

Advances in Anatomy, Embryology and Cell Biology

Inge Brouns
Isabel Pintelon
Jean-Pierre Timmermans
Dirk Adriaensen

Novel Insights in the Neurochemistry and Function of Pulmonary Sensory Receptors

 Springer

Reviews and critical articles covering the entire field of normal anatomy (cytology, histology, cyto- and histochemistry, electron microscopy, macroscopy, experimental morphology and embryology and comparative anatomy) are published in *Advances in Anatomy, Embryology and Cell Biology*. Papers dealing with anthropology and clinical morphology that aim to encourage cooperation between anatomy and related disciplines will also be accepted. Papers are normally commissioned. Original papers and communications may be submitted and will be considered for publication provided they meet the requirements of a review article and thus fit into the scope of "Advances". English language is preferred.

It is a fundamental condition that submitted manuscripts have not been and will not simultaneously be submitted or published elsewhere. With the acceptance of a manuscript for publication, the publisher acquires full and exclusive copyright for all languages and countries.

Twenty-five copies of each paper are supplied free of charge.

Manuscripts should be addressed to

Co-ordinating Editor

Prof. Dr. H.-W. KORF, Zentrum der Morphologie, Universität Frankfurt, Theodor-Stern Kai 7,
60595 Frankfurt/Main, Germany
e-mail: korf@em.uni-frankfurt.de

Editors

Prof. Dr. F. BECK, Howard Florey Institute, University of Melbourne, Parkville, 3000 Melbourne, Victoria, Australia
e-mail: fb22@le.ac.uk

Prof. Dr. F. CLASCÁ, Department of Anatomy, Histology and Neurobiology
Universidad Autónoma de Madrid, Ave. Arzobispo Morcillo s/n, 28029 Madrid, Spain
e-mail: francisco.clasca@uam.es

Prof. Dr. D.E. HAINES, Ph.D., Department of Anatomy, The University of Mississippi Med. Ctr.,
2500 North State Street, Jackson, MS 39216-4505, USA
e-mail: dhaines@anatomy.umsmed.edu

Prof. Dr. N. HIROKAWA, Department of Cell Biology and Anatomy, University of Tokyo,
Hongo 7-3-1, 113-0033 Tokyo, Japan
e-mail: hirokawa@m.u-tokyo.ac.jp

Dr. Z. KMIĘC, Department of Histology and Immunology, Medical University of Gdansk,
Debinki 1, 80-211 Gdansk, Poland
e-mail: zkmiec@amg.gda.pl

Prof. Dr. R. PUTZ, Anatomische Anstalt der Universität München,
Lehrstuhl Anatomie I, Pettenkoferstr. 11, 80336 München, Germany
e-mail: reinhard.putz@med.uni-muenchen.de

Prof. Dr. J.-P. TIMMERMANS, Department of Veterinary Sciences, University of Antwerpen,
Groenenborgerlaan 171, 2020 Antwerpen, Belgium
e-mail: jean-pierre.timmermans@ua.ac.be

211

Advances in Anatomy, Embryology and Cell Biology

Co-ordinating Editor

H.-W. Korf, Frankfurt

Editors

F.F. Beck • F. Clascá • D.E. Haines • N. Hirokawa
Z. Kmiec • R. Putz • J.-P. Timmermans

For further volumes:

<http://www.Springer.com/series/102>

Inge Brouns, Isabel Pintelon,
Jean-Pierre Timmermans,
Dirk Adriaensen

Novel Insights in the Neurochemistry and Function of Pulmonary Sensory Receptors

With 24 figures

 Springer

Dr. Inge Brouns
University of Antwerp
Department of Veterinary Sciences
Laboratory of Cell Biology and Histology
Groenenborgerlaan 171
2020 Antwerp
Belgium
inge.brouns@ua.ac.be

Dr. Isabel Pintelon
University of Antwerp
Department of Veterinary Sciences
Laboratory of Cell Biology and Histology
Groenenborgerlaan 171
2020 Antwerp
Belgium
isabel.pintelon@ua.ac.be

Prof. Dr. Jean-Pierre Timmermans
University of Antwerp
Department of Veterinary Sciences
Laboratory of Cell Biology and Histology
Groenenborgerlaan 171
2020 Antwerpen
Belgium
jean-pierre.timmermans@ua.ac.be

Dr. Dirk Adriaensen
University of Antwerp
Department of Veterinary Sciences
Laboratory of Cell Biology and Histology
Groenenborgerlaan 171
2020 Antwerpen
Belgium
dirk.adriaensen@ua.ac.be

ISSN 0301-5556
ISBN 978-3-642-22771-4 e-ISBN 978-3-642-22772-1
DOI 10.1007/978-3-642-22772-1
Springer Heidelberg Dordrecht London New York

Library of Congress Control Number: 2011939070

© Springer-Verlag Berlin Heidelberg 2012

This work is subject to copyright. All rights are reserved, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilm or in any other way, and storage in data banks. Duplication of this publication or parts thereof is permitted only under the provisions of the German Copyright Law of September 9, 1965, in its current version, and permission for use must always be obtained from Springer. Violations are liable to prosecution under the German Copyright Law.

The use of general descriptive names, registered names, trademarks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

Product liability: The publishers cannot guarantee the accuracy of any information about dosage and application contained in this book. In every individual case the user must check such information by consulting the relevant literature.

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

*Dedicated to emeritus
Prof. Dr. Dr. h.c. Dietrich W. Scheuermann,
former Chair of Histology and Microscopic
Anatomy, and Dean of the Faculty of
Medicine at the University of Antwerp.
He was one of the pioneers of pulmonary
neuroepithelial body research and a mentor
of many young scientists in the field.*

Abstract

Afferent nerves in the airways and lungs contribute to optimisation of the breathing pattern, by providing local pulmonary information to the central nervous system. Airway sensory nerve terminals are consequently tailored to detect changes readily in the physical and chemical environment, thereby leading to a variety of respiratory sensations and reflex responses.

Most intrapulmonary nerve terminals arise from fibres travelling in the vagal nerve, allowing a classification of “sensory airway receptors”, based on their electrophysiologically registered action potential characteristics. Nowadays, at least six subtypes of electrophysiologically characterised vagal sensory airway receptors have been described, including the classical slowly and rapidly adapting (stretch) receptors and C-fibre receptors. The architecture of airways and lungs makes it, however, almost impossible to locate functionally the exact nerve terminals that are responsible for transduction of a particular intrapulmonary stimulus.

With the advances in immunohistochemistry in combination with confocal microscopy, airway sensory receptor end organs can now be examined and evaluated objectively. Based on their “neurochemical coding”, morphology, location and origin, three sensory receptor end organs are currently morphologically well characterised: smooth muscle-associated airway receptors (SMARs), neuroepithelial bodies (NEBs) and visceral pleura receptors (VPRs). The present information on the functional, morphological and neurochemical characteristics of these sensory receptors leads to important conclusions about their (possible) function.

Currently, *ex vivo* lung models are developed that allow the selective visualisation of SMARs, NEBs and VPRs by vital staining. The described *ex vivo* models will certainly facilitate direct physiological studies of the morphologically and neurochemically identified airway receptors, thereby linking morphology to physiology by identifying *in situ* functional properties of a given receptor end organ.

Acknowledgements

This work was supported by grants of the Fund for Scientific Research-Flanders (FWO; G.0081.08 to D.A. and I.B.) and the University of Antwerp (GOA BOF 2007 to DA, KP BOF 2011 to IB).

Special thanks to the past and present colleagues of the research group studying airway sensory receptors, who have been involved in part of the reported research: Dr. I. De Proost, Dr. J. Van Genechten, Dr. R. Lembrechts and Dr. K. Schnorbusch.

The skilful technical assistance of F. Terloo, R. Spillemaeckers, G. Vermeiren, L. Svensson and C. Moers is highly appreciated. Thanks to D. De Rijck, J. Van Daele, and S. Thys for help with imaging and illustrations; D. Vindevogel for aid with the manuscript; and S. Kockelberg and H. De Pauw for administrative help.

Contents

1	Sensory Nerve Terminals in Intrapulmonary Airways and Lungs	1
1.1	Airway Sensory Nerves and Breathing	1
1.2	Activation of Airway Sensory Nerves	2
1.2.1	Mechanical Stimuli	3
1.2.2	Chemical Stimuli	3
1.3	Studying Airway Afferents	4
2	Electrophysiologically Identified Airway Receptors: Main Characteristics	7
2.1	Slowly Adapting (Stretch) Receptors	9
2.2	Rapidly Adapting (Stretch) Receptors	11
2.3	C-Fibre Receptors	12
3	Morphology and Location of Electrophysiologically Identified Sensory Airway Receptors	17
4	The Neurochemical Coding of Airway Afferents	19
4.1	Antibody Markers for Potential Pulmonary Mechanosensory Nerve Terminals	20
5	Morphologically Identified Sensory Receptor End-Organs in the Airways, Lungs and Visceral Pleura	23
5.1	Smooth Muscle-Associated Airway Receptors	24
5.1.1	General Morphology and Origin of SMARs	24
5.1.2	Functional Morphological Characteristics of SMARs	27
5.1.3	Functional Implications	31
5.2	Pulmonary Neuroepithelial Bodies	33
5.2.1	General Morphological Aspects of Pulmonary NEBs	34
5.2.2	Selective Innervation of Neuroepithelial Bodies	35
5.2.3	Functional Morphological Characteristics and Neurochemical Coding of Pulmonary NEB Cells	54
5.2.4	Neuroepithelial Bodies and the Various Associated Nerve Terminals Form Distinct Units with Great Functional Potential in the Airway Epithelium	67