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Editorial

Endothelins

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It is timely indeed to produce a focused issue on endothelins ten years after the discovery of this new family of peptides. Although already in the mid-1980's the group of Robert Highsmith in Cincinnati observed that cultured endothelial cells paradoxically contracted isolated blood vessels they only suspected that a peptide produced by endothelial cells was involved. In 1988 Yanigasawa and Masaki demonstrated that indeed a 21-amino-peptide, which they called endothelin-1 was produced by endothelial cells in culture. Furthermore, they were able to show that various cardiovascular mediators, in particular constrictors such as angiotensin II and vasopressin, growth factors such as transforming growth factor β-1 and coagulation factors such as thrombin stimulated the de novo synthesis of the protein. Because of its remarkable potency and long lasting action as a vasoconstrictor, endothelin attracted a lot of interest in physiology and cardiovascular disease. The demonstration that endothelin also could act as a mitogen further suggested that it may act as an important regulator of the circulation in health and in particular in disease. Measurements of plasma endothelin levels demonstrated that in cardiac shock, congestive heart failure, pulmonary hypertension, acute myocardial infarction and many other conditions, endothelin concentrations were elevated. The importance of these observations, however, was unclear particularly as endothelin is considered primarily a paracrine regulatory system rather than a circulating hormone. The cloning and characterization of ET_A and ET_B-receptors on vascular smooth muscle and the endothelium in the vessel wall as well as in other organs of the circulation such as the heart and the kidney allowed a better understanding of the action of these peptides and led to the development of receptor antagonists. The use of endothelin receptor antagonists has markedly stimulated this area of research as it allowed to delineate the functional importance of these peptides in the cardiovascular system both as regulators of vascular tone and structure. In addition, endothelin receptor antagonist are a new class of cardiovascular drugs at the clinical horizon which may be used in the future to treat patients with hypertension, coronary artery disease and/or heart failure.

In this timely focused issue on endothelins, Tomoh Masaki [1], the discoverer of endothelin, reviews the history of this important basic observation. In addition, Michael Kirchengast reviews the role of endothelin in restenosis, Ton Rabelink [2] the potential of endothelin receptor antagonists in renal protection and Pierre Moreau [3] their possible role to treat arterial hypertension. Furthermore, the focused issue presents 18 original research papers devoted to several aspects of endothelin-mediated responses in the cardiovascular system and the effects of specific endothelin receptor antagonists. The great variety of topics covered reflects the broad interest in these new peptides and the receptor antagonists in cardiovascular research.

References

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[3] Moreau P. Endothelin in hypertension: A role for receptor antagonists? Cardiovasc Res 1998;39(3):534–542.

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