Editorial

Chromaffin cells at the beginning of the 21st century

Survival of a man, as well as of a beast, critically depends on the rapid release of two related hormones, adrenaline and noradrenaline, which provide for a general mobilization of vital resources (Garcia *et al.* 2006). These hormones are synthesized and liberated from post-ganglionic sympathetic neurones and from a set of neuro-endocrine cells (which form the inner part of the adrenal gland) generally known as 'chromaffin cells'. In addition, adrenal chromaffin cells release a wide variety of peptides (e.g. opioids, or VIP), purines (ATP, ADP, AP_4A) and proteins that can act as prohormones (DBH, granins).

The story of chromaffin (i.e. demonstrating affinity to chromium salts) cells began a little more than 100 years ago in Prague, when Alfred Kohn produced the first detailed description of these cells (Kohn 1898, 1902, 1903): he identified these cells as secretory and discovered their close relation to the neurones in the sympathetic ganglia. The structure of the adrenal gland received considerable attention from morphologists (notably from R.E. Coupland) when microscopy techniques became widely available. Díaz-Florez *et al.* in this issue contribute to update this subject with their paper, which is accompanied by a set of images that illustrate the structure and function of these cells.

Development of tissue culture techniques in the 1970s extended earlier classical studies performed on perfused adrenals *in situ* or *in vitro* and allowed for extensive usage of biochemical, electrophysiological, electrochemical, fluorescence microscopy and molecular biology techniques. In 1976, Lloyd Green and Arthur Tischler created the PC12 cells from a rat phaeochromocytoma; subsequently these cells were used for important studies of cell differentiation and enzyme activity as well as secretion. In this issue, Westerink and Ewing have revisited the contribution of PC12 cells to our knowledge of secretory pathways.

Almost 40 years ago Douglas (1968), using data obtained from perfused cat adrenals, promulgated the theory of stimulus-secretion coupling, which highlighted Ca^{2+} ions as signals coupling cellular excitation with initiation of secretion. Since then, chromaffin cells became one of the most popular and widely used cellular models for investigating the molecular mechanisms of secretion. Here, De Diego *et al.* present a comprehensive description of stimulus-secretion coupling and the role of neurotransmitter receptors and ion channels. Further, the specific role of nicotinic cholinoreceptors in stimulus-secretion coupling is overviewed by Sala *et al.*, whereas the role of muscarinic receptors is covered by Olivos and Artalejo. Additional amplification of initial depolarization caused by activation of nicotinic receptors is achieved by opening of voltage-gated sodium channels; their contribution to the regulated secretion is discussed by Wada *et al.* The central role in stimulation-secretion coupling belongs to Ca^{2+} ions passing through voltage-gated Ca^{2+} channels. Marcantoni *et al.* and Fox *et al.* overview the biophysical and functional role of the various Ca^{2+} channel types expressed by chromaffin cells in normal conditions as well as under stress, while the current understanding of Ca^{2+} handling by cell organelles is presented by García-Sancho and Verkhratsky.

The principal functional organelle of chromaffin cells is represented by secretory vesicles, also known as chromaffin granules. Their transport from the *trans*-Golgi apparatus to the plasma membrane is conducted by cytosolic proteins; these are described by Trifaró *et al.* The main intravesicular proteins are chromogranins, which are involved in many cellular functions such as granule sorting, buffering of soluble components and providing a source of bioactive peptides as overviewed by Montero-Hadjadje *et al.* The molecular physiology of exocytosis is a topic of the paper by Shuzo Sugita. Further, the actual exocytotic process visualized by evanescent wave techniques (total internal reflection fluorescent microscopy – TIRFM) allows trailing of the single vesicle in the narrow submembrane area, as described by Holz and Axelrod. Electrophysiology and electrochemistry applied to the study of secretion were first assayed in chromaffin cells and then expanded to other cells; however, chromaffin cells are still considered one of the favourite models to study the exocytosis/endocytosis processes by capacitance recordings, amperometry and patch-amperometry, as presented by Borges *et al.*

Maintenance of regulated exocytosis is inseparable from membrane retrieval accomplished through endocytosis, which also can be followed by TIRFM; these investigations are overviewed by Barg and Machado. Finally, adrenomedullary tissues are implicated in various forms of pathology and the relevant diseases are summarized by Fung *et al.*

The spread of chromaffin cells as universal models was very much determined by their common experimental availability and by the large number of laboratory techniques, which have been developed to study

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them. Although this special issue of *Acta Physiologica* cannot comprise all the aspects of the seminal research carried out with chromaffin cells since William Douglas's time, we have tried to present the reader with a comprehensive view on the chromaffin cell physiology and pathophysiology. This special issue represents a collection of papers, written by the most distinguished experts in the field of chromaffin cells, who gathered for the biannual 'chromaffin cell' meeting held in October 2007 in Liguria, in the city of Sestri Levante (http://www.14thisccb.unito.it/).

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