VOLUME V

THE CELL

Biochemistry, Physiology, Morphology

Edited by

JEAN BRACHET

ALFRED E. MIRSKY

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Biochemistry, Physiology, Morphology

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Bruxelles, Belgique

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PREFACE

The excellent reception accorded the first volume has been very encouraging. It is most rewarding for the contributors to realize that this treatise is filling a real need for a synthesis of up-to-date knowledge in the many active fields of research on the cell.

The chapters in these volumes deal with many different types of cells. Of course what one would desire is to have presented cells of the whole animate creation. "We ought not to hesitate nor to be abashed," said Aristotle, "but boldly to enter upon our researches concerning animals of every sort and kind, knowing that in not one of them is Nature or Beauty lacking." Selection, however, was necessary so that not all areas could be covered.

J. BRACHET
A. E. MIRSKY

July, 1960

THE CELL: *Biochemistry, Physiology, Morphology*

COMPLETE IN 5 VOLUMES

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CHAPTER 1

Gland Cells

By M. GABE and L. ARVY

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I. Introduction

Glandular function is a special case of secretion, which is a phenomenon common to all cells.

The secretory process is usually defined as the result of a cellular activity proceeding in three stages: (1) absorption by the cell of certain compounds present in the surrounding medium; this passage of materials

through the cell membrane is usually called *ingestion*; (2) formation inside the cell of the product(s) of secretion; this stage of the cell activity is called *synthesis* by Junqueira and Hirsch (1956); (3) elimination of the product(s) of secretion into the external or internal environment; this last stage is called *extrusion*.

The secretory process thus defined is evidently a very widespread phenomenon; it would be hard to find in any multicellular organism, a single type of cell not capable of absorbing various materials from its environment, and, after their more or less complete transformation eliminating them. Therefore is it possible to state with Prenant *et al.* (1904) that "secretion is a general property, but not a function of the cell." Consequently, glandular activity must be more closely defined.

Among the substances rejected by the cell in the course of its activity, some have merely passed through it without undergoing any chemical change. These are the "recrements" (Frey-Wyssling's *Rekrete*, 1945), such as water and certain ions, for instance, and the extrusion of these substances is obviously not the result of secretory activity.

Other substances are produced by catabolic phenomena, i.e., the splitting of complex molecules into simpler ones; their elimination is called excretion, and this activity of the cell must be distinguished from secretion proper.

Still other substances are the end products of the synthetic work of the cell; they differ chemically from the compounds absorbed from the environment and are, to a certain extent, specific for the type of cells which produce them; their rejection into the extracellular environment is often preceded by the storing of either the finished secretory product or its precursor; the cell may store these in particulate form and the storage represents the final stage of intracellular synthesis. The secretory product, no longer an integral part of the protoplasm after its accumulation in the cell, can be expelled either in particulate form or after redissolution in the cytoplasm. Only these substances are truly the products of secretion.

The notion of glandular cell implies functional specialization. Indeed, one of the criteria of the glandular nature of a cell is the primary function of periodical or continuous manufacture and extrusion of a secretory product. Another criterion may be the nature of the substance synthesized. The term glandular activity cannot legitimately be used to designate the formation of the common products of cell metabolism; the substance formed must possess a certain specificity for its process of formation properly to be termed glandular activity. There is unquestionable glandular activity in unicellular organisms, but it is obvious that only multicellular organisms can possess glandular cells.

II. Criteria of Glandular Activity in a Cell

The glandular nature of a cell is determined by means of morphological, histophysiological, physiological, and biochemical data.

A. Morphological Criteria

The general morphology of a glandular cell may vary considerably, and it seems impossible at present to find a pattern applicable to all cases. Descriptions based on the structure of the mammalian salivary glands or pancreas are no more than crude approximations. There is no doubt that a well-developed ergastoplasm, an abundance of mitochondria arranged in definite patterns, and grouped Golgi bodies are indications of the possible glandular nature of a cell, but there are innumerable exceptions to this rule. In fact, the general appearance of a cell and the shape and arrangement of its principal organelles are merely clues leading the experienced histologist to suspect, but not to affirm, that he is dealing with a gland cell.

One morphological criterion of the glandular nature of a cell deserves special mention: this is the accumulation, at some stages of the functional cycle, of a secretory product in particulate form. Whenever the presence of such a product can be shown by means of histological techniques, the argument in favor of the glandular nature of the cell is considerably strengthened. The opposite, however, is not true: in a great many gland cells there is no accumulation of particulate material to indicate their activity. A typical example of this is the parathyroid gland cell. It possesses the general characteristics of a gland cell; cytological study of its experimental hyperfunctioning shows (De Robertis, 1940, 1941a) that the fundamental organelles undergo the transformation typical of active gland cells; physiological experimentation and biochemical studies clearly show that parathyroid gland cells do manufacture a specific substance; removal of parathyroid glands results in well-known serious disturbances, which are completely reversed by injections of parathyroid extract. Yet, up to date, no histological technique has enabled us to detect the accumulation of a particulate secretory product in parathyroid cells.

It should be pointed out that these negative results may be merely due to the inadequacy of our means of investigation. In the thyroid cell, for instance, all attempts at detecting the "intracellular colloid" had failed until Gersh and Caspersson (1940) used ultraviolet microspectrography. A few years later it was discovered that fixation by freezing and drying preserved the secretion product in thyroid cells in a form stained by Heidenhain's azan (De Robertis, 1941b). Today, the presence of this sub-

stance can consistently be detected by the periodic acid-Schiff method in preparations fixed by any appropriate chemical method.

Thus, morphological study provides indications of the glandular nature of the cell; this becomes highly probable when accumulation in the cell of particulate material can be observed at some stage of the secretory cycle, followed by its expulsion into the external environment at another stage. The absence of a particulate secretory product is never sufficient justification for formally rejecting the possibility of a glandular function.

B. Histophysiological Criteria

Together with the static study of a cell by histological techniques, valuable evidence of the glandular nature of the cell can be obtained by investigation under well-defined experimental conditions of the various functional stages and by observation of the target area of a secretion, and it becomes possible, in some cases, to determine accurately the site where the synthesis of a secretory product takes place in a given cell category of a complex organ. For example, a parallel investigation of the testis and the target organs of the male hormone shows (Ancel and Bouin, 1904) that the androgenic hormones are actually elaborated by the interstitial cells. Similarly it is possible to locate accurately the site of elaboration of the gonadotropic hormones (Herlant, 1956) by comparative study of the pituitary and the reproductive system in animals with a sexual cycle of sufficient duration. In immature or castrated animals, the epithelial cells of the seminal vesicle or the prostate lack the morphological characteristics of gland cells; injections of appropriate amounts of androgenic hormones bring about the apparition of the morphological characteristics of glandular activity together with the physiological secretory phenomena.

It is thus possible by histophysiological means to ascertain the glandular nature of a cell when morphological techniques alone can, at best, lead to presumptions. It is also possible to determine, at the cellular level, the site of elaboration of a secretory product in complex organs; and, in some cases, to obtain precise information on the functional significance of the product synthesized.

C. Physiological Criteria

The use of physiological methods is obviously of great help in the study of glandular cells. In some cases physiological methods provide the conclusive proof when morphological investigation gives no evidence of the glandular nature of a given cell. It may be appropriate here to recall that the concepts of gland and gland cell originated in Ludwig's investigations (1851) on the effects of electrical stimulation of the glosso-

pharyngeal nerves. The true nature of some vertebrate endocrine glands had of course been suspected because of their structure, but only the results of surgical ablation and injection of extracts provided conclusive evidence of the glandular nature of the thyroid, parathyroids, and pituitary. It is often possible by ligature of the excretory duct of an exocrine gland to determine the functional significance of the product elaborated. Supplemented by histological investigations this method can help to determine the site and mechanism of elaboration of the secretory products. Injections of organ extracts are often very helpful in investigating the nature of a secretory product.

In spite of their importance, physiological criteria are not always adequate. They allow the cellular localization of a secretory process only in organs consisting of a single type of cell. The positive results of injection of extracts confirm, of course, the presence in the organ under investigation of a physiologically active product, but not that this product is formed in this organ, since it could be a substance manufactured somewhere else and simply stored there. The progress of our knowledge of the elaboration of the so-called postpituitary hormones (for references see Bargmann, 1954) is a particularly good case in point.

D. Biochemical Criteria

The investigation of any gland involves as essential steps a biochemical study of the secretory product, the elucidation of its chemical structure, and, if possible, its synthesis. This part of the work makes it possible to give chemical significance to the vague notion of a "secretion product." With respect to physiology, biochemical data often permit a better understanding of the functional significance of the products elaborated. The morphological study itself often benefits from the biochemist's work, since accurate knowledge of the chemical composition of the products secreted by the gland cells can help to detect the product itself, or its precursors, in the cytoplasm of the adenocytes. Thus, apart from its intrinsic value in studying the functions of a gland cell, biochemical study can help to determine and demonstrate the glandular nature of a given category of cells.

To sum up, demonstration of the glandular nature of a given category of cells consists of four steps not necessarily taken in the following order: (1) morphological stage, during which the investigator is looking, on the one hand, for the general morphological characteristics of the cell, and on the other, for the accumulation and extrusion of a particulate secretory product; (2) histophysiological stage, which helps to determine the secretory cycle of the cell; this step often provides information on the significance of the product elaborated; (3) physiological stage, which, in some

cases, provides the proof of the glandular nature of the given category of cells and determines the role played by the secretory product; (4) biochemical stage, leading to the replacement of the term "secretion product" by a specific chemical name and a structural formula.

The definition of the gland cell given above obviously implies exclusion of some categories of cells which are, however, undoubtedly secretory in nature. There is no fundamental difference between the elaboration of the secretion granules in the exocrine pancreatic cell on the one hand, and of the vitellus in the oöcyte on the other; and yet, vitellogenesis cannot be accepted as glandular activity because the "secretion product" accumulated in the cytoplasm in particulate form is not extruded in the external or the internal medium. On the other hand, the active participation of the gland cell in manufacturing the secretion product represents one of the essential elements of its definition. This notion, widely accepted since the investigations of R. Heidenhain and his school (for references see Heidenhain, 1880) has unfortunately been forgotten by some more recent authors (Chèvremont, 1956; Verne, 1956) who recognize the existence of "glomerular glands" in which "the cell does not seem to elaborate any product; it merely extracts from the external medium substances which it selects and eliminates without noticeably altering them" (Chèvremont, 1956, p. 320). Such cells, whose very definition corresponds to that of the excretory cells, will be excluded from the present study.

III. Static Study of the Gland Cell

The static inventory of the constituents of the gland cell is complicated by the extreme diversity of structures encountered as soon as we go beyond the best-known mammalian exocrine glands. Moreover, in order to avoid repetition it will be necessary to retain here only those characteristics which are typical of the gland cell and to refer the reader to the other chapters of this book for the general description of nuclear and cytoplasmic organelles.

A. Size

The dimensions of gland cells vary widely. In mammals, the long axis of most gland cells is not more than 15 or 20 μ; there are, however, exceptions. Thus in the cells of the supraparotid gland of the male albino rat the length of the cell can, at some stages of the secretory cycle, reach 45–50 μ (Guyiesse-Pélissier, 1923; Gabe, 1955) (see Fig. 1). The size of gland cells having identical functional significance and elaborating the same chemical compounds can vary markedly with the species; thus the gland cells of urodele amphibians are much larger than the corresponding