8th Annual Vivian W. Pinn Symposium Meeting Summary: Synergy in Science: Innovations in Autoimmune Disease Research and Care

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National Institutes of Health
Office of Research on Women's Health

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Introduction and Welcome

(VideoCast timestamp 0:00 - 15:37)
Janine Austin Clayton, M.D., FARVO, Director of the Office of Research on Women's Health

The National Institutes of Health (NIH) has long prioritized autoimmune disease research, supporting more than 1,400 grants and administrative supplements related to autoimmune disease in Fiscal Years (FYs) 2021 and 2022, with funding reaching nearly $1 billion in FY21. In FY23, Congress directed NIH to establish the Office of Autoimmune Disease Research in the Office of Research on Women's Health (OADR-ORWH), allocating $10 million to identify emerging areas of innovation and research opportunity; coordinate development of a multi-institute and center strategic research plan; coordinate and foster collaborative research across institutes and centers; annually evaluate the NIH autoimmune disease research portfolio; and develop a publicly accessible central repository for autoimmune disease research. In its first year, OADR-ORWH funded and co-funded 41 awards. Funding included six EXposome in Autoimmune Disease Collaborating Teams PLANning Awards (EXACT-PLAN). The EXACT-PLAN Notice of Special Interest was developed by OADR-ORWH in partnership with the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the National Institute of Environmental Health Sciences (NIEHS), and NIH institute, center, and office partners. The initiative focuses on supporting the design, development, and implementation of a future national, interdisciplinary, collaborative, team science research network that will advance the study of the exposome in autoimmune disease.

Furthermore, NIH's commitment to fostering collaboration and innovation in autoimmune disease research is exemplified by initiatives such as the Team Science Leadership Scholars Program. This program, launched by ORWH in collaboration with National Institute of Arthritis and Musculoskeletal and Skin Diseases and the Office of Data Science Strategy, is embedded within the Accelerating Medicines Partnership® Autoimmune and Immune-Mediated Diseases (AMP® AIM) program. AMP® AIM provides the necessary structure and expanse to advance leadership and mentoring skills of promising researchers committed to working within a large network of stakeholders. This network includes experts in various research topics, including psoriasis, psoriatic arthritis, rheumatoid arthritis, Sjögren's disease, and systemic lupus erythematosus, as well as experts in the molecular analysis of tissue and other biological specimens, data analysis, biorepository, and data management.

ORWH also partnered with five ICs to create two Notices of Funding Opportunities (NOFOs), Understanding Chronic Conditions Understudied Among Women, categorized under the R01 and R21 grant mechanisms. The purpose of the NOFOs is to invite applications on chronic conditions understudied among women and/or that disproportionately affect populations of women who are understudied, underrepresented, and underreported in biomedical research. This initiative underscores NIH's dedication to addressing gaps in women's health research and ensuring that diverse populations are adequately represented in scientific studies.

On March 18, 2024, President Joe Biden signed a new Executive Order that builds upon the establishment of the White House Initiative on Women's Health Research. This Executive Order announced new actions to improve women's health research by prioritizing investments in women's health research; integrating women's health across the federal research portfolio; galvanizing new research on women's midlife health;

and assessing the unmet needs to support women's health research. Dr. Clayton and ORWH Deputy Director Vivian Ota Wang, Ph.D., were honored to attend the historic signing alongside NIH Director Monica Bertagnolli, M.D., and Deputy Director for Program Coordination, Planning, and Strategic Initiatives Tara A. Schwetz, Ph.D. In alignment with the White House Initiative on Women's Health Research, ORWH has issued a NIH-wide Women's Health Research Notice of Special Interest to highlight interest in receiving research applications focused on diseases and health conditions that predominantly affect women (e.g., autoimmune diseases, depressive disorders, Alzheimer's disease and Alzheimer's disease related dementias, gender-based violence); present and progress differently in women (e.g., cardiovascular disease, HIV, reproductive aging and its implications); or are female specific (e.g., uterine fibroids, endometriosis, menopause). Applications are due on June 20, 2024.

Dr. Clayton announced the release of the *NIH-Wide Strategic Plan for Research on the Health of Women 2024–2028*. The plan outlines strategic goals to guide and inform NIH-supported research on the health of women. ORWH employed a data-driven, iterative process to develop this strategic plan, while gathering information from many sources, contributors, and activities during the past several years. Various stakeholders, including representatives from institutes, centers, and offices, federal partners, and other community partners, actively contributed to the strategic plan's development and finalization.

Dr. Clayton acknowledged Vivian W. Pinn, M.D., for her numerous contributions, including the creation of NIH's first strategic plan for women's health research and the establishment of the Building Interdisciplinary Research Careers in Women's Health (BIRCWH) and Specialized Centers of Research Excellence (SCORE) on Sex Difference programs. Dr. Pinn has promoted policies and programs for the entry, recruitment, retention, and sustained advancement of women in biomedical and research careers. In recognition of these efforts, this symposium has been named in her honor.

Opening Keynote: Understanding the Immunome: Past, Present, and Future

(VideoCast timestamp 15:38 - 1:04:51)
Jane Buckner, M.D., President, Benaroya Research Institute, Affiliate Professor, Department of Medicine, Division of Rheumatology, University of Washington

Autoimmunity involves diseases where the immune system attacks healthy tissue. These diseases manifest differently but share common features. Examples of autoimmunity include conditions such as Hashimoto's disease, type 1 diabetes (T1D), psoriasis, and rheumatoid arthritis. Autoimmune diseases are chronic, debilitating, costly, and currently incurable, affecting approximately 50 million Americans. These conditions impact not only the patients but also their families and caregivers. Notably, women are disproportionally affected, and these diseases can occur at any age.

The immune system's role in autoimmunity involves T cells, which typically protect against viruses, bacteria, and cancers. In autoimmunity, T cells that react to self-antigens become activated, triggering the autoimmune response and promoting the production of autoantibodies and inflammation. Autoimmune diseases develop over time, starting with the presence of autoantibodies before symptoms or tissue inflammation occur. Genetic factors contribute to susceptibility, because autoimmune diseases often run in families, but environmental factors such as infections, injuries, lifestyle, and stress also play a significant role.

Research into autoimmunity focuses on understanding the factors that initiate and perpetuate these diseases. Current efforts include studying the immune features that differentiate affected individuals from those without autoimmunity and identifying mechanisms leading to these differences. Advancing the understanding of autoimmune diseases involves generating hypotheses through model systems, studying unique populations, and developing patient cohorts. These cohorts include control populations to ensure accurate comparisons. Identifying altered immunologic pathways in autoimmune diseases helps determine whether these features are shared across different autoimmune conditions and informs treatment strategies. Studying disease evolution in at-risk individuals and conducting in vivo interventions, such as clinical trials and specific drug studies, further aids in understanding and treating autoimmune diseases.

Genome-wide association studies conducted in the early 2000s identified numerous genes associated with autoimmunity, including hundreds of genes linked to T1D. Among these, *PTPN2*, a gene involved in the inhibition of interleukin-2 (IL-2) signaling, emerged as significant. IL-2 is essential for T cell growth and survival, particularly regulatory T cells (Tregs). Studies revealed that individuals with genetic variants of *PTPN2* exhibited impaired IL-2 responses, suggesting a link between these genetic factors and T1D. Further studies showed that T1D patients had a diminished ability to maintain Tregs, leading to a possible imbalance where effector T cells are not adequately regulated.

Exploring therapeutic approaches, researchers have attempted to increase Tregs in T1D patients by administering IL-2. Although this approach increased Treg numbers and normalized IL-2 response, the treatment did not improve beta cell function and occasionally worsened the patient's condition, highlighting the need for more targeted therapies. Another approach involved expanding Tregs in vitro and reintroducing these cells to patients. While safe, this method failed to improve beta cell function, suggesting that current strategies may not adequately address the complexity of autoimmune regulation. These findings underscore the challenges in treating autoimmune diseases, where simply boosting Tregs or IL-2 is insufficient.

The specificity of Tregs makes these cells unique compared to other therapeutic approaches. Tregs are designed to recognize healthy tissue and inhibit the action of effector cells against it. This specificity is mediated by a T cell receptor, which recognizes self-antigens and suppresses inflammation. Harnessing this specificity, researchers aimed to develop antigen-specific Tregs as a more targeted therapy for autoimmune diseases. However, several challenges emerged in this approach. Islet-specific T cells, for example, are rare in diabetes, complicating the isolation of a pure population of islet-specific Tregs. Additionally, Tregs can become effector cells, posing a risk if antigen-specific Tregs lose their regulatory function. Furthermore, T1D individuals exhibit reduced sensitivity to IL-2, potentially affecting the stability of engineered Tregs (EngTregs). To overcome these challenges, researchers turned to gene editing technologies such as CRISPR/Cas9. By genetically engineering conventional T cells to express a T cell receptor specific to islet antigens and inducing the expression of FOXP3, a key regulator of Treg stability and function, researchers created antigen-specific Tregs. These EngTregs demonstrated suppressive activity specifically against islet antigens, both directly and in bystander T cells. Moreover, this approach showed promise beyond T1D. By targeting other antigens implicated in autoimmune diseases such as rheumatoid arthritis, researchers expanded the potential applications of antigen-specific Tregs.

Despite these advances, certain limitations must be considered. The EngTregs approach relies on the patient's own cells (autologous therapy), rendering the treatment expensive and impractical for widespread use. Efforts are under way to develop off-the-shelf therapies to overcome this limitation. Other strategies, such as incorporating chimeric antigen receptors into Tregs, are also being explored to enhance the cells' therapeutic efficacy. The first clinical trials involving antigen-specific Tregs are under way, offering hope for more targeted and effective treatments for autoimmune diseases. Furthermore, understanding the timing of intervention is crucial. Studies have shown that impairments in IL-2 signaling occur early in the development of autoimmunity, suggesting that targeting IL-2 or Tregs may be most effective in the early stages of disease progression.

Notably, studying unique populations, such as individuals with Down syndrome, has provided valuable insights into immune dysregulation and autoimmunity. Individuals with Down syndrome have a significantly elevated risk of autoimmune diseases such as T1D, Hashimoto's disease, and celiac disease, with half this population experiencing one or more of these conditions by adulthood. To further investigate this susceptibility, researchers have established a cohort of individuals with Down syndrome spanning various age groups through the NIH INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromE (INCLUDE) project. By comparing the immune profiles of individuals with Down syndrome to age- and sex-matched controls and individuals with T1D, researchers have identified significant differences in T cell populations associated with autoimmunity. Specifically, individuals with Down syndrome exhibit marked increases in T cell populations implicated in autoimmunity. These findings suggest that Down syndrome may predispose individuals to autoimmunity through dysregulated immune responses. Moreover, research on immune aging has revealed intriguing parallels between Down syndrome and autoimmune diseases such as T1D. By comparing immune age between controls and individuals with Down syndrome, researchers have observed a significant acceleration of immune aging in the latter group, particularly among those with autoimmune conditions. This observation emphasizes the potential role of immune aging and inflammation in both Down syndrome and autoimmune diseases, paving the way for identifying therapeutic targets to prevent or treat autoimmune diseases not only in individuals with Down syndrome but also in the broader context of autoimmunity research.

Inside Innovation: Intramural Impact at the National Institutes of Health

Understanding the Genetics of Childhood-Onset Systemic Lupus Erythematosus in Global Populations

(VideoCast timestamp 1:04:52 - 1:20:38)

Laura Lewandowski, M.D., M.S., Head, Lupus Genomics and Global Health Disparities Unit, National Institute of Arthritis and Musculoskeletal and Skin Diseases

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that can affect any organ system and currently has no cure. SLE is a leading cause of death among young women in the United States. Childhood-onset lupus (cSLE), which accounts for about 20% of SLE cases, is particularly severe. cSLE exhibits higher disease activity, requires more intensive therapy, and results in serious complications such as brain and kidney inflammation, leading to greater organ damage compared to adult-onset SLE. The incidence of SLE shows a strong female predominance, which is less pronounced in prepubertal children but increases significantly during adolescence and adulthood.

Research into SLE in global populations, especially in less resourced areas such as sub-Saharan Africa and Southeast Asia, remains limited. The scarcity of pediatric rheumatologists in these regions hampers a comprehensive understanding of the global burden of cSLE. However, an important study conducted in South Africa established the largest registry of children with SLE in sub-Saharan Africa. This study revealed that children in the region suffer from more severe disease, greater organ damage, and higher mortality rates compared to their counterparts in North America.

Genetic studies of SLE have primarily focused on adult populations of European ancestry, resulting in significant disparities in understanding the genetic drivers of the disease in diverse populations. SLE has heritable components, as evidenced by high concordance rates in identical twins. Research has identified two main types of genetic variants associated with SLE: common variants with small effect sizes and rare variants with significant and often damaging effects. cSLE, which carries a higher genetic load, presents a valuable opportunity to study the genetic contributions to the disease in greater depth.

Research methodologies, including transmission disequilibrium analysis, have been used to identify both common and rare variants in cSLE patients and their unaffected parents. While initial studies did not yield statistically significant findings regarding common variants, numerous rare variants with potentially significant biological impacts were identified. Furthermore, pathway analysis has provided deeper insights into the mechanisms underlying SLE, uncovering both well-known pathways and novel ones.

Advancing the understanding of SLE requires inclusive studies involving large, diverse cohorts. Such research is crucial for transitioning from broad clinical phenotypes to precise molecular phenotypes, paving the way for better-targeted therapies and improved outcomes for SLE patients globally. Addressing the disparities in genomic research and ensuring sustained funding and infrastructure for global research are critical steps toward achieving this goal.

Anticytokine Autoantibodies: Who Knew?

(VideoCast timestamp 1:20:39 – 1:36:43)

Steven M. Holland, M.D., Director, Division of Intramural Research, National Institute of Allergy and Infectious Diseases

Around 140 years ago, Robert Koch's groundbreaking discovery of *Mycobacterium tuberculosis* marked a pivotal moment in disease understanding, prompting the formulation of Koch's postulates—a set of criteria to establish the causative relationship between a microorganism and a disease. Subsequent research confirmed *M. tuberculosis* as the causative agent of tuberculosis, laying the foundation for studying disease mechanisms. Despite *M. tuberculosis* being the most virulent strain of mycobacteria, approximately 150 other strains of mycobacteria exist, with many not inducing such severe disease.

The emergence of the HIV epidemic in the 1980s shed light on mycobacterial dissemination, particularly in immunocompromised individuals, highlighting the critical role of immune function in combating mycobacterial infections. Consequently, research expanded beyond HIV-infected individuals to investigate disseminated

mycobacterial diseases, leading to a focus on nontuberculous mycobacteria (NTM). Although NTM are commonly present in the environment and typically pose no threat to healthy individuals, certain populations, such as those with compromised immune systems or underlying lung conditions, are more susceptible to NTM-related diseases. NTM infections can manifest as skin and pulmonary conditions. However, disseminated NTM disease poses a particularly severe threat because it affects multiple organs and systems. This form of the disease is primarily observed in children with conditions such as Mendelian susceptibility to mycobacterial disease, a rare genetic disorder that impairs the body's ability to effectively combat mycobacterial infections.

NTM disease is intricately linked to a cellular pathway involving macrophages, IL-12, IL-23, and interferon-gamma (IFN-γ), which are crucial for effectively eradicating intracellular mycobacterial pathogens. Studies have unveiled a distinct syndrome prevalent among Southeast Asian immigrants, marked by disseminated NTM disease alongside widespread opportunistic infections. This syndrome, which disproportionately affects women, is often accompanied by symptoms such as weight loss, fevers, and skin lesions indicative of bone infections. Notably, specific human leukocyte antigen alleles overrepresented in Southeast Asians have been associated with this syndrome, suggesting an autoimmune etiology. Further investigation has revealed cross-reactivity between IFN-γ and *Aspergillus* antigens, providing insight into the syndrome's underlying mechanisms. This observation suggests that exposure to the fungus *Aspergillus* may trigger an autoimmune response in individuals with certain genetic predispositions, leading to the onset of NTM disease and associated symptoms. Treatment strategies for this syndrome have progressed significantly, with rituximab emerging as a promising therapy aimed at targeting B cells that produce autoantibodies. Despite such advances, questions remain regarding the syndrome's prevalence among Southeast Asian immigrants and its notable gender disparity. This syndrome serves as a valuable model for understanding the intricate interplay between genetics, environmental influences, and gender in autoimmune diseases characterized by multiple opportunistic infections.

Genetic and Environmental Risk Factors of Autoimmune Diseases

(VideoCast timestamp 1:36:44 – 1:49:55)

Alison Motsinger-Reif, Ph.D., Chief, Biostatistics and Computational Biology Branch, Principal Investigator, National Institute of Environmental Health Sciences

The Personalized Environment and Genes Study (PEGS), sponsored by NIEHS, is a North Carolina–based cohort aimed at investigating the interplay between environmental factors and health outcomes. Initiated in 2002, the cohort comprises nearly 20,000 individuals, with comprehensive health and exposure data available for almost half of the cohort. The demographic makeup of PEGS reflects diversity across various socio-economic and cultural parameters.

From 2013 to 2020, three surveys were used to collect phenotype and exposure data in the cohort. The PEGS Health and Exposure Survey collected data on general demographics, family medical history, information on lifestyle factors such as smoking and alcohol use, and data on occupational exposures. The NIEHS PEGS Exposome Survey was administered to collect comprehensive information about endogenous and exogenous exposures throughout life. Part A focused on external exposures, including chemical and environmental exposures at work and home from childhood to the present. Part B included questions about internal exposures, including medications, and lifestyle factors such as physical activity, stress, sleep, and diet. In

addition to the survey-based exposure data, address histories, including longest-lived childhood address, were collected. These addresses have been used to link participants with a growing list of geospatial exposure estimates, including air pollution and distance to toxic release and agricultural operation sites.

Participants with extensive exposure data underwent whole genome sequencing to enable comprehensive genetic studies. Whole genome sequencing offers insights into various genetic variants, including single nucleotide variants, copy number variations, structural variants, telomere length, and high-resolution human leukocyte antigen complex variation. An exposome-wide association study, similar to genome-wide association studies, was conducted to explore associations between the genome and relevant phenotypes. This method utilized logistic regression while adjusting for covariates such as sex, race, body mass index, and age. Results revealed numerous associations between exposures and autoimmune diseases, with notable findings related to smoking, occupational exposures, lifestyle factors, and psychological aspects.

The findings from the exposome-wide association study analysis are accessible through the PEGS Explorer, a web tool designed to disseminate and visualize complex correlations among exposures. The PEGS Explorer empowers researchers to explore associations between exposures and disease outcomes, facilitating a deeper understanding of these relationships. This development marks a significant stride toward personalized health care interventions and informed public health policies.

Fireside Chat: Turning Hope into Action – Empowering Communities to Advance Science

(VideoCast timestamp 1:25:37 – 2:35:08)

David Fajgenbaum, M.D., M.B.A., M.Sc., Co-Founder and President, Every Cure Director, Center for Cytokine Storm Treatment & Laboratory at the University of Pennsylvania, Castleman Disease Collaborative Network; and Victoria Shanmugam, MBBS, MRCP, FACR, CCD, Director, Office of Autoimmune Disease Research in the Office of Research on Women's Health

Dr. Shanmugam introduced Dr. Fajgenbaum, the founding director of the Center for Cytokine Storm Treatment and Laboratory (CSTL) and co-founder of the Castleman Disease Collaborative Network (CDCN). Through the discussion, Dr. Fajgenbaum chronicled his journey as both a physician and patient battling idiopathic multicentric Castleman disease (iMCD). Currently experiencing his longest remission period of 10 years, Dr. Fajgenbaum credits a precision treatment he identified, previously unused for iMCD, for this milestone. In addition to this groundbreaking discovery, he has advanced 15 other treatment approaches for iMCD and cancer.

Dr. Fajgenbaum recounted his journey from being a healthy college athlete to experiencing severe illness that led to multiple hospitalizations and eventually a stay in the intensive care unit. After advocating for a lymph node biopsy, he received the distressing diagnosis of iMCD. Despite initial treatments with rituximab and tocilizumab (IL-6 blockade), he experienced several relapses and required a combination of chemotherapies. During this challenging period, Dr. Fajgenbaum realized that hope alone was insufficient and decided to take decisive action. He began profiling his own and other patients' immune systems to identify existing drugs that could be repurposed for treating iMCD. This proactive approach was driven by the lack of novel targets and the impracticality of developing a new drug.

During his time as a medical student, Dr. Fajgenbaum devised a strategy to advance research of iMCD. He engaged patients, physicians, and researchers to identify key research questions, and then recruited experts to address these questions. This collaborative effort led to the formation of a community dedicated to prioritizing research needs and pooling resources. Through direct collaboration with patients, Dr. Fajgenbaum spearheaded the establishment of a central institutional review board, streamlining the global collection of samples and overcoming the limitations of individual research centers. This innovative approach not only facilitated the acquisition of ample patient samples but also fostered an environment conducive to significant breakthroughs, which would have been challenging within isolated centers.

Dr. Fajgenbaum's previous experiences played a crucial role in his efforts to advance iMCD research. The death of his mother during his undergraduate years inspired him to pursue a career in medicine and medical research. This tragedy also led him to establish Actively Moving Forward, a nonprofit supporting grieving college students on more than 200 campuses. The skills and insights he gained from building Actively Moving Forward, such as community organization and addressing systemic issues, were instrumental in galvanizing the iMCD community and advancing research.

Dr. Fajgenbaum's academic background further equipped him to tackle the challenges in rare disease research. After completing his medical studies, he pursued a master of business administration degree, which provided him with a robust framework for analyzing and addressing complex problems. His expertise in organizational management, strategic planning, and resource allocation proved invaluable in transforming research on iMCD and other rare diseases. He also credited his success to the incredible team he built around him, which included classmates from various disciplines. Their collective expertise helped create a unified strategy to advance the science of iMCD. Through this collaborative approach, Dr. Fajgenbaum was able to leverage diverse skills and perspectives, driving significant progress in the field.

Dr. Fajgenbaum recently co-founded Every Cure, a nonprofit organization aimed at maximizing the therapeutic potential of Food and Drug Administration (FDA)-approved drugs across various diseases. His innovative approach to medical research includes harnessing artificial intelligence (AI) for drug repurposing. Recognizing that many existing FDA-approved drugs have the potential to treat diseases beyond their original indications, Dr. Fajgenbaum is using AI and machine learning algorithms to analyze large data sets and identify potential drug-disease matches. By evaluating the strength of evidence for each match, Every Cure prioritizes drugs for further research, regardless of their potential profitability. This approach aims to ensure that patients can benefit from existing medications that might otherwise go underutilized.

Notably, Every Cure recently received a grant from the Advanced Research Projects Agency for Health (ARPA-H) to develop an AI platform aimed at revolutionizing drug repurposing. This platform leverages global biomedical knowledge to evaluate every drug against every disease, refining existing data into a comprehensive tool. Initially, the platform will focus on FDA-approved drugs and those included in established guidelines, with research-grade scores for other drugs to follow. This initiative seeks to democratize access to crucial medical information and address gaps in biomedical knowledge, particularly those affecting women and underrepresented populations. Additionally, Every Cure is assembling a medical team to identify and conduct clinical trials on promising drug-disease combinations, even in the absence of pharmaceutical company incentives. By integrating feedback from clinicians and researchers, the organization aims to

enhance the accuracy and applicability of the AI platform, ultimately guiding more effective clinical trials and treatments.

Dr. Fajgenbuam closed with a number of publications where the audience can find out more about his work, including through various articles in the popular press and in his book *Chasing My Cure: A Doctor's Race to Turn Hope into Action*.

Closing Capstone: Making a Difference

(VideoCast timestamp 2:35:08 - 3:26:35)

Gail Kerr, M.D., FRCP (Edin), FACR, MACR, Professor of Medicine, Chief, Division of Rheumatology, Washington, D.C. Veterans Affairs Medical Center; MedStar Georgetown University Hospital; Howard University Hospital

Dr. Kerr's 28-year tenure at the Department of Veterans Affairs (VA) provided her with opportunities to serve a large veteran population, in which arthritis is notably prevalent, especially among females. She led initiatives to gather rheumatologists and improve patient care, culminating in the formation of the VA Rheumatology Consortium in 2001. This consortium fostered collaboration and various advances, including the creation of chronic disease registries such as the VA Rheumatoid Arthritis Registry, a national biologic repository and longitudinal clinical database that serves as a resource for VA research with the long-term objective of improving the lives of U.S. veterans with rheumatoid arthritis.

At Howard University, Dr. Kerr's research team developed a new registry called the Ethnic Minority Rheumatoid Arthritis Consortium (EMRAC) to address the lack of representation of ethnic minorities in existing registry databases. With eight participating centers, EMRAC aimed to include predominantly ethnic minority patients, collecting clinical data without serum samples. The registry amassed 1,500 patients, with a diverse demographic makeup including 40% White, 30% Black or African American, 13% Hispanic and Latino, and 10% Asian, providing valuable insights into rheumatoid arthritis demographics. Findings from EMRAC highlighted disparities in disease severity, progression, and treatment outcomes among different ethnic groups, emphasizing the need for tailored interventions. Two key interventions emerged: a web-based program for earlier referral from community clinics and patient education on the importance of treatment adherence. These interventions led to improved access to care, medication adherence, and disease management outcomes. Additionally, research explored disparities in biologic therapy utilization, revealing system-level discrepancies rather than racial disparities alone. Further analysis suggested modifications to cost-sharing practices to improve access for vulnerable populations. Such modifications hold the potential to mitigate disparities and promote a more inclusive and equitable environment within rheumatology.

Dr. Kerr's involvement with the Academy for Workforce Advancement to Enrich Rheumatology Diversity (AWARD) Program underscores her commitment to addressing disparities in the rheumatology workforce. Sponsored by the Arthritis Foundation, AWARD aims to increase diversity in rheumatology and tackle historical and ongoing disparities by fostering community, coordinating national efforts, and developing specific strategies for rheumatology. The academy will offer mentorship and sponsorship opportunities, along with a curriculum focusing on racial and social justice. Trainee leadership-building activities will also be a key component, empowering participants to become advocates for diversity and inclusion in the field. In its

second phase, the program aims to recruit, retain, and advance rheumatologists from historically underrepresented communities, further enhancing diversity within the specialty.

Despite commendable efforts and initiatives such as AWARD, significant challenges persist within the field of rheumatology. Chief among these challenges is the ongoing shortage of rheumatologists, a pressing issue that disproportionately affects both rural and urban areas, leaving many patients without access to specialized care. Moreover, the field continues to grapple with alarmingly high attrition rates, particularly among female rheumatologists, who often find themselves forced to navigate formidable work-life balance challenges. The persistence of compensation disparities further exacerbates these challenges, with women consistently earning significantly less than their male counterparts across various specialties, including rheumatology. This persistent pay gap not only undermines the financial well-being of female rheumatologists but also poses a significant threat to their career longevity and retirement savings.

Furthermore, within academic settings, women remain grossly underrepresented in senior roles, leadership positions, and research authorship, a stark manifestation of systemic inequities deeply entrenched within the field. Addressing these disparities demands a concerted effort that extends beyond mere acknowledgment; this effort necessitates the implementation of tangible metrics for analysis and the revision of organizational policies to foster a culture of equity and inclusion within rheumatology and academia at large. Such proactive measures can dismantle the barriers that impede the full realization of its potential as a diverse, inclusive, and equitable discipline committed to advancing the well-being of all patients with rheumatic diseases.

Concluding Remarks

(VideoCast timestamp 3:26:36 - 3:36:43)

Vivian W. Pinn, M.D., Director (Retired), Office of Research on Women's Health

Autoimmune diseases have been a priority for ORWH since its establishment because of the profound impact these diseases have on women's health. Over time, considerable strides have been made, particularly in uncovering the genetic underpinnings of these conditions and elucidating the factors contributing to sex-based differences in their prevalence. This symposium served as a platform to showcase the latest breakthroughs in this field. Dr. Buckner provided a compelling synthesis of the genetic landscape of autoimmune diseases, marking a significant evolution in our understanding since ORWH's inception.
The establishment of OADR within ORWH was the culmination of collaborative efforts uniting researchers, health care practitioners, and advocates. This initiative arose from appeals within the advocacy community to prioritize autoimmune conditions, acknowledging the pressing need for dedicated research and focused attention, particularly given their disproportionate impact on women. Through the collective endeavor of OADR-ORWH, a unified effort is under way to advance understanding, diagnosis, and treatment, ensuring that the necessary attention and resources are directed toward women's health.

Dr. Fajgenbaum's remarkable journey, from patient to leading researcher, highlights the profound impact of personal experiences on scientific advancement. Moreover, ORWH's commitment to interdisciplinary collaboration, exemplified by initiatives such as BIRCWH and SCORE, underscores the essential role of synergy in driving scientific progress forward. Dr. Kerr's comprehensive approach, integrating clinical practice, research validation, and initiatives for workforce diversity, serves as a prime example of this collaborative ethos in action.

Dr. Pinn extended congratulations to Drs. Clayton and Shanmugam, alongside the ORWH team, for orchestrating yet another impactful symposium, expressing her honor and delight in being associated with such a remarkable event. This symposium not only highlighted the latest breakthroughs but also showcased the ongoing commitment to addressing autoimmune diseases and promoting women's health through collaborative efforts spearheaded by ORWH and its partners.