Preface

In early summer 2011, the medical community lost one of its best physician-scientists, Dr. Stephen F. Lowry. As luck would have it, it was the same day the author of this note was presenting a joint paper at an international conference. His loss was insurmountable in many ways. Dr. Lowry was an outstanding surgeon, a preeminent scientist, a great educator, and an inspiring administrator. His many prestigious appointments and accolades testify to this and are eloquently summarized in this volume by Dr. Lowry's long-time scientific collaborator Dr. S. E. Calvano.

Dr. Lowry had a true passion to mentor young(er) physicians and scientists. For those of us who had the good fortune to know and be mentored by him, it had come almost as a shock to see a world-renowned, highly decorated scientist actually spending meaningful time with junior faculty, and their students, providing ample guidance and assistance, driven exclusively by a genuine interest to help them without expecting anything in return. The honesty of his interest in others and his willingness to help, advise, and encourage was a breath of fresh air and an astounding departure from what is

often the norm. It was an almost surreal experience in this day of tremendous competition and pressure. His door was always open, and his unbelievably busy calendar would always find an opening for a short meeting to discuss an idea, a scientific career, or a personal concern, even if for him that meant being late for a meeting with the Dean. His immediate response to an e-mail request, no matter how insignificant it may have appeared to someone else, was astonishing and reassuring. Dr. Lowry had a deep and fundamental respect for everyone regardless of their stature, position, seniority, background, or perceived importance. Maybe Dr. Lowry himself best expressed his philosophy when saying, "… while virtually every patient encounter has been rewarding, each in its own way, my greatest joy has been to be a part of the career development of many internationally renowned physician/scientists. The opportunity to mentor the next generation of these patient-oriented investigators is both a privilege and an honor!"

Dr. Lowry's most recent scientific interests explored the possibility of developing a systems biology approach to the analysis of *in vivo* responses to

sepsis and systemic inflammation. Our hope with this volume is to discuss a compendium of approaches that are aligned with Dr. Lowry's vision that a systems-wide perspective would be needed for assessing patient risk and response to therapy. We are fortunate to have complied a number of outstanding contributions that span a wide range of topics related to inflammation. These vary from bioinformatics analysis to bedside monitoring, from animal to patient models, and from equation-to agent-based approaches.

Calvano opens this volume with a brief account of Dr. Lowry's contributions. Sunderram and Androulakis discuss why and how systems biology approaches would help elucidate the mechanistic underpinnings of the links between chronic intermittent hypoxia, resulting from obstructive sleep apnea, and the development of hypertension. Tsoka et al. discuss a number of computational and scientific approaches for evaluating immune-level responses to melanoma facilitating the identification of biomarkers and elucidating immunological pathways that could serve as potential therapeutic targets.

Lon et al. illustrate the current state of the art in modeling drug effects in the treatment of inflammation, demonstrating how such a continuum of models would enable better drug assessment, and, eventually, translation of drug properties from *in vitro* and animal observations to patients. Scheff et el. discuss the implications of the physiologic variability in the context of controlling the inflammatory response through the analysis of an *in silico* model of human endotoxemia. This work summarizes to a great extent the systems biology of inflammation work that defined an axis of Dr. Lowry's interest during the recent years.

An and Christley discuss how agent-based modeling has been used in the study of inflam-mation, emphasizing its ability to encompass multiple scales of biological process as well as spatial considerations, coupled with an intuitive modeling paradigm, suggesting that this modeling framework is well suited for addressing the translational dilemma and to augment the generation and evaluation of knowledge by the biomedical research community at large. An et al. explore the need for a mechanistic understanding that links the clinical phenomenon of physiologic variability with the underlying patterns of the biology of inflammation, asserting that this can be facilitated through the use of dynamic mathematical and computational modeling integrating cellular biology, physiology, control theory, and systems engineering across biological scales. Finally, Jopling and Buchman provide a review of the history of sepsis science and treatment from an engineering perspective, through the eyes of a surgeon, in order to advance our understanding and illuminate strategies that might mitigate the clinical condition.

We sincerely hope that this collection of review papers will highlight the importance of Dr. Lowry's most recent passion, namely, the challenges and opportunities for modeling and interpreting the complex biology of severe injury and inflammation.

This volume is but a small token of respect and appreciation to, above all, a great mentor who is already, and will always be, sorely missed. His advice to "do the right thing" should become our guiding principle.

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