

## Preface: James N. Miller: A Journey Fighting Infectious Diseases

This special issue is dedicated to honoring the distinguished professor James N. Miller on the recent celebration of his 90th birthday. The contents of the issue are the result of the contributions of various authors, who have either trained or collaborated with James in his pioneering research on syphilis and Lyme diseases. These contributors represent only a fraction of the large number of Ph.D. trainees, postdoctoral fellows, and national and international collaborators who have been involved with James Miller's research. It is an honor for me as the editor to develop this special issue in recognition of his myriad achievements and breakthroughs throughout the years.

We include four tributes dedicated to James Miller. In the tribute *Dr. Miller: Virtuoso of All Spirochetes*, author Jarlath Nally (United States Department of Agriculture) states that on his list of respected individuals that he keeps to remind himself of their contributions, James, with whom he trained at the University of California at Los Angeles (UCLA), is at the top. Nyles W. Charon's (West Virginia University) *University of California at Los Angeles and James Miller: A Powerhouse* states that James's method of training had a golden touch and that his trainees have moved to academic institutions to become leaders in the field of spirochetes to date. Dr. Charon labels James as a great mentor. In Linda K. Bockenstedt's (Yale School of Medicine) *A Tribute to James N. Miller*, she explains that in his role as a successful research scientist, James had the ability to reinvent his research every ten years and made significant breakthroughs with his fellows and collaborators. Interestingly, Dr. Bockenstedt lists by decade the major contributions made by James, beginning in 1955. She also indicates that as an avid educator, James has benefited more than one generation of scientists, who have followed his path in the areas of syphilis and Lyme disease. Benjamin Bonavida's (UCLA) *A Tribute to James N. Miller: Colleague–Friend–Mentor* describes how the author met James in the 1970s, when he was recruited to

be an assistant professor in the same department as James. Dr. Bonavida states how James has been his mentor throughout his academic career. Both remain close friends and continue to exchange ideas on both research and research-unrelated activities.

Eight chapter reviews are also included in this issue. David A. Haake's (UCLA) *The Miller Hypothesis* describes how James Miller pioneered the identification of pathogenic proteins via their antigenicity, by triggering a specific immune response to each protein, a concept that Dr. Haake refers to as "The Miller Hypothesis." This initial work resulted in the discovery of several leptospiral proteins. Dr. Haake trained with James and continues in his research on the identification of several pathogenic leptospiral proteins. In Caroline E. Cameron's (University of Victoria, British Columbia, Canada) *A Journey Through Time: The Foundational Studies of Dr. James N. Miller and Their Influence on Current-Day Syphilis Research*, the author offers a historical description of James's numerous breakthrough achievements as he established the foundation of syphilis knowledge. James had the insight and vision to research fundamental questions using careful and novel applications. Dr. Cameron, who does not know James personally, indicates that she is highly grateful for the significant influence that James has had on her career. Dr. Šmajš and associates (Masaryk University, Czech Republic) wrote *Why Are There Two Genetically Distinct Syphilis-Causing Strains?* Regarding syphilis, these authors describe one group of strains that is related to the reference strain TPA-Nichols (Nichols-like strains) and a second group, the TPA SS14 strain (SS14-like strains). They question the existence of these two strains and ask why there has not been isolated strains with intermediate sequences between these two groups. They discuss possible reasons and the isolation of each of these two strains in different geographic locations, although it remains unknown as to the reasons for diversification of the two strains and the predominance of the SS14-light strains in the human population. In Troy

Bankhead's (Washington State University) *Role of the VlsE Lipoprotein in Immune Avoidance by the Lyme Disease Spirochete* *Borrelia burgdorferi*, the author discusses the pathogenesis of the pathogenic bacterial agent of Lyme disease, *B. burgdorferi*, as it can evade the immune response. The discussion is centered on the role of VlsE lipoprotein-mediated immune avoidance in *B. burgdorferi*, although the author is careful to show that there remains no direct proof that this phenomenon occurs. A thorough discussion is presented, including the implications of developing a vaccine overriding the protective effects of VlsE. In D. Scott Samuels and Leah R.N. Samuels's (University of Montana) *Gene Regulation during the Enzootic Cycle of the Lyme Disease Spirochete*, these authors discuss the spirochete *B. burgdorferi*, which causes Lyme disease, in its use of three different gene systems, namely, the expression of genes that regulate transmission from the tick to the vertebrate, regulate survival in the midgut of the tick, and become repressed in the transition between tick and vertebrate. Steven E. Schutzer and P.K. Coyle's (Stony Brook University) *Immune Complex Analysis in Active Lyme Disease* describes the various assays used to detect active infection and discuss some of the shortcomings of several assays. They believe that the preferred assay of antibody complexes is a better indicator of active infection and present supportive data. Drs. Schutzer and Coyle suggest that a battery of platforms, both serological and molecular, may be needed to definitively detect active infection. Stewart Sell's (Albany College of Pharmacy and University of New York at Albany) *Immunopathology of Experimental Models of Syphilis, Influenza, and Asthma* reviews the underlying immunological mechanisms for experimental models of syphilis, influenza, and asthma. Dr. Sell is grateful for James Miller's work on syphilis and the fact that two of the collaborators in his laboratory had trained in James Miller's lab. A general discussion regarding the role of the immune system and its relationship in syphilis, influenza, and asthma is presented. Rebecca A. Porritt and Timothy R. Crother (Cedars-Sinai Medical Center, Los Angeles) coauthored *Chlamydia pneumoniae Infection and Inflammatory Diseases*, in which they discuss the pathogenic role of the intra-

cellular bacteria *Chlamydia pneumoniae* and its part in various pathologies. Emphasis is placed on the role of *C. pneumoniae* in chronic inflammatory diseases. In addition, the authors discuss the indefinitely established role and correlation on a causal relationship between *C. pneumoniae* infection and various diseases; primarily, atherosclerosis, asthma, cancer, arthritis, neurological diseases, and other inflammatory diseases. The authors show how further studies are clearly needed to better understand *C. pneumoniae* infection in diseases and the possible interventions for reducing or eliminating its involvement. Lao and Bonavida chapter "Gonorrhea: Immune Escaper and Immunotherapeutic Strategies" reviews, briefly, the immune suppression induced by the microorganism and the failure to develop an effective vaccine. It is also discussed the similarities between the various mechanisms of the immune resistance of cancer and the immune resistance by gonorrhea. There have been recently several novel immune therapeutic strategies that have been developed to overcome resistance in several cancers. Clearly, such strategies may be replicated for gonorrhea.

The contents of these articles provide a brief survey via several reviews that discuss the general knowledge in the field of spirochetes. They show how published reports by James Miller have resulted in significant advances in research in the field of spirochetes. They are only a sample of James's contributions and the impact that he has made to the field overall.

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