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Thyroid Tissue-Organotypic Culture System

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Editorial Note

Thyroid gland is composed of spheroid structures called thyroid follicles, which consist of both many thyrocytes and a few C cells. Each follicle, which is an essential structural and functional unit of the thyroid, is supported by the stroma that contains interfollicular extracellular matrix (ECM), a capillary network and a few stromal cell types such as fibroblasts and inflammatory cells. Thyrocytes have specific structural polarity: their apical pole with numerous microvilli faces the follicle lumen, and their basal side with basal lamina faces the stroma. This is a specialized structure, compared to other endocrine organs, and results in thyroid hormone biosynthesis and release in a basal-apical (follicle lumen)-basal direction by Thyrocytes.

To investigate both thyroid biology and diseases, monolayer and floating culture systems have been developed and widely used. These methods have certainly facilitated the above-mentioned issues of the thyroid. However, the conventional methods, in which thyrocytes are unable to organize follicle structures, cannot satisfactorily provide thyrocytes with normal cellular integration. In contrast, three-dimensional collagen gel culture system allows thyrocytes to achieve follicle structures with their physiological polarity. This method is, thus, suitable for studying the normal and pathologic behaviour of thyrocytes in a microenvironment which more closely simulates physiological conditions. Given that highly integrated thyrocytes function to maintain body homeostasis through their intercommunication with neighboring thyrocytes, C cells, the other cell types, ECM molecules, and cytokines, the highly integrated thyrocyte-based experimental system seems critical for investigating both thyroid biology and disorders.

Thyrocyte monolayer culture initiated by Pulvertaft et al. in 1959 has been used for studying the proliferation and differentiation of thyrocytes. However, monolayer culture cannot satisfactorily enable thyrocytes to achieve normal structural and functional polarities. In this culture system, thyrocytes organize a continuous epithelial pavement, adhering to the surface of the plastic dish, and they show apical-basal polarity, with their apical side with microvilli facing the culture medium, and the basal (attached) side without basal lamina facing the plastic surface of the culture dish. In the epithelial sheet, some thyrocytes organize dome-like structures. The elevation of the cells from the plastic surface results in the formation of these structures, although the exact mechanism by which this occurs remains unclear. Thyrocytes covering these structures show microvilli on the side which contacts the culture medium, and they form foot processes on the luminal side. The plastic surface just under these structures is comprised of an acellular area.

To maintain body homeostasis, stem cells are considered to produce tissue-specific differentiating cell types (hematopoietic, intestinal, epidermal cells etc.) in response to daily cellular loss. Partial defect of tissue is well known to initiate tissue regeneration such as liver regeneration after its partial defect by injury. Thus, the defect of cell population and tissue is considered to be essential for the initiation of these phenomena. As described above, a tissue fragment is largely subdivided into the following two parts: peripheral zone with lower density of cell population and central zone with higher density of cell population. On the basis of this fact, organotypic culture of tissue fragments seems to be a promising model for investigating tissue regeneration and remodeling in vitro. However, only several organotypic cultures of tissue fragments, including thyroid, brain, adipose, and intestinal tissues are successfully established. Thus, various tissues other than these tissues above should be applied to organotypic culture system. In addition, the injection of various stem cell types, including embryonic stem cells and iPS cells into tissue fragments may allow us to study in vitro organogenesis with their proliferation and differentiation in a tissue microenvironment-dependent way. Since these issues are critical for regenerative medicine, further extensive studies are inevitably needed.

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