The National Psoriasis Foundation (NPF) 2015 Research Symposium, held in San Francisco from July 23 to 25, began with a keynote address from Steven Katz, M.D., Ph.D., Director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) of the National Institutes of Health (NIH). In it, Dr. Katz discussed the agency’s approach to setting funding priorities for medical research, emphasizing the importance of bridging the gap from fundamental knowledge to the application of knowledge. For the next two days, seven scientific sessions put this vision into practice by exploring the many steps along the continuum of basic science and clinical care.

Scientists and clinician-researchers discussed major clinical and scientific developments in the psoriatic disease field. Emerging from these discussions was a new paradigm for research and treatment that builds upon associations and observations to produce novel insights into disease mechanisms and therapeutic targets. Seven scientific sessions comprised the meeting, with a poster session featuring more than 40 posters on the evening of July 24. The Symposium also provided the opportunity for early-career investigators to learn more about leveraging NPF funding into grants from the NIH and other agencies, with a question-and-answer session on July 24 featuring past NPF grantees who have won NIH funding, as well as Ricardo Cibotti, Ph.D., program director for the Immunobiology and Immune Diseases of Skin program at NIAMS.

Joining the approximately 100 basic scientists and clinician-researchers at the Symposium were psoriasis and psoriatic arthritis patients attending the concurrent NPF National Volunteer Conference (NVC). These patients had a visible and vocal role throughout the Symposium. Four scientific sessions began with an introduction delivered by a patient; patients conversed with researchers at the poster session; and the Symposium concluded with a Roundtable, hosted in conjunction with NVC, where patients and researchers sat together at tables designated for various topics, such as itch, comorbidities, or alternative treatments, sharing thoughts and asking questions of each other. Through their personal stories of living with these conditions, patients helped bridge the gap between the patient and provider perspective, and urged researchers to translate laboratory discoveries and clinical advances into successful patient outcomes.

The theme of advancing the field of psoriatic disease research from fundamental knowledge to clinical application was apparent in the first scientific session, and resurfaced in subsequent lectures throughout the event. The Symposium began with a call from Abrar
Qureshi, M.D., a dermatologist at Brown University and a member of the NPF Medical Board, to advance comorbidity research beyond the identification of associations among psoriasis, psoriatic arthritis, and other conditions. His lecture, "Fundamentals of Psoriatic Disease Comorbidities," was part of the opening session of the Research Symposium, titled "The Fundamentals of Psoriatic Disease — A Clinical Overview." Epidemiological and population-based studies have yielded an extensive list of comorbidities and risk factors for psoriatic disease, including cardiovascular disease, nonalcoholic fatty liver disease, and metabolic syndrome. Many important lessons about psoriatic disease have emerged through studying the associations between psoriatic disease and these comorbid conditions. Dr. Qureshi concluded his talk by challenging the audience to build upon key discoveries in comorbidity research by investigating the mechanisms and pathways that tie these diseases together.

Before Dr. Qureshi's talk, Mark Lebwohl, M.D., a dermatologist at the Icahn School of Medicine at Mount Sinai and chair emeritus of the NPF Medical Board, and Philip Mease, M.D., a rheumatologist at the University of Washington, provided an overview of the pathogenesis and treatment of psoriasis and psoriatic arthritis, respectively. Dr. Lebwohl started his talk by noting that in the past decade, there have been more new treatments introduced for psoriasis than for any other dermatologic disease. The growth and innovation in treatment modalities can be traced to the discovery that psoriasis was not a disease of the epidermis, but instead involved the immune system. He continued by recounting major discoveries regarding psoriasis pathogenesis. After researchers identified the role of the T cell in psoriasis, the role played by cytokines such as tumor necrosis factor-alpha (TNF-alpha), interleukin (IL)-23, and IL-17 also became apparent. Today, drugs targeting IL-23 that are in development are "as close to a cure as we have ever gotten," Dr. Lebwohl said. Yet the need remains for better treatments, including treatments for pediatric psoriasis and better topical therapies. The need for improved topicals was reiterated during the roundtable discussions among patients and doctors that concluded the Symposium.

Dr. Mease also discussed treatment options during his talk on psoriatic arthritis, noting that biologics targeting TNF-alpha worked well at inhibiting structural damage. He commented that secukinumab, a biologic targeting IL-17, and apremilast were useful treatments with good safety profiles. Psoriatic arthritis is a heterogeneous disease with many clinical manifestations, including enthesitis, dactylitis, spine disease, and nail changes. Treating skin and joint manifestations, as well as comorbidities, requires teamwork among the primary care physician, dermatologist, rheumatologist, and other specialists, Dr. Mease emphasized.

In a lecture delivered during the final Symposium session, Elaine Husni, M.D., a rheumatologist at Cleveland Clinic and a member of the NPF Medical Board, as well as co-chair of the Symposium, offered practical guidance on how to establish an interdisciplinary clinic to care for all aspects of psoriatic disease and comorbidities. According to several patients, this guidance is much-needed. During the roundtable, patients voiced the concern that while dermatologists and rheumatologists seemed largely aware of psoriatic disease comorbidities, specialists from other fields were not always alert to the connection between psoriatic disease and associated conditions. As one example of the importance of both identifying psoriatic arthritis early, and treating any comorbidities, Dr. Mease called attention to recent findings indicating that newly diagnosed psoriatic arthritis patients have an increased risk for cardiovascular disease.

Highlighting the significance of this particular comorbidity, the Symposium featured an entire session dedicated to cardiovascular disease. Titled "Bringing Research on Cardiovascular Comorbidities from Bench to Bedside," this session showcased the importance of translational research in understanding the mechanisms involved in psoriatic disease — in this case, the role played by inflammation in cardiovascular outcomes such as atherosclerosis, heart attack, and stroke. Pairing Nicole Ward, Ph.D., a researcher in the dermatology department at Case Western Reserve University, recipient of five NPF research grants, and Symposium co-chair, with Nehal Mehta, M.D., a cardiologist who studies cardiovascular disease in psoriasis and psoriatic arthritis at the NIH and a member of the NPF Medical Board, the session demonstrated bench-to-bedside collaboration in action.

Dr. Mehta opened the session with a case study of a patient who had mild, untreated psoriasis as well as
cardiometabolic disease. After reviewing research linking psoriasis, inflammation, and atherogenesis, Dr. Ward then delved into the biological mechanisms driving this connection. As a basic scientist, she said, she is able to study cause and effect using animal models in a way that is not possible in clinical research. By exploring the question of whether mice with psoriasis-like disease ever develop cardiovascular disease, she found that her mouse model of psoriasis — the KC-Tie2 mouse — developed spontaneous aortic root lesions containing immune cells.

From there, Drs. Mehta and Ward explored possible mechanistic pathways that could lead to cardiovascular disease in psoriasis patients. Dr. Mehta discussed his studies of vascular inflammation in people with psoriasis, and Dr. Ward discussed her work in mouse models. Dr. Ward presented her finding that KC-Tie2 mice are prothrombotic, but inhibiting IL-23 and IL-17, two cytokines involved in psoriasis, made clotting time revert back to the levels of control mice. Dr. Mehta shared information about ongoing trials investigating vascular inflammation in psoriasis, which will shed light on whether systemic treatment for psoriasis can decrease this inflammation and reduce cardiovascular risk.

The Symposium returned to the topic of mouse models the following day, when Brian Nickoloff, M.D., a senior medical fellow for Eli Lilly, presented a session titled “Challenges in Translational Psoriasis Research.” In his lecture, “Translating Insights from Animal Modeling to Dermatology,” Dr. Nickoloff focused on the role of mouse models in translational research, emphasizing the key insights that have been gleaned from working with the xenograft mouse model of psoriasis. Among these insights are the identification of psoriasis as an immunological disease, and the importance of T cells and cytokines in disease pathogenesis. However, Dr. Nickoloff also urged the audience to remain cognizant of the challenges of using animal models, particularly the differences between the murine and human immune systems.

Despite these challenges, many disease fields have gained significant insight from the use of animal models.1,2,3 Among these is the field of microbiology, whose intersections with psoriatic disease were the focus of a session titled “Hot Topics in Psoriatic Disease: The Microbiome.” As with many Symposium sessions, this session, which explored the role of microbiota in the immune response, underscored the importance of moving beyond association studies to better understand mechanisms at work in disease development. In this case, the associations were between particular microbial populations and psoriatic disease, and the mechanisms explored were the role that microbial dysbiosis may play in triggering psoriasis and psoriatic arthritis.

The session began with Shruti Naik, Ph.D., a cancer researcher at The Rockefeller University and winner of a 2015 NPF Discovery Grant. Her lecture, titled “Skin Microbiota in Health and Disease,” traced the mechanisms by which skin commensals led to the production of T cells. As Dr. Naik discussed, *Staphylococcus epidermidis* can protect against an infection from *Candida albicans*, because *S. epidermidis* engages the immune system by inducing production of CD8+ T cells. After sharing that finding, she continued, “How do you go from putting bacteria on the skin to making a T cell? There are a lot of steps in between.” Central to this process are dendritic cells. Dr. Naik explained, which control the dialogue between commensals and the cutaneous immune system, and specifically, control the capacity of T cells to produce IL-17 in response to bacterial challenges.

Following Dr. Naik’s overview of how microbiota interact with the immune system, Jose Scher, M.D., a rheumatologist at New York University, focused on the role of microbes in psoriatic arthritis with a lecture titled “The Microbiota and Psoriatic Arthritis.” His lecture shifted attention from the skin microbiome to the gut microbiome. One function of the gut microbiome is to shape the immune system. Studies in mouse models have shown that, in animals raised under germ-free conditions, introducing gut-residing segmented filamentous bacteria can trigger arthritis in an animal predisposed to the disease.5 His studies of the gut microbiome in people with psoriatic arthritis have found there to be decreased bacterial diversity, with some kinds of bacteria more prevalent than others.6 Studies also have shown that bacteria of the genus *Prevotella* are prevalent in new-onset rheumatoid arthritis patients.7 These taxonomic observations offer insights into the role of dysbiosis in triggering arthritis. However, he said, “We need to understand what these microbes are truly doing, rather than just looking at taxonomy.” Moving beyond taxonomy would require scientists...
to delve deeper into the functionality of microbes. Understanding the metabolic activity of bacteria is key to understanding their influence on the immune system, Dr. Scher noted. Future directions in the study of the microbiome and immune disorders could lead researchers to develop ways of manipulating the microbiome to study human disease, and possibly uncover therapeutic options based on the microbiome, he concluded.

The session ended with a lecture from Andrew Johnston, Ph.D., a researcher in the dermatology department at the University of Michigan and winner of a 2015 NPF Discovery Grant. Dr. Johnston’s lecture, titled “Psoriasis and the Tonsil Microbiome,” narrowed the focus of the session further to pinpoint the role of streptococcal bacteria in triggering guttate psoriasis. His research focus springs from the observation that many people experience onset of psoriasis, or a worsening of their psoriasis, following a streptococcal throat infection or tonsillitis. He presented research indicating that the tonsils of people with psoriasis have more lymph nodes, are more dense and active, and host more skin-homing T cells than the tonsils of patients who do not have psoriasis.

His lecture took up Dr. Scher’s challenge of investigating the functionality of microbes in immune disorders by proposing a role for tonsillitis in psoriasis. He suggested that streptococcal bacteria on the tonsils can drive skin-homing T cell responses. Upon entering the skin, they may move into the epidermis, where they activate more T cells and ultimately lead to psoriasis. The proposed model is plausible, but untested. Like Dr. Scher, Dr. Johnston emphasized the need to understand more functional information about bacteria, including the role of metabolites. His NPF-funded study analyzes the tonsil microbiome of people with psoriasis, investigating the various species represented. Perhaps even more important than identifying the species involved, he suggested, is understanding the role they play, particularly if different bacteria can play the same role in disease. During the roundtable, he noted that the idea had been raised that a biobank for microbes — a biome-bank — could be a useful research tool.

The previous day, a session on the topic of genetics and psoriatic disease also stressed the importance of moving past identification to better understand functionality. Frank Nestle, M.D., a dermatologist at King’s College in London, and Anne Bowcock, Ph.D., a professor of cancer genomics at Imperial College London, spoke about genetic risk factors for psoriatic disease, making the case that, beyond simply identifying risk factors, researchers must identify the role these factors play in immune function. In this way, genetic studies could lead to new approaches for treating psoriasis and psoriatic arthritis. Speaking at the roundtable, J.T. Elder, M.D., Ph.D., a dermatologist at the University of Michigan and past NPF grant recipient, commented that genetic studies needed to advance in a way that offer patients practical information, such as whether someone with psoriasis will develop psoriatic arthritis, or whether their children will develop psoriatic disease.

In his talk, titled “Psoriatic Disease from the Bench to Bedside,” Dr. Nestle discussed the genetic risk factors for psoriatic disease that have been discovered. Although more than 30 risk loci have been validated, they still only explain 22% of disease prevalence. Much remains to be discovered before the genetic contribution to psoriasis will be fully understood. One of the most pressing needs is investigating the immune traits associated with these risk factors. Dr. Nestle discussed the clinical potential of this research strategy. Once scientists understand the immune function of a particular locus, they can go back into the patient population to identify the immune phenotype associated with this gene. This, in turn, could lead to the development of new hypotheses about biomarkers, disease mechanisms, and treatment response.

Dr. Bowcock’s lecture, titled “Translating GWAS to Patient Care,” also emphasized the potential contribution of genetic studies to understanding disease pathogenesis. She presented her work on the CARD14 gene, which was the first gene to be identified that harbors rare mutations that can lead to psoriasis, as well as generalized pustular psoriasis, palmoplantar pustular psoriasis, and psoriatic arthritis. Dr. Bowcock stressed that even genetic factors that confer a small risk for psoriasis can be useful for the study of disease pathways. Once a genetic association points the way toward a certain disease pathway, other genes in this pathway also can be targeted, which can subsequently help identify new therapeutic targets.

Emerging therapies for psoriasis and psoriatic arthritis were reviewed in the session “Clinical Trials Outcomes — Designs of the Future.” Craig Leonardi,
M.D., associate clinical professor at St. Louis University Medical School, opened his lecture titled “The Future of Clinical Trials in Psoriasis” by noting that psoriasis treatment has changed dramatically in the past 15 years. He reviewed current and cutting-edge therapies, discussing their therapeutic targets and mechanisms of action, as well as the high efficacy rates of new biologics. He also offered guidance to clinicians on how to sort through these options to choose the best treatment for their patients and identified the Number Needed to Treat (NNT) as a useful rubric for doctors. Dr. Leonardi noted that ixekizumab and secukinumab have two of the lowest NNTs among biologic treatments for psoriasis.

Dr. Mease followed Dr. Leonardi with his second lecture of the Symposium, titled “The Future of Clinical Trials in Psoriatic Arthritis.” Turning the audience’s attention to the topic of outcomes measures, Dr. Mease reviewed the various means of establishing efficacy in clinical trials. Among these measures are joint activity, pain, physical function, skin activity, and health-related quality of life. Emphasizing the importance of including the patient perspective in devising outcomes measures, he discussed recent revisions that emerged from patient focus groups, such as the impact of disease on economic status and other quality-of-life issues.

As both Drs. Mease and Leonardi discussed, well-designed clinical trials for psoriasis and psoriatic arthritis provide a wealth of information on safety and effectiveness, as well as insights into how best to treat psoriatic disease and its associated comorbidities. The rise of “big data” analysis offers clinicians and researchers access to real-world data in addition to data from clinical trials. The final session of the Symposium, "Controversies and Challenges in Psoriatic Disease Clinical Care," featured two lectures on the use of big data in psoriatic disease research.

In his lecture, titled “Big Data in Psoriasis,” Jashin J. Wu, M.D., director of dermatology research at Kaiser Permanente Los Angeles Medical Center and a member of the NPF Medical Board, reviewed the types of data sets that can be used in clinical research. The examples he discussed included repurposed data, such as that taken from insurance claims, and clinical data that can be reanalyzed to answer different research questions, such as the Nurses’ Health Study I and II. Although conducting big data-driven clinical research can yield useful answers to clinical questions—such as Dr. Wu’s Kaiser Permanente study that found that treating psoriasis with TNF-alpha inhibitors can reduce myocardial infarction risk—it also comes with challenges. Aside from only being useful for retrospective studies, these data sets do not capture the use of alternative or over-the-counter treatments, and do not always account for disease severity. In addition, misclassified data, such as in prescribing off-label drug use, can affect the results.

Jeffrey Greenberg, M.D., chief scientific officer of Corrona LLC, next highlighted the value of registries, such as Corrona, to collect clinical data. Registries can provide more clinically rich insights than big data can, because they can include disease severity and outcomes data. He emphasized the distinction between epidemiological research, which he conducts through Corrona, and big data research, and also the ways in which data-driven research may differ from traditional scientific studies. Using big data may require a different methodology than traditional scientific research. Some researchers contend that big data doesn’t use the traditional scientific method because studies don’t necessarily have a hypothesis. However, supporters of big data maintain that big data searches for correlations, and therefore don’t require a hypothesis.

Moving from clinical research to clinical care and care delivery, the two other lectures in this session covered emerging treatment strategies and healthcare protocols in the world of psoriatic disease. April Armstrong, M.D., associate dean for clinical research at the University of Southern California Keck School of Medicine and a member of the NPF Medical Board, opened the session with a lecture titled “Using Telehealth to Treat Psoriasis.” According to a 2012 survey, only a small percentage of dermatologists who practice telehealth methods practice live, interactive dermatology.

Fueled by a sociodemographic changes, a growing demand on behalf of patients for “anytime/anywhere” health care, and physicians’ need for different work models, researchers have begun developing a telehealth model that involves the primary care physician. This collaborative connected health model, which Dr. Armstrong is studying through a Patient-Centered Outcomes Research Institute grant, enables patients or primary care providers to send
images to a dermatologist for analysis. Despite the many advantages to this model, challenges include technology limitations, workflow changes, and reimbursement issues.

The final lecture of the Symposium rounded out this session by approaching coordinated healthcare from a different perspective: that of the dermatologist and rheumatologist partnering in care for psoriatic disease patients. In an earlier session, Dr. Mease had underscored the need for collaboration between dermatologists and rheumatologists to treat psoriatic disease comprehensively. To conclude the Symposium, Dr. Husni delivered a lecture titled “Optimizing Interdisciplinary Care for the Complex Patient,” in which she shared her experiences establishing a multidisciplinary clinic treating psoriatic disease patients. Addressing how dermatologists can screen psoriasis patients for signs of psoriatic arthritis, and when to refer patients to a rheumatologist, Dr. Husni cited the usefulness of the Psoriasis Arthritis Screening and Education questionnaire, which covers symptoms such as joint pain, fatigue, and difficulty performing everyday activities.

By providing practical expertise to assist dermatologists and rheumatologists in caring for the whole psoriatic disease patient, Dr. Husni’s lecture exemplified the guiding principles of the Symposium, which brought together wide-ranging medical expertise to advance the state of research and care for psoriasis and psoriatic arthritis. Different clinical specialties, healthcare protocols, and scientific methodologies converged to build upon past milestones and generate insights into the pathogenesis and treatment of these diseases.

As the Symposium unfolded, many lectures heeded the call to delve deeper into the functional mechanisms driving psoriasis and psoriatic arthritis, whether those mechanisms involved clinical or basic science questions. Dr. Qureshi asserted the need for comorbidity research to move beyond association studies to investigate the biological pathways linking related conditions, while Drs. Bowcock and Nestle examined the potential of genetic studies to yield insights into immune functioning. Drs. Mehta and Ward demonstrated how translational and clinical research could come together to investigate the cause-and-effect involved in one particular comorbidity, cardiovascular disease, and Dr. Scher issued a call for microbiome studies to move beyond taxonomy into functionality, touching on the potential for more advanced functional studies to create new therapeutic possibilities.

The Symposium interwove the history of psoriatic disease research with the history of disease progression. Speakers built upon associations and observations to introduce a more advanced understanding of mechanistic pathways and therapeutic targets, at the same time highlighting the patient perspective through the stages of symptomology, diagnosis, and treatment. As we look ahead to the next NPF Research Symposium, to be held in 2017, these insights will help forge the future direction of NPF-funded research.

REFERENCES