## Bridging the gap



Translational medicine has been described as a "two-way street" between bench and bedside. Experimental findings and models in

the basic laboratory can help to steer clinicians to increase the efficiency by which we use new therapeutic strategies in humans. Of equal importance is the feedback from clinicians to researchers on the effects of these treatments and potential for new pathways based on clinical observation, sometimes in other disease states. This feedback loop has been critical in the field of pulmonary vascular disease, as we have shifted focus over the past decades from finding the perfect "selective" pulmonary vasodilator to investigating therapies with anti-

proliferative and anti-inflammatory properties. Clinicians frequently use the term "remodeling" of the pulmonary vascular bed, but without the ability to safely and routinely perform lung biopsies, we are dependent on the basic scientists to report the impact of novel therapies on the pulmonary vascular bed. Unfortunately, even the basic scientists struggle with less than perfect animal models for pulmonary vascular disease. These challenges highlight the importance of close communication among the basic scientists, clinical researchers, and clinicians in the field of pulmonary vascular disease.

In this issue, Jim White, MD, PhD, serves as guest editor and he and authors shed light on many of the complex pathways implicated in the pathogenesis of PAH and some of the novel therapies and strategies to target these pathways. The authors provide a comprehensive review and at times a "translation" of where the science is moving and how it may affect our clinical practice in the future. In the absence of a cure, we need to continue to bridge the gap between basic scientists and clinical researchers if we hope to uncover new targets for the treatment of pulmonary vascular disease. In this issue of *Advances*, authors eloquently provide the reader with some of the tools to start to bridge these gaps.

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## **Guest Editor's Memo**



This issue of *Advances* is about looking forward, but I'd like to start by looking backward for some perspective. About 10 years ago, a small company called Actelion launched

the first effective oral therapy for pulmonary arterial hypertension, bosentan, while another startup, United Therapeutics, launched subcutaneous treprostinil. Rather suddenly, our patients had 2 options other than intravenous epoprostenol, and a broader number of cardiology and pulmonary physicians became interested in recognizing, evaluating, and treating patients with pulmonary hypertension. Since that time, an enormous investment from industry partners and governmental authorities around the world has resulted in significant rewards. In the US, there now are 3 different parenteral therapies, 2 inhaled therapies, and 4 oral therapies. We are making meaningful clinical use of plasma brain natriuretic peptide levels and more sophisticated measurements of right ventricular function to risk stratify our

patients. We continue to explore the benefits of combination therapy, and we are documenting patient outcomes in large scale registries more completely than ever before. Our collective work as an investigative community and the dedication of our patients to better their own lives has changed this disease in radical, measurable ways. The amazing volunteers and employees of the Pulmonary Hypertension Association have been central to this success.

Today, as I write this introduction, the US Food and Drug Administration is evaluating the New Drug Applications for imatinib and oral treprostinil; they will likely be receiving the dossiers on macitentan and riociguat before the end of the year. The US National Institutes of Health will soon award 6 large grants to do patient-oriented research on right ventricular function, and industry-sponsored clinical development programs are recruiting new investigative sites and patients worldwide at a quick pace. It remains a very exciting time to be a clinician caring for these patients and a scientist working toward a better understanding of the disease state.

For this issue, the editorial board decided to focus on the advances in basic science that will likely change the way we care for patients in the next decade. We considered a large number of potential topics and selected the 3 that we thought would be most interesting to our readers. I reviewed the literature about in situ thrombosis, platelet activation, and warfarin use for our patients. I explored the vascular biology related to thrombin signaling and briefly summarized the novel anti-coagulants that we might consider as alternatives to warfarin (preferably in the context of a large, randomized trial). The investigative team from Vanderbilt reviewed the fascinating history that led to the identification of bone morphogenetic protein receptor 2 (BMPR-2) mutations in families with pulmonary hypertension. Then they provided an update (including unpublished data) of their work to better understand the strikingly low