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INTRODUCTION

Psoriasis, a chronic dermatological condition, has confounded clinicians for centuries. Progress in understanding its genetic basis, comorbidities, pathogenesis, and treatment strategies has burgeoned over time. The recent presentations of the International Psoriasis Council Think Tank comprehensively explored the historical, current, and future perspectives of psoriasis management, shedding light on its evolution through time (Lomholt, 1963).

HISTORICAL PERSPECTIVES

The historical landscape of psoriasis research was illuminated by pioneers such as Gunnar Lomholt (after whom this symposium was named), whose seminal contributions in the mid-20th century laid the groundwork for understanding psoriasis genetics and prevalence. In 1963, Lomholt presented a groundbreaking thesis titled "Psoriasis: Prevalence, Spontaneous Course, and Genetics," aimed at elucidating the genetic features of psoriasis and clarifying its prevalence and natural course when untreated (Lomholt, 1963). His census surveys in the Faroe Islands unveiled a 2.84% prevalence, evenly distributed across genders, with onset typically occurring at ages 12−13 years.

James T. Elder presented a historical perspective to highlight the importance of these epidemiological observations. He went on to explain how family and twin studies confirmed Lomholt's conclusions and how this knowledge eventually led to large-scale international studies that attempt to define the genetic architecture of psoriasis, provide clues to disease biology, and potentially identify new drug targets. As he explained, future genetic studies can help us understand the natural history of the disease. These foundational studies set the stage for the exploration of psoriasis beyond its clinical manifestations as discussed in detail at the symposium.

CONTEMPORARY INSIGHTS

In the contemporary era, Tamar Nijsten's exploration of Big Data in psoriasis research signifies a paradigm shift in data utilization. The vast and complex datasets generated in health care, characterized by volume, velocity, variety, variability, and veracity, open new avenues for understanding psoriasis at deeper, multidimensional, and multiomic levels. Nijsten cautioned about the potential information stress and overload, emphasizing the potential of machine learning to surmount these challenges.

Michael Simpson's research on genetic associations and the role of HLA-C*06:02 in psoriasis endotypes highlights the intricate relationship between genetics, clinical features, and treatment response. He presented data showing differences in clinical features in individuals with psoriasis who are HLA-C*06:02 positive and HLA-C*06:02 negative. Polygenic risk scores can be used to further stratify psoriasis, including severity. The clinical significance of this has been highlighted by data showing the predictive ability of HLA-C*06:02 in determining response to biologics. Simpson also presented pharmacogenomic data revealing the association between the development of antidrug antibodies and HLA-DRB1. Perhaps in the future, genotyping patients before starting therapy will allow us to use drugs in a more personalized way.

Alex Tsoi's emphasis on comorbidities, identified through patient claim databases and *trans*-disease meta-analysis, contributes to a holistic understanding of psoriasis. Employing Mendelian randomization as a tool to infer causal relationships, Tsoi's work advances our comprehension of the broader implications of psoriasis beyond its cutaneous manifestations, underscoring the interconnectedness of psoriasis with various health conditions. The work challenges much current dogma concerning the relationship between psoriasis and cardiometabolic comorbidities with potentially significant implications for how we manage psoriasis and its comorbidities.

Johann E. Gudjonsson's elucidation of psoriasis as a spectrum of clinical phenotypes, driven by complex interactions between immune and stromal cell populations, offers a blueprint for targeted interventions. He provided an in-depth view of psoriasis pathogenesis, unraveling genetic

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Abbreviations: GPP, generalized pustular psoriasis; RWE, real-world evidence; TDM, therapeutic drug monitoring

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predisposition loci corresponding with T cells, dendritic/myeloid cells, keratinocytes, and fibroblasts. Gudjonsson stressed the dynamic and complex interaction between these cell types, with IL-17, TNF, IFNs, and IL-36 associated with underlying disease, the relative contribution of each immunological circuit correlating with disease subtype, and severity of psoriatic skin lesions.

FUTURE PERSPECTIVES

The future of psoriasis management is intricately linked to advancements in genetics, immunology, and therapeutic strategies. Gudjonsson's portrayal of psoriasis as a spectrum driven by complex immune–stromal interactions provides a framework for future targeted interventions. Hervé Bachelez's discussion on immunogenetic dissection of pustular forms of psoriasis reveals the power of single-gene disease models. Indeed, pathogenic variants targeting different innate immune genes have been identified mainly in patients with generalized pustular psoriasis (GPP), such as *IL36RN*, *CARD14, AP1S3*, and *MPO*. These genetic studies identified IL-36 as a key pathogenic cytokine in GPP and paved the way for the successful development of anti–IL-36 receptor mAbs for therapeutic purposes, leading to the recent approval of spesolimab in this indication. The correlations between each genetic background and the clinical response to different targeted therapies (anti–IL-36R, anti–IL-17, anti–IL-23) will be of great interest in the perspective of precision medicine approaches. Preliminary findings support the major pathogenic contribution of the IL-17–driven inflammatory cascade in patients with *CARD14* variant, which needs to be prospectively investigated.

Liv Eidsmo's exploration of inflammatory memory in patients with psoriasis suggests that altering the microenvironment and prolonged T-cell starvation may pave the way for achieving long-term remission. The increased understanding of immunological memory and tissue-resident memory T cells requires a paradigm shift toward earlier treatment with highly efficacious medication for those presenting with severe psoriasis rather than a stepwise graded approach.

Oliver Fitzgerald's insights into psoriatic arthritis highlighted the need for further understanding based on distinct genetic HLA subsets for more effective and targeted treatments. The recognition of distinct entities within the spectrum of psoriatic arthritis further emphasizes the complexity of the disease and the need for tailored interventions. A large European study is currently underway to try and address these important issues.

Catherine Smith's discussion on therapeutic drug monitoring (TDM) underscores the importance of optimizing drug exposure to mitigate suboptimal responses to biologic therapy. Proactive or reactive approaches to TDM hold potential benefits for personalized outcomes and cost-effectiveness during maintenance treatment, offering a glimpse into the future of precision medicine in psoriasis.

Advocating for holistic therapeutic care, Ulrich Mrowietz emphasized addressing risk factors, trigger factors, and comorbidities in patients with psoriasis. Common treatment targets for psoriasis and comorbid conditions advocate a holistic approach to future patient care, acknowledging the interplay between various factors in the management of this complex condition.

Lone Skov highlighted the need for real-world evidence (RWE) in psoriasis research. Most randomized controlled trials have a short follow-up duration, with strict eligibility criteria. RWE, derived from health records, insurance claims databases, and patient registries, offers long-term efficacy and drug survival data. Skov outlined the key findings from several RWE studies, providing evidence regarding long-term effectiveness, sequential treatments, and safety.

CONCLUSION

In conclusion, the trajectory of psoriasis management has transitioned from historical explorations of genetic predispositions to a contemporary era of big data analytics and targeted molecular therapeutics. The future promises a nuanced understanding, where genetic insights, immunological memory, and RWE converge to shape individualized and effective management strategies. Navigating this trajectory requires embracing historical lessons; leveraging present technologies; and charting a course toward personalized, targeted treatments. The unfolding chapters in psoriasis research and treatment hold the potential to alleviate the burden of this chronic condition and enhance the QOL for affected individuals, marking a significant paradigm shift in the holistic care of patients with psoriasis.

Abstracts of the presentations of the symposium have been published before (Barker et al, 2023)

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CONFLICT OF INTEREST

FYXL received fees for consultancy services or lecturerships from Amgen, Bristol-Myers Squibb, Eli Lilly, Janssen, Leo Pharma, Novartis, Pierre Fabre, Sanofi, and UCB. HB had paid consulting activities for Anaptysbio, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Janssen, Lilly, and UCB Pharma and grant research support from Boehringer Ingelheim and Pfizer. JG received research grants from Bristol-Myers Squibb, Prometheus/Merck, Almirall, Janssen, AbbVie, Boehringer Ingelheim, and Novartis and is on the advisory board of AbbVie, Janssen, Eli Lilly, Bristol-Myers Squibb, Boehringer Ingelheim, Novartis, and UCB. LS has attended advisory boards and/or spoken at sponsored symposia and/or received research funding from AbbVie, Almirall, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly, Galderma, Janssen, Novartis, Pfizer, LEO Pharma, Sanofi, and UCB. CZ has attended advisory boards and/or spoken at sponsored symposia from AbbVie, Almirall, CSL, Eli Lilly, Galderma, Jansen Cilag, Leo Pharma, Novartis, and UCB. PCMvdK received fees for consultancy services or lecturerships from Almirall, AbbVie, Eli Lilly, Novartis, Janssen Pharmaceutica, Leo Pharma, Bristol Mayer Squib, UCB, Boehringer Ingelheim, and Dermavant. JNWNB has attended advisory boards and/or spoken at sponsored symposia and/or received research funding from AbbVie, Almirall, Amgen, Anaptys Bio, Boehringer Ingelheim, Bristol-Myers Squibb, Johnson and Johnson, Eli Lilly, Novartis, Sandoz, and UCB.

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