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The Why's and Wherefore's of this Vascular Biology Section of Current Opinion in Hematology

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This is my first attempt to organize an issue of *Current Opinion in Hematology*. Indeed, my first attempt to organize any comparable compilation of articles. When the Editor-in-Chief, Tom Stossel, recruited me to organize the Vascular Biology Section, he said it would be the easiest job I'd ever done. Not quite true, but not a difficult job, and certainly an enjoyable task. The first task was to decide on a theme. One could choose to focus on a single topic and delve into it in great depth. That would require success in recruiting from a group of authors with a highly specialized interest and could lead to articles with extensive overlap. So, I decided that a broader topic was in order. Certainly, "the endothelium" was a safe choice for a vascular biology section. Each of the eight contributions in this issue of the Current Opinion in Hematology deals with some aspect of the endothelium. The authors were given a topic from within their area of expertise and asked to provide up-to-date perspectives on a particular molecule, signaling pathway and/or mechanism within this area with an emphasis on developments during the past year.

There is a unifying theme that links all eight articles. They deal with the communication between endothelial cells and their environment. This communication is bi-directional. To usurp terms that are used frequently in the integrin field, the signaling pathways can be both "outside-in" and "inside-out". Outside-in signals are generated via receptors on the endothelial cell surfaces. These receptors are exemplified by Protease-activated Receptor-1, described by Grimsey and Trejo, and by Neuropilin, discussed by Kofler and Simons. These receptors recognize ligands in the microenvironment of endothelial cells that transduce outside-in signaling events. Endothelial cells can also adsorb exosomes from tumors that infuse miRNA and other informative molecules that can influence intracellular responses including angiogenesis as described by Ohyashiki in his article. Endothelial cells sense changes in blood flow and wall shear stress at their extracellular surface and such mechanosensing can alter gene expression and intracellular signaling. In their article, McCormick and Tzima focus on the responses of endothelial cells in the heart to wall shear stress. Inside-out communication from endothelial cells is evidenced by the influence of released VWF from endothelial cells. Xiang and Hwa discuss mechanisms by which VWF synthesis and release are controlled in physiological and pathological settings in their contribution. Membrane anchored proteases on endothelial cells provide another mechanism by which endothelial cells can influence their extracellular environment. These membrane-anchored proteases are discussed by Antalis, Conway, Peroutka and Buzza. Endothelial cells

can also influence one another in cis via inter-junctional communication. Lertkiatmongkol, Liao, Mei, Hu and Newman relate how the recently solved crystal structure of portions of PECAM-1 provides insights into its functional outputs. Proteins of the extracellular matrix, either as endogenous components of the subendothelium or recruited from plasma, accumulate at sites of endothelial damage, where they influence thrombus formation and dissolution. This aspect of vessel wall biology and injury is considered in the article by Wang, Gallant and Ni. We have attempted to amalgamate these diverse topics into a single scheme in Fig. 1. I make no attempt to summarize the content of the articles. They should be read. They are concise, and they are excellent. They provide an opportunity for readers to not only gain a background but also up-to-date information in topical areas in vascular biology from leading authorities in the field.

In selecting the senior authors, I considered the contributions to high impact journals and the invited speakers at national and international meetings. Everyone we asked, with only one exception, agreed to provide an article. I am very grateful to all the authors and particularly for their provision of their articles in a timely fashion. Choices had to be made in selecting topics are authors. Omissions were unintentional. I particularly apologize to members of my institution who made many outstanding contributions to Hematology during the past year but I was counseled to select against home grown authors.

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Fig 1. Schematic diagram linking the contents of the Vascular Biology Section of Current Opinion of Hematology.