HHS Public Access

Author manuscript

Clin Immunol. Author manuscript; available in PMC 2021 September 01.

Published in final edited form as:

Clin Immunol. 2020 September ; 218: 108519. doi:10.1016/j.clim.2020.108519.

Editorial: Psoriatic arthritis; Overcoming the challenges by creating opportunities

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Abstract

Over the past few years, there have been several scientific advances related to the discovery of interleukin 23 (IL-23) and IL-17 which led to the development of new treatment options and overall improved clinical care of Psoriatic Arthritis (PsA) patients. Many of these efforts and milestones, alongside new developments, are captured in this Clinical Immunology special edition. We also take the opportunity to highlight the overall scientific progress in PsA research and also highlight some areas of concern that continue to represent barriers in the PsA arena that need to be addressed. These areas are 1) basic & translational research, 2) clinical diagnosis 3) treatment and 4) medical education and awareness.

1. Basic & translational research

PsA research is surprisingly challenging as it requires the involvement of many different scientific backgrounds within life-sciences including immunology, bone biology and skin biology. Recent developments in genetics research, focused on the IL-17A and IL-17F as described in the original research report by Shao et al., [1] as well as the implications of the IL-23/IL-17A axis in the innate immune responses are discussed by Hille et al., [2]. The role of regulatory T cells in PsA is discussed by Liu et al., [3] and Daihui and Adamopoulos [4] tackle the complex role of IFNγ in regulating signals that can inhibit and/or induce PsA pathology. The ever-growing fields of microbiome and bioinformatics are also highlighted by Le et al., [5].

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Despite the effort of many investigators, unfortunately, the amount of basic and translational original research papers in PsA is rather limited. As a result, many PsA scientific principles have been “borrowed” by other autoinflammatory, autoimmune or infectious diseases without being validated properly for their applicability in PsA pathophysiology. One of the reasons for is that funding of long-term research program grants in PsA is impaired due to the lack of research centers that will rise to the task of interdisciplinary research. The need of dedicated research centers for PsA that bring together a diverse scientific team is paramount to address the gaps of knowledge in PsA. Part of this problem is due to the lack of PsA-specific grant-review boards. Despite the effort of many grant-funding bodies most basic and/or translational research grants automatically fall in study sections composed of either immunology, bone or skin biology experts without necessarily appreciating the overlap as it is commonly observed in PsA. Many times, reviewers request to separate studies of bone from skin and vice versa which defeats the purpose of basic research in PsA pathophysiology and identifying cellular and molecular mechanisms that can be exploited for therapeutic intervention. Interestingly, misunderstanding the importance of the “overlap” principle also presents significant obstacles and challenges in clinical care especially in clinical diagnosis.

2. Clinical diagnosis

In the article by Stoll and Mellins [6], the controversy of PsA in childhood is discussed and Rida and Chandran [7] eloquently present the challenges of early PsA diagnosis in adults. As discussed in both reports while imaging, serology or biopsies are definitive diagnosis for many conditions, that is not the case the PsA. Indeed, in the National Psoriasis Foundation (NPF) 2019 Annual Survey, the majority of patients reported not receiving a diagnosis of PsA for up to a year after experiencing symptoms. This is problematic since permanent joint damage can occur in as little as six months. The survey also indicated that 68% of patients with psoriasis that had a Psoriasis Epidemiology Screening Tool (PEST) score of >3 - indicating a high likelihood of having PsA - have never seen a rheumatologist. The challenge of receiving a proper diagnosis is one of most frequent remarks received by the NPF and the Arthritis National Research Foundation (ANRF) from individuals during their PsA journey. To overcome this challenge the NPF launched in 2018 the PsA Diagnostic Test Grant to fund efforts for the development of a reliable, reproducible and readily available diagnostic test for PsA. In 2019, six proposals were funded as the proof of concept phase, with research underway to progress the most promising approaches toward implementation. Success of these teams would represent a huge milestone in the care of individuals living with PsA and would undoubtedly result in improved health outcomes. Similarly, ANRF has also funded pilot research grants in the disease area as well and we optimistically expect to see the results of these studies in the near future.

3. PsA Treatment

2018 marked a key step forward in the field of Psoriatic Arthritis with the publication of new treatment guidelines developed jointly by the American College of Rheumatology (ACR) and the NPF, in collaboration with community stakeholders. Notably, the shortage of available patient data in some key areas examined during the process of developing the latest

guidelines necessitated grading the quality of evidence as low, or very low. As such, most recommendations in the ACR/NPF treatment guidelines were qualified as conditional, underscoring the need for more clinical research and focused investigations in PsA. That is coupled to the exigency of robust patient data acquisition, collection, and analysis efforts - particularly in gap areas in PsA such as early detection, diagnosis, natural history and treatment options.

Treatment of PsA remains a challenge as despite approval of at least twelve treatments in the US, outcomes have not improved significantly. As discussed in the article by Toussi et al., [8] up to 45% of patients do not achieve primary outcome measures in clinical trials and nearly 60% of patients surveyed by NPF still find their disease burden unacceptable with treatment. This highlights the need for new treatment options through current treatment optimization, precision medicine and new target discovery which is thoroughly discussed by Castillo and Scher [9].

Again, these lofty goals will only be achieved through collaboration, between researchers from multiple disciplines, and clinical rheumatologists and dermatologists. Organizations like ANRF and NPF have facilitated many joint programs to move the science and education forward by soliciting grants each year focused on PsA that has translational and clinical relevance. This year, NPF launched a groundbreaking initiative, the Psoriasis Prevention Initiative, a funding mechanism that requires a multi-institutional, multidisciplinary, team-based approach to investigating the prevention of onset of disease, the prevention of relapse or the prevention of the onset of comorbidities. Finding a way to prevent the development of PsA in those patients with PsO would be of critical importance. Finally, treatment options in general, and early treatment regimens in particular, are influenced by many factors including comorbidities, which are eloquently discussed by Perez-Chada and Merola [10], as well as disparities, stigmas, access to care, cost, mental health and many other socioeconomical determinants of health that are beyond this editorial but should be noted.

4. Medical Education and Awareness

The need for far-reaching education and awareness programs, including within the healthcare community is palpable. Patients experiencing symptoms have to find a rheumatologist with a knowledge of PsA and with the shortage of rheumatology specialists, this can be an obstacle to care. This is especially true outside metropolitan areas and large medical centers. The NPF and other patient advocacy organizations has developed educational materials for PsA pathophysiology, screening, comorbidity evaluation and treatment to educate rheumatologists about PsA at all stages of their training. Grand Rounds programs in underserved areas and virtual offerings, especially during the pandemic are critical to serve our community. ANRF has a robust research education and outreach presence across their multiple channels and platforms to disseminate the latest news in Arthritis, Rheumatology and Autoimmune Diseases through free newsletters, webinars, fact sheets and other digital and print mediums. Other collaborative programs are also in development between NPF and ANRF. Of note, NPF is launching a medical school curriculum program to expose first- and second-year medical school students to the basics of psoriatic disease for our next generation of health care providers. Dermatologists are

encouraged to use the PEST screener and recognize risk factors and signs of concern for PsA beyond joint pain. To foster collaboration between rheumatologists and dermatologists, PPACMAN and the NPF have partnered to offer programs for trainees and providers. Access to accurate and concise information is a necessity in a disease area like PsA. This elevates the standards of care and benefits healthcare providers, enabling them to deliver the best-in-class care and treatment options for their patients. In turn, such access also assists patients in their self-empowerment journey as partners and informed decision makers in their own health and welfare.

5. Concluding remarks

Work behind the scenes, by leading foundations and societies that promote innovation and collaborative networks have made significant contribution in the field of PsA and have addressed many areas of contention to overcome multiple hurdles. In this context, important work has been done by GRAPPA and OMERACT (Outcome Measures in Rheumatology) on health outcomes, and by PPACMAN (Psoriasis and Psoriatic Arthritis Clinics Multicenter Advancement Network) related to clinical care, collaboration, PsA screening, and comorbidity. Other large-scale, public-private partnership initiatives like the “Accelerated Medicines Partnerships (AMP)” effort for psoriatic disease would model previous AMP programs and involve collaboration with industry, the NIH and researchers from many disciplines. This would be the US complement to the recently announced International Medicines Initiative call for PsA in the European Union.

Finally, this is, by no means, a comprehensive list, instead, these gaps are ones that can benefit more than others from the forward momentum gained in understanding the pathophysiology of PsA recently, including the rise of some effective, targeted therapies in the course of the last decade. However, as the challenges present themselves, so do the opportunities for new directions, new collaborations and new discoveries, making the arena of PsA research one of the most exciting areas in translational research.

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