
Preface

The endothelins are a remarkable family of signaling peptides: molecular biology predicted the existence of their receptors and synthetic enzymes prior to both the identification of the encoded proteins and the synthesis of antagonists and inhibitors for use as pharmacological tools. Although considerable advances have been made, culminating in the design of endothelin antagonists with therapeutic potential in cardiovascular disease, much remains to be discovered.

Tantalizingly, new research frontiers are emerging. To support further progress, *Peptide Research Protocols: Endothelin* encompasses experimental protocols that interrogate all facets of an endogenous mammalian peptide system, from peptide and receptor expression through synthetic pathway to peptide function and potential role in human disease.

Chapters describe the use of molecular techniques to quantify the expression of mRNA for both endothelin receptors and the endothelin-converting enzymes. Peptides, precursors, receptors, and synthetic enzymes may be localized and quantified in plasma, culture supernatants, tissue homogenates, and tissue sections using antibodies, while additional information on receptor characterization may be obtained using radioligand binding techniques. Several protocols cover in vitro assays that determine the function of the endothelin peptides in isolated preparations, that characterize new endothelin receptor ligands, or provide information on the tissue-specific processing of endothelin precursor peptides. Finally, in vivo protocols illustrate the role of the endothelin peptides in healthy human individuals, describe animal models that reveal the alteration of the endothelin system in cardiovascular disease, and therefore predict the therapeutic potential of drugs that manipulate endothelin synthesis or function. A particular strength of *Peptide Research Protocols: Endothelin* is that, although each protocol may be used independently, many of the techniques are written to be complementary. The sequencing of the human genome presents new challenges in understanding the role in human physiology and pathophysiology of novel encoded proteins and peptides. The protocols described in this book have proved successful in endothelin research and the experimental strategies described have a wider relevance for determining the functional importance of the emerging orphan receptors and their cognate peptidic ligands.

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<http://www.springer.com/978-0-89603-993-3>

Peptide Research Protocols

Endothelin

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2002, X, 242 p., Hardcover

ISBN: 978-0-89603-993-3

A product of Humana Press