

Mechanisms of Phospholipase C Activation by the Vasoactive Intestinal Polypeptide/Pituitary Adenylate Cyclase-Activating Polypeptide Type 2 Receptor

CHRISTOPHER J. MACKENZIE*, EVE M. LUTZ†, MELANIE S. JOHNSON,
DEREK N. ROBERTSON, PAMELA J. HOLLAND, AND RORY MITCHELL

Medical Research Council Membrane and Adapter Proteins Co-operative Group, Membrane Biology Group, Department of Biomedical Sciences, University of Edinburgh, Edinburgh, United Kingdom EH8 9XD; and Medical Research Council Brain Metabolism Unit, Edinburgh, United Kingdom EH8 9JZ

ABSTRACT

The vasoactive intestinal polypeptide/pituitary adenylate cyclase-activating polypeptide type 2 (VPAC₂) receptor was shown to induce both [³H]inositol phosphate ([³H]IP) and cAMP production in transfected COS7 cells and in GH₃ cells where it is natively expressed. Neither cholera toxin nor forskolin could elicit an equivalent [³H]IP response, suggesting independent coupling of the two pathways. The VPAC₂ receptor-mediated [³H]IP response was partially inhibited by pertussis toxin (Ptx) and by the G $\beta\gamma$ -sequestering C-terminal fragment of G19C2 (G19C2-ct) in COS7 and GH₃ cells, whereas responses of control receptors were unaffected. Blockers of receptor-activated Ca²⁺ influx pathways (Ca²⁺ and SKF 96365) also partially inhibited

VPAC₂ receptor-mediated [³H]IP responses. This inhibition was not present in the component of the response remaining after Ptx treatment. A range of blockers of voltage-sensitive Ca²⁺ channels were ineffective, consistent with the reported lack of these channels in COS7 cells. The data suggest that the VPAC₂ receptor may couple to phospholipase C through both Ptx-insensitive and Ptx-sensitive G proteins (G_{12/13} and G_{q/11}, respectively) to generate [³H]IP. In addition to G $\beta\gamma$, G_{12/13} activation appears to regulate receptor-activated Ca²⁺ entry. This is consistent with the possibility that not only G_{12/13}-responsive and G $\beta\gamma$ -responsive isoforms of phospholipase C but also Ca²⁺-responsive forms may contribute to the overall [³H]IP response. (*Neuroendocrinology* 142: 1209–1217, 2001)

THE 28-AMINO acid vasoactive intestinal peptide (VIP) belongs to a family of structurally related hormones that include pituitary adenylate cyclase-activating polypeptide (PACAP), secretin, GH-releasing hormone, and glucagon. VIP has well documented effects as a potent vasodilator and stimulator of electrolyte secretion and smooth muscle relaxation. In the central nervous system it is involved in regulating cerebral blood flow and circadian rhythms. It is a secretagogue for melatonin synthesis and release from pineal gland, PRL release from pituitary, insulin release from pancreas, and catecholamine release from adrenal medulla. VIP has a protective role in limiting oxidative damage in various tissues. Furthermore, dramatic changes in the amounts of VIP, PACAP, and their receptors in the spinal cord after peripheral nerve injury suggest an important role in neuropathic pain states (1–5).

The pleiotropic effects of VIP are mediated through G protein-coupled receptors that may activate several signal

transduction pathways in addition to cAMP production. Two distinct receptors for VIP have been cloned, the vasoactive intestinal polypeptide/pituitary adenylate cyclase-activating polypeptide type 1 (VPAC₁) from rat lung (6) and the VPAC₂ from rat pituitary and olfactory bulb (7). The neuropeptide PACAP³⁸ and its 27-residue amino-terminal form PACAP-27 (which shares approximately 68% identity with VIP) are similarly potent at these receptors in stimulating cAMP production. Receptors for VIP/PACAP belong to group II of the G protein-coupled receptor family, which includes receptors for secretin, PTH, and calcitonin (8). Members of this family couple to adenylate cyclase (AC), and a number have been shown to couple additionally to phospholipase C (PLC) (9, 10).

Preliminary studies indicated that the VPAC₂ receptor-mediated activation of [³H]inositol phosphate ([³H]IP) formation in transiently transfected COS7 cells occurred through a mechanism that was in part pertussis toxin (Ptx) sensitive (11). Here we investigated the hypothesis that this response is due to the stimulation of a PLC isoform by a mechanism involving the $\beta\gamma$ -subunits of the Ptx-sensitive G proteins, G_i and G_{12/13}, and whether there is any role for receptor-operated Ca²⁺ entry in the response. As well as in transfected COS7 cells, studies were carried out in GH₃ cells, which natively express the VPAC₂ receptor at low levels.

Materials and Methods

Drugs and chemicals

Tissue culture media were obtained from Life Technologies, Inc. (Paisley, UK); diethylaminoethyl (DEAE) dextran was obtained from

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Address all correspondence and requests for reprints to Dr. R. Mitchell, Medical Research Council Membrane and Adapter Proteins Co-operative Group, Membrane Biology Group, Department of Biomedical Sciences, University of Edinburgh, Hugh Robson Building, George Square, Edinburgh, United Kingdom EH8 9XD. E-mail: rory.mitchell@ed.ac.uk.

* Present address: Department of Physiology and Pharmacology, University of Strathclyde, 27 Taylor Street, Glasgow, United Kingdom G4 0NR.

† Present address: Department of Bioscience and Biotechnology, University of Strathclyde, 204 George Street, Glasgow, United Kingdom G1 0DW.

Pituitary Adenylate Cyclaseactivating Polypeptide

**John Stephen White, Dorothy Chong
White**



Pituitary Adenylate Cyclaseactivating Polypeptide:

Pituitary Adenylate Cyclase-Activating Polypeptide Hubert Vaudry,Akira Arimura,2012-12-06 Pituitary Adenylate Cyclase Activating Polypeptide is the first volume to be written on the neuropeptide PACAP It covers all domains of PACAP from molecular and cellular aspects to physiological activities and promises for new therapeutic strategies Pituitary Adenylate Cyclase Activating Polypeptide is the twentieth volume published in the Endocrine Updates book series under the Series Editorship of Shlomo Melmed MD **Handbook of Biologically Active Peptides** Abba Kastin,Abba J.

Kastin,2011-04-28 Peptides play a crucial role in many physiological processes including actions as neurotransmitters hormones and antibiotics Research has shown their importance in such fields as neuroscience immunology pharmacology and cell biology The Handbook of Biologically Active Peptides presents for the first time this tremendous body of knowledge in the field of biologically active peptides in one single reference The section editors and contributors represent some of the most sophisticated and distinguished scientists working in basic sciences and clinical medicine The Handbook of Biologically Active Peptides is a definitive all encompassing reference that will be indispensable for individuals ranging from peptide researchers to biochemists cell and molecular biologists neuroscientists pharmacologists and to endocrinologists Chapters are designed to be a source for workers in the field and will enable researchers working in a specific area to examine other related areas with which they would not ordinarily be familiar Chapters are designed to be a source for workers in the field and will enable researchers working in a specific area to examine other related areas that they would not ordinarily be familiar Fascinating relationships described in the book include the presence of some peptides originally found in frog skin that persist in the human human and brain where they can affect food intake and obesity P.A.C.A.P. CHRISTINE..

OUSTRIC,1996 *Pituitary Adenylate Cyclase Activating Polypeptide — PACAP* Dora Reglodi,Andrea Tamas,2016-10-08 The first comprehensive book to cover all aspects of the last 25 years of PACAP pituitary adenylate cyclase activating polypeptide research this book contains contributions from virtually all the leading researchers in the field and addresses some of the following topics evolutionary aspects of PACAP distribution and occurrence of PACAP and its receptors hormonal effects of PACAP intracellular signaling effects on cellular proliferation and differentiation protective effects of PACAP behavioral effects of PACAP developmental aspects of PACAP other physiological effects of PACAP cardiovascular thermoregulatory human studies drug design metabolism and transport This compendium can serve as an important reference for researchers and students in PACAP research and can also be a thorough introduction for those in related fields

Psychoneuroimmunology Robert Ader,2007 Psychoneuroimmunology is the study of interactions among behavioral neural and endocrine and immunologic processes of adaptation These two volumes provide a clearly written extensively referenced summary of some of the behavioral neural and endocrine regulators of immune responses and immunologically mediated disease processes and of the behavioral and neuroendocrine effects of immune system activity Several chapters

expand upon topics reviewed in earlier editions of this series most chapters cover active areas of research that have not previously been reviewed As illustrated in this fourth edition interdisciplinary research continues to provide evidence that the brain and immune system represent a single integrated system of defense

Pituitary Adenylate Cyclase Activating Polypeptide (PACAP) Guo, Xi,1996 *Pituitary Adenylate Cyclase Activating Peptide (PACAP)* Kristian Moller,1997

Studies of Pituitary Adenylate Cyclase-activating Polypeptide (PACAP) and Vasoactive Intestinal Peptide (VIP) and Their Effects on Pituitary Hormone Secretion in the Ewe Kitja Sawangjaroen,1997 *Handbook of Amygdala Structure and Function* Janice H. Urban,J. Amiel Rosenkranz,2020-04-02

Handbook of Amygdala Structure and Function Volume 26 provides an updated overview on the functional neuroanatomy of amygdala nuclei with an emphasis on interconnections basolateral central amygdala medial amygdala and their integration into related networks circuits prefrontal cortex bed nucleus nucleus accumbens The design of this volume builds upon the foundations of functional neural circuits and the corresponding cellular electrophysiology important for the homeostatic control of amygdala function This volume contains a dedicated section on the anatomical organization of the amygdala nuclei emphasizing the role of neurotransmitters and neuropeptides that integrate signals and regulate behavior Additional chapters discuss cellular physiology plasticity and the integration of electrical signals that contribute to neural activity The final section of the book connects the role of amygdala dysfunction and the development of disorders in human health and disease

Involvement of Bioactive Peptides in the Control of Cell Survival, Proliferation and Plasticity in Physiological and Pathological Conditions, 2nd Edition

David Vaudry,Dora Reglodi,2021-12-02 Publisher's note In this 2nd edition the following article has been added Editorial *Involvement of Bioactive Peptides in the Control of Cell Survival Proliferation and Plasticity in Physiological and Pathological Conditions*

Neuropeptide GPCRs in neuroendocrinology Jae Young Seong,Hubert Vaudry,2014-11-07 The human genome encompasses 860 G protein coupled receptors GPCRs including 374 non chemosensory GPCRs Half of these latter GPCRs recognize neuro peptides as natural ligands GPCRs thus play a pivotal role in neuroendocrine communication In particular GPCRs are involved in the neuroendocrine control of feeding behavior reproduction growth hydromineral homeostasis and stress response GPCRs are also major drug targets and hence possess a strong potential for the development of innovative pharmaceuticals The aim of this Research Topic was to assemble a series of review articles and original research papers on neuropeptide GPCRs and their ligands that would illustrate the different facets of the studies currently conducted in this domain

Estrogen Effects on Fertility and Neurodegeneration - Classical versus Non-Classical Actions Zsuzsanna Nagy,Allan Herbison,Andrea Kwakowsky,Gergely Kovacs,Klaudia Barabas,2023-08-07

Physiology and Pathophysiology of the Islets of Langerhans Bernat Soria,2013-11-21 Proceedings of the First International Meeting of the Pancreatic Islet Study Group held in the Alicante Spain November 25 28 1994

Stress: Physiology, Biochemistry, and Pathology

George Fink,2019-01-12 Stress impacts the daily lives of humans and all species on Earth Physiology Biochemistry and

Pathology the third volume of the Handbook of Stress series covers stress related or induced physiology biochemistry and pathology Integrated closely with new behavioral findings and relevance to human conditions the concepts and data in this volume offer readers cutting edge information on the physiology of stress A sequel to Elsevier s Encyclopedia of Stress 2000 and 2007 this Handbook of Stress series covers the many significant advances made since then and comprises self contained volumes that each focus on a specific area within the field of stress Targeted at scientific and clinical researchers in neuroendocrinology neuroscience biomedicine endocrinology psychology psychiatry the social sciences and stress and its management in the workplace this volume and series are ideal for graduate students post doctoral fellows and faculty interested in stress and its consequences Chapters offer impressive scope with topics addressing stress related or induced physiology biochemistry and pathology Articles carefully selected by eminent stress researchers and prepared by contributors representing outstanding scholarship in the field with each chapter fully vetted for reliable expert knowledge Richly illustrated with explanatory figures and tables Each chapter has a boxed Key points call out section The volume is fully indexed All chapters are electronically available via ScienceDirect Affordably priced self contained volume for readers specifically interested in the physiology biochemistry and pathology of stress avoiding the need to purchase the whole Handbook series Cumulated Index Medicus ,1996 *Neuropeptides in Neuroprotection and Neuroregeneration* Fred Nyberg,2012-06-19 Although the genomic era is no longer in its infancy the life sciences are still facing questions about the role of endogenous proteins and peptides in homeostasis and pathologies Delving into one of the most current fields of interest in biology and medicine Neuropeptides in Neuroprotection and Neuroregeneration describes the impact of neuropep

Regulatory Mechanisms in Gastrointestinal Function (1995) Timothy S. Gaginella,2017-11-22 Regulatory Mechanisms in Gastrointestinal Function includes a collection of contemporary topics in gastrointestinal research The control of gastroduodenal electrolyte transport and the influence of drugs on bicarbonate secretion are reviewed in detail The importance of the interactions between calcium and cyclic AMP in intestinal secretion is emphasized in a comprehensive chapter that systematically addresses each link in the mechanisms that regulate chloride secretion Other important topics included in the book are neural reflex modulation of intestinal epithelial transport the influence of the microcirculation on intestinal secretion and nitric oxide as a mediator of physiologic and pathophysiologic secretion The expertise of the authors has resulted in a breadth of important contemporary topics covered in depth Proteins, Peptides and Amino Acids SourceBook John Stephen White,Dorothy Chong White,2002-04-15 Proteins Pep tides and Amino Acids SourceBook is the second in a series of reference books conceived to cover the explosive growth in commercially available biological reagents The success of our first reference work Source Book of Enzymes published in 1997 encouraged us to continue this series Choosing proteins peptides and amino acids as the subject matter for the second volume was simple given their preeminence in regulating biochemical processes and their importance to modern molecular biology The SourceBook series was inspired

by our difficulty in locating a suitable replacement for a depleted reagent in the midst of an urgent research project To our dismay we found the reagent supplier out of business and the product line no longer available Other reagent catalogs on our library bookshelf offered a narrow selection and incomplete functional information We were ultimately able to locate a satisfactory alternative only by making countless inquiries and paging through innumerable product catalogs and technical data sheets We needed but could not find a single resource that cataloged available compounds organized them in a logical and accessible format provided critical technical information to distinguish one from another and told us where we could buy them

International Review of Cytology Kwang W. Jeon, 2006-06-07 *International Review of Cytology* presents current advances and comprehensive reviews in cell biology both plant and animal Authored by some of the foremost scientists in the field each volume provides up to date information and directions for future research Articles in this volume address endogenous ligands of PACAP VIP receptors in the autocrine paracrine regulation of the adrenal gland ultrastructural dynamics of human reproduction from ovulation to fertilization and early embryo development chromosomal variation in mammalian neuronal cells automated interpretation of protein subcellular location patterns cell and molecular biology of human lacrimal gland and nasolacrimal duct mucins

Neuroendocrine Control of Energy Homeostasis in Non-mammalian Vertebrates and Invertebrates Suraj Unniappan, Ian Orchard, María Jesús Delgado, 2020-07-31 This eBook is a collection of articles from a Frontiers Research Topic Frontiers Research Topics are very popular trademarks of the Frontiers Journals Series they are collections of at least ten articles all centered on a particular subject With their unique mix of varied contributions from Original Research to Review Articles Frontiers Research Topics unify the most influential researchers the latest key findings and historical advances in a hot research area Find out more on how to host your own Frontiers Research Topic or contribute to one as an author by contacting the Frontiers Editorial Office frontiersin.org about contact

Pituitary Adenylate Cyclaseactivating Polypeptide Book Review: Unveiling the Magic of Language

In a digital era where connections and knowledge reign supreme, the enchanting power of language has become more apparent than ever. Its capability to stir emotions, provoke thought, and instigate transformation is truly remarkable. This extraordinary book, aptly titled "**Pituitary Adenylate Cyclaseactivating Polypeptide**," compiled by a highly acclaimed author, immerses readers in a captivating exploration of the significance of language and its profound effect on our existence. Throughout this critique, we shall delve into the book's central themes, evaluate its unique writing style, and assess its overall influence on its readership.

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