

Preface

Pituitary adenylate cyclase activating polypeptide (PACAP) was discovered in 1989 in the US-Japan Biomedical Research Laboratories of Tulane University, led by Akira Arimura. Atsuro Miyata and Akira Arimura isolated two peptides from ovine hypothalamus, with 38 and 27 amino acid residues that could stimulate adenylate cyclase in pituitary cells, resulting in the name of the peptide (Miyata et al. *Biochem Biophys Res Commun* 1989). In the last 25 years since its discovery, research has proved that PACAP has a very widespread occurrence. Its receptors, the specific PAC1 receptor and the receptors also binding VIP (VPAC1 and 2 receptors), also have widespread distribution in various tissues. The distribution, the splice variants of the receptors, and the diverse signaling explain the miscellaneous actions of the neuropeptide. PACAP belongs to the vasoactive intestinal peptide/secretin/glucagon peptide family and is implicated in a large array of physiological and also pathological processes. Several review articles published in the last 10 years provide excellent sources for reviews on occurrence, as well as the different effects and therapeutic relations of PACAP (the most comprehensive review so far is seen in Vaudry et al. *Pharmacol Rev* 2009). The present book is a collection of reviews from leading PACAP research investigators from all around the world.

PACAP is one of the most well-conserved peptides throughout evolution, indicating important roles in basic biological processes. The first section of this volume contains reviews on evolutionary aspects of the peptide—from molecular evolution to different roles in annelids and molluscs. Soon after its discovery, it became evident that PACAP plays a role in neuronal cell proliferation, differentiation, and migration. Thanks to the vast amount of data in this area, PACAP is now considered a trophic factor. Reviews on these developmental aspects of the peptide will comprise the next section. The following section is focused on the theme of receptors and signaling, with overviews of novel directions in peptide transport and pharmacological properties. The sections following these contain reviews on the physiological functions in various organs and systems, starting with effects in the endocrine system, thermoregulation, circadian rhythm, and cardiac excitability. Afterwards, there are discussions about actions in the gastrointestinal and urinary tracts, normal and pathological bone and cartilage development, and roles in the reproductive

system. PACAP has been shown also to play a role in various physiological barriers, especially the transport of PACAP through the blood brain barrier have been well studied. PACAP does not only affect neuronal function directly, but numerous glial effects have also been shown, as described in two further reviews. A separate chapter will deal with functions of PACAP in sensory systems, such as the olfactory, auditory, and visual system, the last focusing on the protective effects of PACAP in the retina. One of the most intensively studied aspects of PACAP is its strong neuroprotective effect, so the next section contains three reviews dedicated to these protective effects in both the central and peripheral nervous system. Very active investigation is currently underway regarding the role of PACAP in pain conditions, especially in migraines. A section is dedicated to chapters providing an overview of PACAP in pain. As PACAP partially shares receptors with vasoactive intestinal peptide, a neuropeptide closely related to PACAP and the inflammatory functions of which had long been known, the effects of PACAP in the immune system were described relatively early after the peptide's discovery. A vast amount of data have been collected since the first descriptions related to the immune functions of PACAP, summarized in three reviews of the next section. Another very intensively researched area is the role of PACAP in psychological processes and disorders, from depression to anxiety. A section consisting of six reviews provides an overview of these studies. Finally, there are three chapters that describe the clinical aspect of PACAP in relation to cancer, human milk and human blood, and the role of PACAP as a potential biomarker.

In essence, this volume is a detailed yet general reference resource, touching upon the different aspects of this interesting neuropeptide that has diverse effects and increasing therapeutic consideration.

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