Biologic response modifiers (BRMs) are often discussed with a narrow focus on the “biological therapies,” ie, the pharmacologically administered form of cytokines, eg, interferon or antagonists of cytokines, eg, tumor necrosis factor blocking agents. In conceptualizing this issue of Infectious Diseases Clinics of North America, my focus was first and foremost, to make available to the readers a reference with up-to-date information on the endogenously produced BRM and their role in disease pathogenesis as well as in host defense, both of which determine the outcomes. These have been covered very well Khardori; Masihi and Schäfer; Mullangi and colleagues; and Sundareshan and colleagues. The second focus was on broadening the definition of BRMs particularly from the infectious diseases point of view. Historically, vaccination and administration of “anti-sera” raised in animals were the first and second attempts at modifying the interaction with microbial agents by augmenting the natural defenses. Speil and Rzepka discusses the role of vaccines and vaccine adjuvants not only in infectious diseases but more recently also in cancers and autoimmune disorders. Hsu and Safdar takes the readers from the early (pre-antibiotic) days of antitoxin sera raised in animals injected with the toxin to the current uses of polyclonal and hyperimmune globulins in the prevention and management of infectious diseases. This is followed by the discussion on the use of monoclonal antibodies in infectious diseases. In addition, Jan ter Meulen has provided extremely useful information on the pipeline of these agents for clinical use as of 2011.

The third focus was on detailing the use of BRM therapies in infectious disease as Vivek Kak discusses the failures of various immunologic biological response modifiers in sepsis and the modest if any improvement in outcome by the only clinically available agent, ie, recombinant activated protein C. Although this therapeutic agent provides triple intervention in the form of profibrinolytic, anticoagulant, and anti-inflammatory actions, the stage at which it is currently given is perhaps the stage of “no return”. Rosenblum and colleagues highlights the complex interactions between infections, vaccines, vaccine adjuvants, and syndromes of unclear etiology. The last two articles discuss the fourth and the final focus, which is the fact that therapeutic BRMs are a two-edged sword. Their use involves evaluation of risk-benefit ratio and pre- and posttherapy preventive measures.
It seems every day more and more BRMs are being identified. The complexity and diversity of their interactions with the host continue to unravel. The following quote describes it all “I suspect that the host is caught up in mistaken, inappropriate and unquestionably self destructive mechanisms by the very multiplicity of defenses available to him, defenses which do not seem to have been designed to operate in net coordination with each other. The end result is not defense, it is an agitated ‘committee directed, harum-scarum effort to make war’” (Louis Thomas, *The Immunopathology of Infection*, 1971). However, as in life in general, it seems most of the real work is done outside the “committees,” which explains the success stories outnumbering adverse outcomes in infectious diseases. Human ingenuity made it possible that the prevention and management of infectious diseases contributed the most to the current state of human health and longevity.

It is obvious that this issue was made possible and of the highest quality because of the contributions made by the authors. However, I owe special thanks to Mrs Nancy Mutzbauer for the assistance she provided me in bringing this issue of *Infectious Disease Clinics of North America* to fruition.

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