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GRAPPA 2023 Basic Science Workshop: What to Expect From Animal Models for Psoriatic Arthritis and Psoriasis

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ABSTRACT. Animal models help to drive research into psoriasis and psoriatic arthritis (PsA), particularly when studies in humans are not feasible. There are no animal models that perfectly mimic psoriatic disease (PsD) and so the pros and cons of each existing model must be considered for appropriate experimental design. Roughly, the existing animal models for PsD can be divided into 4 categories: (1) spontaneous models, (2) transgenic models, (3) inducible models, and (4) xenotransplantation models. Animal models in PsD are extremely important for dissecting and understanding molecular mechanisms of the disease process and for developing novel drugs. Animal models remain highly valuable for research in PsD in 2 scenarios. The first scenario is when complex interventions or analyses are required that are not feasible in humans due to technical, safety, or economic reasons. The second is when well-controlled study environments are required, such as dietary modifications, that would be challenging in humans. This topic was presented as part of the basic science workshops during the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) 2023 annual meeting.

Key Indexing Terms: animal model, GRAPPA, psoriasis, psoriatic arthritis

Animal models aid in understanding disease pathogenesis and underlying cellular and molecular mechanisms. In psoriatic disease (PsD), animal studies contributed to our current knowledge of the inflammatory proliferative cascades and in the development of novel, effective, safe therapies.[1-3] There is no known naturally occurring PsD in nonprimates. Therefore, currently used animal models—almost exclusively using rodents—mimic aspects of the disease but are never a perfect representation.[2] Both the advantages and limitations of each model must be considered when planning studies. For example, animal models displaying both skin and joint inflammation are limited. The most useful models of both skin and joint symptoms are HLA-B27–positive rats,[4] the minicircle-driven interleukin (IL)-23 overexpression mouse model,[5] and β-glucan–induced disease in SKG mice.[6]

Extensive overviews of currently used animal models for PsD are available elsewhere.[2,3] In short, these models can roughly be divided into 4 categories. The first category comprises the spontaneous models mimicking a part of the human disease, like the psoriatic arthritis (PsA)-like joint inflammation in the aging DBA/1 mice.[7] There are also multiple models of spontaneous skin inflammation, but with substantial differences from human psoriasis (PsO), like the absence of an epidermal T-cell infiltrate, so these models are not widely used.[8] The second category is transgenic animals with overexpression or loss of function approaches like HLA-B27–positive rats,[4] myeloid-selective A20 deficiency in mice,[9] and systemic tumor necrosis factor (TNF) overexpression such as the $TNF^{\Delta ARE}$ mice.[10] Third, inducible models, such as topical imiquimod application[11] for inducing PsO-like inflammation, the minicircle-driven IL-23 overexpression mouse model,[5] and the β-glucan–induced arthritis in SKG mice[6] resembling PsA, offer the advantage of synchronized disease onset and reproducibility. Last, transplantation approaches, like the human skin xenograft model in severe combined immunodeficiency (SCID) mouse, have been used to study skin PsO and for PsO drug development.[12]

Animal models are essential for developing innovative technologies, not only for safety reasons but also because they offer the possibility for more in-depth analysis. For example, high-resolution imaging techniques like micro–positron emission tomography/computed tomography, which have become widely available in recent years, were first tested in animal models.[13] Animal models also remain crucial for drug development.[2,12]

Animal models have recently been used to advance the field, particularly in understanding environmental factors that may

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influence PsA. Risk factors for developing PsA include genetic factors and the PsO phenotype, such as severity of PsO lesions and involvement of nail or scalp, but environmental factors also have a substantial effect.[1] These environmental factors include mechanical loading of the joints and dietary intake, but they are rarely considered in clinical trials. This can be explained in part by the difficulty of gathering the necessary information from trial participants and categorizing these data appropriately, since not enough is known yet about which environmental factors to investigate. It is even harder to examine these factors in prospective studies since strict controlled circumstances would be necessary. As animal experiments are always performed in a well-controlled and stable environment, animal models are particularly useful for this type of research. Diet[14,15] and mechanical loading[16,17] have been studied in animals and can help optimize the design of future prospective trials in humans.

To conclude, the basic research workshop at the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) annual meeting and this summary report highlight that animal models remain of importance when studying PsD, particularly within 2 scenarios. First, animal models should be employed when complex interventions or analyses are required that are not feasible in human participants due to technical, safety, or economic reasons. Second, animal models can be important in exploratory research when studies in humans would be unsafe, such as when developing novel drugs or investigating environmental factors that are difficult to control in clinical studies.

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REFERENCES

1. Scher JU, Ogdie A, Merola JF, Ritchlin C. Preventing psoriatic arthritis: focusing on patients with psoriasis at increased risk of transition. Nat Rev Rheumatol 2019;15:153-66.
2. Lories RJ, Neerinckx B. Animal models of psoriasis and psoriatic arthritis. In: Adebajo A, Boehncke WH, Gladman DD, Mease P, editors. Psoriatic arthritis and psoriasis. Cham: Springer; 2016:103-9.
3. Neerinckx B, Van Mechelen M. Chapter 123. Animal models of spondyloarthritis. In: Hochberg MC, Gravallese EM, Smolen JS, van der Heijde D, Weinblatt ME, Weisman MH, editors. Rheumatology. 8th ed. Philadelphia: Elsevier; 2023:1056-60.
4. Hammer RE, Maika SD, Richardson JA, Tang JP, Taurog JD. Spontaneous inflammatory disease in transgenic rats expressing HLA-B27 and human beta 2m: an animal model of HLA-B27-associated human disorders. Cell 1990;63:1099-112.
5. Adamopoulos IE, Tessmer M, Chao CC, et al. IL-23 is critical for induction of arthritis, osteoclast formation, and maintenance of bone mass. J Immunol 2011;187:951-9.
6. Ruutu M, Thomas G, Steck R, et al. β-glucan triggers spondylarthritis and Crohn's disease-like ileitis in SKG mice. Arthritis Rheum 2012;64:2211-22.
7. Braem K, Carter S, Lories RJ. Spontaneous arthritis and ankylosis in male DBA/1 mice: further evidence for a role of behavioral factors in "stress-induced arthritis." Biol Proced Online 2012;14:10.
8. Gudjonsson JE, Johnston A, Dyson M, Valdimarsson H, Elder JT. Mouse models of psoriasis. J Invest Dermatol 2007;127:1292-308.
9. Matmati M, Jacques P, Maelfait J, et al. A20 (TNFAIP3) deficiency in myeloid cells triggers erosive polyarthritis resembling rheumatoid arthritis. Nat Genet 2011;43:908-12.
10. Kontoyiannis D, Pasparakis M, Pizarro TT, Cominelli F, Kollias G. Impaired on/off regulation of TNF biosynthesis in mice lacking TNF AU-rich elements: implications for joint and gut-associated immunopathologies. Immunity 1999;10:387-98.
11. van der Fits L, Mourits S, Voerman JSA, et al. Imiquimod-induced psoriasis-like skin inflammation in mice is mediated via the IL-23/IL-17 axis. J Immunol 2009;182:5836-45.
12. Kundu-Raychaudhuri S, Datta-Mitra A, Abria CJ, Peters J, Raychaudhuri SP. Severe combined immunodeficiency mouse-psoriatic human skin xenograft model: a modern tool connecting bench to bedside. Indian J Dermatol Venereol Leprol 2014;80:204-13.
13. Kundu-Raychaudhuri S, Mitra A, Datta-Mitra A, Chaudhari AJ, Raychaudhuri SP. In vivo quantification of mouse autoimmune arthritis by PET/CT. Int J Rheum Dis 2016;19:452-8.
14. Shi Z, Wu X, Yu S, et al. Short-term exposure to a western diet induces psoriasiform dermatitis by promoting accumulation of IL-17A-producing γδ T cells. J Invest Dermatol 2020;140:1815-23.
15. Shi Z, Wu X, Santos Rocha C, et al. Short-term western diet intake promotes IL-23-mediated skin and joint inflammation accompanied by changes to the gut microbiota in mice. J Invest Dermatol 2021;141:1780-91.
16. Van Mechelen M, Martens T, Vanden Berghe P, Lories R, Gulino GR. Impact of barrier tissue inflammation and physical activity on joint homeostasis in mice. Rheumatology 2022;61:1690-8.
17. Cambré I, Gaublomme D, Burssens A, et al. Mechanical strain determines the site-specific localization of inflammation and tissue damage in arthritis. Nat Commun 2018;9:4613.