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Letter to the Editor

Immune Cells Express Endocrine Markers

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Abstract: Evidence are now given that immune cells expressed endocrine markers like neuropeptides, biogenic amine, neuropeptide processing enzymes, regulated secretion pathway. In clear, immune cells expressed like the nervous system an endocrine phenotype. This give the following question: what can we now consider as immune or endocrine?

Key words: **endocrinology; neuroimmunity; immunity**

As suggested by Kvetnoy and colleagues [1] in the letter to NEL editor entitled "Claude Bernard was right: hormones may be produced by « non-endocrine » cells", Claude Bernard was the first in 1855 to suppose that not only endocrine glands but many organs in the organism have the ability for "internal secretion" [2]. The evidences that identical biogenic amines and peptides hormones are found in neurones and in amine precursor and uptake decarboxylation (APUD) cells located in different organs firstly confirmed his visions of the endocrinology [2]. The existence of a diffuse neuroendocrine system (DNES) concept was born [2]. Recently, Weigent and Blalock demonstrated that communication and reciprocal regulation between the nervous, endocrine and immune systems are essential for the stability of the organism, these three systems use the same signalling molecules. [3] Among others, cytokines, hormones and neuropeptides have been identified as messengers mediating the communication between the three systems [4–8]. Moreover, in the last few years various animal models have served to study neuroimmune mechanisms confirming the view of communication between the neuroendocrine and immune systems via neuropeptide signalling and through specific receptors [6–8].

Immune cells are able to synthesise neuropeptides acting as signalling molecules but also in organism defence [8–14]. Peptides with antibacterial properties have been shown to be derived from neuropeptide precursors such as proenkephalin and chromogranin B [8–14]. The role of neuropeptide precursors in immunity, through the release of antibacterial peptides, is an entirely novel concept. The biosynthetic pathway that leads to the production of biologically active neuropeptides begins with the synthesis of large inactive precursor proteins which are cleaved at specific paired or single basic residues within the Golgi secretory pathway [15]. It is a family of subtilase-like pro-protein convertases (SPCs) [15] that is largely responsible for these processing events that activate precursor proteins into neuropeptides. The SPCs

have been extensively studied in both neural and endocrine systems. However, much less is known concerning their expression, regulation and role within the immune system at the basal level [15, 16] or their function during microbial challenge [4]. We recently demonstrate that SPC functions are important since differential expression of SPCs and the resulting cleavage patterns determine the nature and biological activity of the peptide products. Thus, depending on the pattern of SPC expression, a single protein precursor can give rise to different peptides with diverse biological activities like antimicrobial substances (secretolytin, enkelytin/peptide B, dermaseptins [9–13, 17] or chemoattractant factors (Methionine-enkephalin) [7, 8].

Finally, the important point is the presence of at least four different types of granules formed during maturation of neutrophil granulocytes in the bone marrow [18]. Recent data support the concept that the (lysosomal type) azurophil granules are secreted through the endosomal pathway [19]. Taken together, these data suggest that regulated exocytosis from neutrophil granulocytes belongs to the general mechanism of secretion.

Considering all the above data, the aim of this letter is to point out that some revisions of the fundamental postulates of classical endocrinology need to be now undertaken.

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