 3 key unmet needs in psoriatic disease (PsD): (1) BioDAM PsA, to identify biomarkers as predictors of structural damage in psoriatic arthritis (PsA); (2) PreventPsA, to evaluate biomarkers of the development of PsA among patients with psoriasis (PsO); and (3) PredictorPsA, to identify biomarkers predicting treatment response in patients with early PsA. These have now been incorporated into 4 parallel and complementary international research initiatives.

The first research initiative resulting from GRAPPA-CRN activities is the Axial PsA Molecular and Clinical Characterization Study, a pilot investigator-initiated study (IIS) to evaluate biomarkers associated with axial involvement in PsA that will be funded by Janssen. The second initiative is the Health Initiatives in Psoriasis and PsOriatic arthritis ConsoRTium European States (HIPPOCRATES), a European research consortium formed with research objectives that are aligned with the GRAPPA-CRN unmet needs. The third initiative is the US-based Preventing Arthritis in a Multi-Center Psoriasis At-Risk Population (PAMPA), who defined consensus terminology for preclinical phases of PsA and are involved in the PAMPA Preventive study. The fourth initiative is the Accelerating Medicines Partnership Autoimmune and Immune-Mediated Diseases (AMP AIM) program 2.0. AMP AIM has also incorporated 2 of the GRAPPA-CRN unmet needs into its proposed program for research in PsD.

Prof. Oliver FitzGerald opened the meeting with an overview of the agenda for the 2021 GRAPPA-CRN meeting. The first part was keynote lectures from 2 esteemed speakers, Profs. Iain McInnes and Soumya Raychaudhuri. The second part provided an update on the 4 research initiatives. The presentations were followed by a panel discussion and concluded with recommendations for GRAPPA-CRN's next steps.

Keynote Lectures

1. How can molecular medical technologies elucidate unmet needs in PsD? The keynote lecture from Prof. McInnes reviewed the clinical heterogeneity of PsD, the involvement of a variety of often inaccessible tissues, and the recognition of associated comorbid conditions. He proposed that PsD may represent several disease phenotypes with likely unique pathogenic mechanisms operating at different disease sites (eg, axial skeleton vs skin), and that the timing of analysis may also affect the outcomes measured (eg, early vs established disease). An overview was presented on potential technological approaches starting with lessons from genetics in PsA that demonstrate interrelationships with associated clinical diseases.[1] Tissue and RNA resources for disease pathotypes in rheumatoid arthritis (RA) were presented, based on tissue and transcriptional evaluations from the Pathobiology of Early Arthritis Cohort, which sampled synovial biopsies from patients with early inflammatory arthritis followed prospectively.[2] Advances in cellular phenotyping of tissue and fluid were presented next, including multiparameter flow cytometry, mass cytometry–based methods, and combinatorial options using RNA sequencing (RNA-seq) and spatial transcriptomics, as well as technologies such as the Hyperion Imaging System (Fluidigm), which enables cellular analysis within the context of the tissue microenvironment.

Several examples of different technological approaches in immune-mediated diseases were presented. This included the characterization of PsD polyfunctional T cells in synovial tissue by flow cytometry and correlation with disease activity,[3] the identification of inaccessible group 3 innate lymphoid cells producing interleukin (IL)-17 in the human enthesis,[4] and single-cell sequencing of synovial tissue to deconstruct macrophage subsets associated with remission in RA.[5] For example, MerTK-positive synovial tissue macrophages produce inflammation-resolving mediators, and coculture with stromal cells result in unique tissue repair reprogramming signatures by synovial fibroblasts. Further, single-cell sequencing and spatial transcriptomics in human tendon disease identified dysregulated immune homeostasis, and a preliminary tendon atlas was described.[6]

Epigenetic approaches have been utilized to identify treatment response signatures in RA; for example, differences in genomic architecture represented by chromosome confirmation signatures.[7] Proteomic approaches, such as the Proximity Extension Assay (Olink Proteomics), was used to compare upadacitinib and adalimumab in PsA and revealed differential patterns of biomarker downregulation by the treatment utilized.[8] A metabolome mass spectrometry approach identified several metabolites, including itaconate, which correlated with disease activity in RA and Disease Activity Score in 44 joints response.[9]

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Using nuclear magnetic resonance metabolomics, Colaco et al were able to predict cardiovascular events using metabolomics profiling in PsD.[10] Prof. McInnes described a multiomics monitoring of drug response in RA in pursuit of molecular remission and advocated for the future use of machine learning and artificial intelligence (AI) to facilitate clinical phenotyping of patients and matching to molecular analyses.[11] In silico clinical trialing provides a computational approach to systematically predict new drug targets or repurposing of existing targets, but requires the application of suitable algorithmic approaches to identify relevant disease-specific mechanisms. Prof. McInnes suggested we now have clear evidence that multiomics-based molecular medicine offers future opportunities to address the unmet needs identified by GRAPPA-CRN.

2. Defining the landscape of tissue inflammation in RA. The second keynote lecture, from Prof. Raychaudhuri, acknowledged that we are unable to define which treatments might be preferable in patients with RA, and outlined the diverse cellular subsets present within the inflamed joint. Technological advances over the last decade that have led to multiomic technologies being simultaneously applied to the same cells were reviewed. Members of the AMP RA/Systemic Lupus Erythematosus (SLE) Network were acknowledged, and the goals of phase I and phase II of the AMP RA/SLE program were summarized. The goals of phase I are to collect data on single cells from synovial joint biopsies (RA vs osteoarthritis [OA]), define key populations, and characterize which populations are expanded with inflammation. The goal of phase II is to characterize heterogeneity in patients with RA, with an overall objective of identifying pathways and cell states as drug targets.

In phase I, synovial tissue samples were acquired and either sent for histology or disaggregated and exposed to mass cytometry or flow cytometry. Cells were sorted into several subpopulations and then bulk or single-cell RNA-seq was performed (Figure 1). In this way, 51 patient data sets were acquired (n = 15 OA; n = 17 leukocyte-poor RA; n = 19 leukocyte-rich RA), for which flow cytometry and bulk RNA-seq was available for all patients, mass cytometry for a smaller number, and single-cell RNA-seq for a limited number.[12] Eighteen unique populations of cell states were identified by both single-cell RNA-seq and mass cytometry, which were enriched in the leukocyte-rich RA population and included THY1^{+}HLA^{high} sublining fibroblast, IL-1β^{+} proinflammatory monocytes, CD11c^{+}T-bet^{+} autoimmune-associated B cells, and PD-1^{+} T peripheral helper and T follicular helper subsets.[12] IL-6 was uniquely produced by THY1^{+}HLA^{high} sublining fibroblasts and naïve B cells, with IL-1β produced by proinflammatory monocytes. Canonical correlation analysis was undertaken to ensure there were no technical artifact limitations. This analysis facilitated the validation of particular clusters, such as the HLA^{high} SC-F2 synovial fibroblast cluster, leading to further characterization of the 16-fold enriched clusters in leukocyte-rich RA of THY1^{+}CD34^{-} HLA-DR^{high} subset compared to OA and leukocyte-poor RA.[13] These inflammatory fibroblasts are localized to the perivascular zone in inflamed synovium[14] and are regulated by endothelium-derived Notch signaling.[15] Further, a lining population of synovial fibroblasts expressing DNASE1L3 was found to be depleted in patients with RA, and this subpopulation may protect from RA development.

Phase II of the project evaluated > 300,000 single cells using RNA-seq in 80 samples, including droplet-based RNA-seq and integrated RNA and surface markers to explore heterogeneity. Principal component analysis has enabled patients to be subcategorized according to cell type composition. Covarying neighborhood analysis is being deployed to define cell states associated with subgroups of patients.[16] Comprehensive data analysis of phase II is continuing.

Initiative Updates

1. Axial PsA Molecular and Clinical Characterization Study. Prof. Philip Mease updated progress on an IIS funded by Janssen. The central hypothesis was that there are liquid and/or tissue biomarkers associated with axial involvement in PsA and

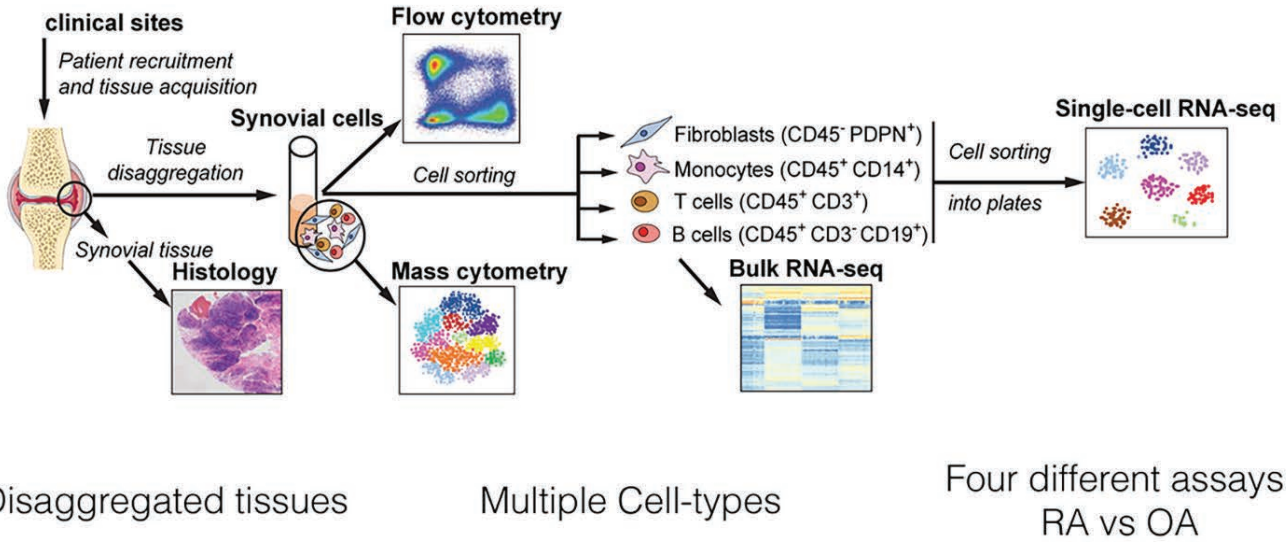

Figure 1. Toward a global picture of synovial cells. RNA-Seq: RNA sequencing. Adapted from Zhang et al.[12]

identification of these biomarkers will assist in the recognition of these patients for appropriate assessment and treatment. The study design is a multicenter pilot study, enrolling 40 patients (20 with and 20 without axial involvement) with data collected at baseline/enrollment only. Patient inclusion criteria are the fulfillment of ClASsification for Psoriatic ARthritis (CASPAR) criteria and < 10 years of active disease, where at least 80% will have an active skin plaque for punch biopsy and at least 50% an inflamed joint for synovial biopsy. The patients will be naïve to biologic (b-) and targeted synthetic disease-modifying antirheumatic drugs (DMARDs). Imaging will include plain radiographs of the sacroiliac joints (prone view), lumbar and cervical spine, and hands and feet. In addition, T2-weighted, fat-saturated (FS) oblique coronal magnetic resonance imaging scans of both sacroiliac joints, and T1 and T2-FS sagittal imaging of cervical, thoracic, and lumbar spine will be obtained.

Data collected will include patient history, demographics, and disease activity measures. Samples will include blood and stool (all patients), skin biopsy in at least 80%, and synovial biopsy in 50% of patients. Samples will be biobanked for phased analysis; phase I includes HLA typing and cytometry by time of flight (CyTOF) on peripheral blood mononuclear cells (PBMCs), skin, and synovial biopsies. The overall analysis will also include (1) PBMC phenotyping; (2) liquid chromatography with tandem mass spectrometry unbiased discovery and targeted proteomics on serum samples as well as serum metabolome studies; (3) synovial and skin single-cell transcriptomics and toponomics; and (4) stool microbiome analysis. Twelve international sites in North America and Europe that have capabilities in skin and synovial biopsies have been identified as participants in this pilot study, with the study due to launch in the near future.

2. HIPPOCRATES. Prof. Stephen Pennington introduced HIPPOCRATES, a European research consortium addressing key unmet clinical needs in PsA. The project is funded over 5 years by the Innovative Medicines Initiative (IMI) in a joint undertaking with European Federation of Pharmaceutical Industries and Associations (EFPIA) industry partners (grant agreement no. 101007757). The research objectives are aligned with those originally identified by GRAPPA-CRN and include the identification of patients with PsO at risk of progression to PsA, the early diagnosis of PsA in patients with PsO and in those with undifferentiated early inflammatory arthritis, the early identification of patients with PsA likely to experience damage progression, and the prediction of patients' response to treatment. Ultimately, the results may allow a precision approach to treating PsA, where treatment decisions are based on combined clinical, genetic, and molecular disease characteristics. The consortium comprises 20 academic centers across Europe, many of whom are GRAPPA-CRN investigators, EFPIA pharmaceutical companies, small–medium enterprises, and patient organizations (GRAPPA, European Alliance of Associations for Rheumatology–People with Arthritis/Rheumatism across Europe, and Europso). Profs. Pennington and FitzGerald at the University College Dublin are the HIPPOCRATES academic coleads, and Drs. Christine Huppertz (Novartis) and Owen Davies (UCB) are EFPIA partner coleads. The project is managed by Eurice, based in Germany, and is divided into 4 scientific work packages (WPs) aligned to the unmet needs and a fifth which, using machine learning and AI approaches, will integrate and analyze data from the 4 WPs. HIPPOCRATES commenced with an online kick-off meeting in May 2021, attended by > 90 individuals, and officially started on July 1, 2021.

WP-1 will address "Early Diagnosis of PsA" and is led by Frank Behrens, Micheala Koehm, and Anne Barton (industry colead BMS). The objective is to perform deep phenotyping of PsO patients with musculoskeletal symptoms or imaging abnormalities to identify and validate a set of clinical, imaging, genetic, and liquid biomarkers, as well as tissue features, to support an early PsA diagnosis. The deliverable is to develop a diagnostic algorithm, which can be used by general practitioners, rheumatologists, and dermatologists.

WP-2 will address "Predicting PsA" and is led by Oliver FitzGerald, Stephen Pennington, and Laura Coates (industry coleads UCB and Novartis). There is increasing recognition of early stages of disease prior to the development of clinical PsA that fulfills CASPAR criteria.[17] WP-2 will use 3 main approaches: (1) collating multiple cohorts and biosamples for PsO cohorts to develop and validate an algorithm for predicting PsA using clinical and biological markers; (2) using machine learning on real-world, routinely collected datasets from across Europe to identify predictive algorithms based on clinical data; and (3) developing a new web-based longitudinal HIPPOCRATES Prospective Observational Study (HPOS) to follow up to 25,000 patients with PsO across Europe in order to identify and test predictors for the development of PsA. This work will culminate in the development of an optimal study design for a future interventional study aiming to prevent PsA in people with PsO. HPOS will recruit 25,000 patients with PsO but without PsA and obtain genomic information from a subset of patients who develop PsA, those at risk of developing PsA (using prediction models), and a control group. Information will be obtained using the Rare UK Diseases study's web-based platform application (University of Oxford). Using a clinical risk tool to identify high and low risk (1500/group), patient-centric sampling (Mitra tips) will be used to collect whole blood samples (target n = 3000) for subsequent HLA genotyping, genetic variant/single-nucleotide polymorphism analysis, and whole exome or genome sequencing.

WP-3 focuses on "Rapid Damage Progression" and is led by George Schett and David Simon (industry colead Pfizer). Four objectives of the WP are (1) to define the longitudinal course of joint and bone damage and of functional decline; (2) to define clinical, imaging, and biochemical predictors of disease progression; (3) to build predictive models to identify patients at risk for disease progression; and (4) to establish adaptive, patient-oriented, individualized therapy strategies to prevent disease progression. WP-3 has 3 associated tasks: (1) to identify a PsA clinical phenotype associated with damage progression and functional decline; (2) to perform an in-depth systemic molecular characterization of patients with PsA and association

with disease progression; and (3) to target tissue characterization of patients with PsA and its relation to disease progression. The outputs of these tasks will be analyzed in WP-5, validated in larger cohorts, and then a tailored risk assessment will be done to identify patients at risk for fast progression and provide an optimal design for a future interventional study.

WP-4 led by Iain McInnes and Stefan Siebert (industry colead Novartis) focuses on "Predicting Treatment Response" in PsA. The 4 objectives include (1) to collate and align existing datasets and samples of therapeutic response (with WP-5); (2) to perform state-of-the-art polyomic molecular/cellular analysis to identify theragnostic biomarkers for clinical evaluation; (3) to define theragnostically significant endotypes using AI-based analytics of clinical and biomarker data (in WP-5); and (4) to use state-of-the-art tissue/blood analytic techniques to develop novel molecular signatures of clinical state with potential for clinical application. Treatments evaluated will include methotrexate, tumor necrosis factor inhibitors (TNFi), and IL-17 inhibitors (IL-17i); treatment responses will include composite measures until ≥ 6 months; and biomarkers will include both discovery and validation. The plan is for (1) genomic and epigenomic characterization of response using existing cohorts/biobanks; (2) metabolomic and proteomic analyses of existing cohorts/biobanks; and (3) deep phenotyping of tissue (synovium, skin) and blood to identify pathways driving TNFi and IL-17i treatment–resistant pathologies vs those driving sustained remission in PsA using cellular indexing of transcriptomes and epitopes by sequencing (CITE-seq; single-cell transcriptomics and proteomics) at baseline integrated with prospective clinical outcome; and (4) epigenetic time of flight (longitudinal epigenetic changes) at baseline and at time of response or nonresponse to TNFi or IL-17i.

WP-5 led by Stefan Rueping and Mark Ibberson focuses on "Data Integration and Analysis" (industry colead UCB). The 4 objectives include (1) securing data management; (2) data analysis for WP-1 to WP-4 to enable hypothesis-free analysis of clinical data beyond current state-of-the-art technologies; (3) central coordination of data analysis; and (4) evaluating trustworthiness of AI models and thus support dissemination into clinical practice.

Key to HIPPOCRATES is the availability of existing patient cohorts and samples. Prof. FitzGerald provided a summary of the impressive patient cohorts already collected in Europe (clinical data, imaging, biosamples) that will be incorporated within the different WPs. WP-6 is entitled "Project Management" and is led by Vera Schneider at Eurice (in addition to Stephen Pennington and Oliver FitzGerald; industry coleads Novartis and UCB).

WP-7, "Dissemination, Exploitation, Sustainability, and Communication" is led by Frances Mair and Maarten de Wit (industry colead Novartis). The executive team and all WPs include PRPs. The vision of HIPPOCRATES is to yield a transformative opportunity to create a sustainable knowledge base and patient biosample resource that will enable a greater understanding of the molecular heterogeneity of PsA, and to promote and accelerate PsD research leading to the development of innovative personalized treatment strategies. In achieving this, HIPPOCRATES hopes to ultimately improve PsA patient outcomes.

3. PAMPA. Prof. Jose Scher provided an overview of the Psoriasis and Psoriatic Arthritis Clinics Multicenter Advancement Network (PPACMAN) PsO to PsA transition program. Several therapeutics achieve PsO Area and Severity Index-90 response in 60–80% of patients with PsO, whereas < 20% of patients with PsA would reach an American College of Rheumatology-70 response in their joints.[18] Early intensive treatments and combinations of available therapeutics have not necessarily improved PsA outcomes, and perhaps once PsA is established it is not amenable to modulation. Therefore, defining patients with PsO alone at increased risk of progression to PsA will enable studies to dissect the involvement of genetic, environmental, and immune factors in PsA transition. The development of a predictive tool for PsA progression should provide a framework for the design of preventive clinical trials.[17]

In order to improve outcomes in PsA, innovative solutions were defined. The first key innovative solution of AMP AIM was to discover a novel inflammatory pathway or cell subset in PsA. AMP AIM has synergy with several academic centers (University of California San Francisco, University of Rochester Medical Center, University of Michigan Medical Center, University of Pennsylvania, Brigham and Women's Hospital), National PsO Foundation, Sage Bionetworks, industry partners, and HIPPOCRATES.[19] The PAMPA study group within PPACMAN has defined consensus terminology for preclinical phases of PsA for use in research studies and its mission is to study the clinical, genetic, environmental, and immune events during the natural history of PsO to PsA transition.[17,20] PAMPA aims to define the at-risk PsO population, predict progression, and prevent PsA. PAMPA will begin the industry-sponsored (Janssen), double-blind, placebo-controlled randomized controlled trial, PAMPA Preventive, where at-risk patients with PsO[17,20] who have had PsO of moderate severity (> 3% body surface area) for > 2 years with musculoskeletal (MSK) power Doppler abnormalities at baseline will receive a bDMARD or placebo for 6 months. The primary outcome is MSK ultrasound improvement at week 20. The study will explore the coprimary outcome of percent of high-risk patients with PsO who fulfill modified CASPAR criteria, secondary PsA transition outcomes, and also biomarker analysis.

4. AMP AIM. Prof. Ritchlin provided an overview of the success of the AMP RA/SLE program and the concept of disease deconstruction in which multiomic high-dimensional characterization of single cells in > 100 synovial biopsies in RA have led to the discovery of new cell populations and states, biomarkers, pathways, and targets for drug development. In AMP AIM, the cornerstone will be disease deconstruction/reconstruction, where disease deconstruction indexes and maps cells. New analytics will be used to see how innate and adaptive cells of the immune system and tissue resident cells interact to cause inflammation and clinical disease (disease reconstruction). These approaches may facilitate the discovery of new mechanisms of disease and targets for intervention.

AMP AIM builds on key outcomes of AMP RA/SLE using deconstruction methods such as CyTOF, CITE-Seq, and assay for transposase-accessible chromatin using sequencing, along with intracellular pathway analysis and clinical correlate evaluation. AMP AIM will introduce high-dimensional information about tissue resident and infiltrating cells in blood and tissue using spatial mapping of cell types and states (eg, Visium, Hyperion) to measure and understand cell–cell interactions and covariant pathways. The initial focus will be to evaluate skin, synovial tissue, and blood in order to characterize clinical/molecular disease endotypes. The second unmet need is the discovery of prognostic and predictive biomarkers (molecular insights), which identify targets to track the transition from PsO to PsA. The third unmet need is the definition of features associated with treatment response and nonresponse to a specific targetable pathway. AMP AIM will enable unprecedented multimodality data integration using several parallel platforms across the diseases being evaluated. There will be a centralized technologies and analytics core; a systems biology core focusing on analyzing and interpreting large-scale molecular data, then integrating the data across multiple cell types, tissue types, and cell states; and a tissue repository center. The Elucidating the Landscape of Immunoendotypes in Psoriatic Skin and Synovium (ELLIPSS) group is the team submitting their proposal to AMP AIM, and an overview of the subcommittees within ELLIPSS (including several GRAPPA-CRN members), along with clinical sites and core teams, was presented.

Discussion Session

GRAPPA-CRN meeting attendees asked the panel (Philip Mease, Stephen Pennington, Oliver FitzGerald, Christine Huppertz, Jose Scher, Christopher Ritchlin, and Vinod Chandran; chaired by April Armstrong and Maarten de Wit) about the lack of PRP involvement in the Axial PsA Molecular and Clinical Characterization Study. As a result, a GRAPPA PRP will now be included in the steering committee. It was acknowledged that the sample size is small, that peripheral features in the axial and nonaxial groups need to be carefully matched, and that this was a pilot study focusing on the mechanics of data and biosample collection in addition to the study hypotheses. The importance of longitudinal studies to address axial PsA was emphasized, and was also recognized with respect to HIPPOCRATES and, in particular, the HPOS study, which will aim to collect samples at several timepoints.

Attendees asked whether HIPPOCRATES had sought advice from Biomarkers in Atopic Dermatitis and Psoriasis (BIOMAP), an IMI endeavor funded with 33 partners in 13 countries, with a budget of € 22 million, that is currently 1 year into the project (www.biomap-imi.eu). There are members of BIOMAP in HIPPOCRATES.

With respect to PAMPA Preventive, entry criteria for MSK abnormalities were discussed. The PsA ultrasound composite score (PsASon), which is able to evaluate both inflammatory and structural PsA lesions, is being adopted.[21] Attendees asked about noninvasive sample collection, such as urine sampling or tape stripping, rather than skin or synovial biopsies. AMP AIM favors deconstruction evaluation of tissues for discovery, but the AMP RA/SLE program has gained valuable data from urine proteomics, and blood biomarkers would be the hope for validation studies for AMP AIM.

General themes from the discussion were to nurture collaboration across the ocean between HIPPOCRATES and AMP AIM, as there are common goals. There is currently progress in coordinating efforts through GRAPPA-CRN, with Profs. FitzGerald and Ritchlin as leaders of the 2 projects in Europe and the US, respectively. It was recognized that the projects are very European/North American–centric. GRAPPA-CRN would be central in evaluating PsA in different ethnic groups and broadening involvement to a more global scale based upon GRAPPA member participation.

Summary

Following the creation of GRAPPA-CRN 5 years ago, significant progress has been made, with support now in place for several parallel research programs based upon the original unmet needs defined by the network. This includes the Janssen-funded Axial PsA Molecular and Clinical Characterization Study program, the IMI-supported HIPPOCRATES program, the Janssen-funded PAMPA Preventive study, and the incorporation of unmet needs into the AMP AIM program. There are also GRAPPA-CRN industry-partnered programs nearing completion, which are addressing unmet needs using industry-provided patient biosamples.

Next steps. The HIPPOCRATES program, an endeavor that came out of the GRAPPA-CRN group led by Profs. FitzGerald and Pennington, has commenced. The ELLIPSS consortium includes key members of GRAPPA-CRN and will know shortly whether they have been successful in obtaining funding from AMP AIM. There are common objectives identified in the Europe- and North America–based consortiums, and the role of GRAPPA-CRN will be to nurture a complementary rather than competitive approach to their goals, to facilitate communication, and to work on mutually agreeable definitions. Another important goal of GRAPPA-CRN is recognizing that the organization is global, and that PsO is experienced by people of different ethnic groups. The importance of the inclusion of such patients in ongoing studies and providing opportunities to researchers across the world was acknowledged.

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