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Letter to the Editor

Claude Bernard was right: hormones may be produced by "non-endocrine" cells

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In recent years attention of the specialists in different fields of biomedicine has focus on an unusual phenomenon, i.e., many so-called "non-endocrine" cells in living organism produce hormones.

In addition to neurons and some types of lymphocytes for which such ability was shown earlier [1–2], a large number of other cells significantly extend this list today. Among them, mast cells, natural killer cells, eosinophilic leukocytes, endothelial cells, thymic epithelial cells, monocytes, platelets, chondrocytes, osteocytes, placental trophoblasts and amnion cells, ovarian Leydig cells, endometrial cells, retinal photoreceptors and amacrine cells, Merkel cells in skin, Paneth cells, and macrophages. The spectrum of hormonal substances produced by these cells is extremely wide and includes serotonin, melatonin, catecholamines, histamine, endorphins, endothelin, matrilysin, natriuretic peptide, vasoactive intestinal peptide, vasopressin, oxytocin, thymosins, insulin and insulin-like substance, somatostatin, prolactin, ACTH, leptin and others [3–7]. This list could be further extended if organs producing nitric oxide (NO) were included. NO also is considered as a gaseous hormonal substance [8]. Moreover, many different peptide complexes (so called "cytomedines") which are able to regulate intercellular communications within of small particularized cellular populations, were evoked from almost all tissues [9].

Taking into account the main feature of a hormone as a biochemical molecule produced within the body which acts on target cells via the blood (endocrine), neural synapses (neurocrine) or via the intercellular space (paracrine) obviously there are many other cells of different origins that meet these criteria independent of the chemical nature of substances produced by them.

Thus, the above data suggest some revision of the fundamental postulate of classical endocrinology—***hormonal function is a specialized feature of endocrine cells having a common origin and similar morphology.*** Apropos of this, the postulate was rather weakened when identical biogenic amines and peptide hormones were found both in neurones and in amine precursor and uptake and decarboxylation (APUD) cells located in different organs. These cells are considered as a common regulatory system—the diffuse neuroendocrine system (DNES) [10]. It is now widely accepted that cells in many organs which produce biologically active substances, i.e., DNES cells, are regulators of homeostasis acting via neurocrine, endocrine and paracrine mechanisms [11].

In this connection, it may be possible to consider the above list of different "non-endocrine" cells as an additional part of the universal system of response, control and organismal protection and that their hormonal substances act as paracrine signal molecules for the local co-ordination of intercellular, intertissue and interorgan relationships. The agents produced by the DNES act as typical hormones, reaching wide spread target cells through the bloodstream. In both cases, some "non-endocrine" cells such as mast cells, eosinophilic leukocytes, monocytes, platelets and macrophages may take up biologically active substances from the blood or intercellular space so as to transport them to sites where they exert their effects.

Thus**, hormonal function, in the strict sense, is not a specific action of some cells, but is a general biological function of many cells independent of their development and primary role.**

This being the case we can only be astonished by the great foresight of Claude Bernard, who more than 100 years ago (in 1855) first supposed that not only endocrine glands but many organs in the organism have the ability for "internal secretion", which is a basic mechanism to regulate homeostasis [12].

In this brief letter we wish to stress once more the significance of Bernard's speculation. Current data and further investigation into the phenomenon of hormonal function of "non-endocrine" cells continues to reveal the complex processes of cell signalling and their role in homeostasis regulation in normal and pathologic conditions.

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