Immunoreactive Growth Hormone Production by Human Lymphocyte Cell Lines

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SUMMARY

1. Two human lymphocyte cell lines, a T-cell line and a B-cell line, were shown to produce and secrete immunoreactive growth hormone (irGH). The irGH molecules secreted by the two cell lines appeared to be de novo synthesized and their molecular size was similar to that of pituitary GH as well as irGH secreted by peripheral blood lymphocytes.

2. Affinity-purified irGH molecules had human growth hormone (hGH)-like mitogenic activity on Nb2 cells. These findings indicate that the irGH molecules produced by H9 and IM9 were similar to hGH in structure.

3. However, the irGH messages could not be amplified by polymerase chain reaction (PCR) primers which had been demonstrated to be able to amplify reverse-transcribed hGH messenger RNA successfully, suggesting that the lymphocyte-derived irGH and pituitary hGH are not exactly identical molecules.

4. We conclude that the H9 and IM9 cells produce a growth hormone-related molecule whose structure is different from that in the anterior pituitary.

INTRODUCTION

In recent years, numerous bidirectional interactions between the immune system and the neuroendocrine system have been described. Alterations in the neuroen-
Endocrine system affect the immune system, and the reverse is also true. One of the proposed mechanisms for the intersystem communication is the production of neuropeptides by the cells of the immune system. Several of the lymphocyte-derived pituitary hormones have been characterized, such as ACTH, endorphin, thyrotropin (TSH), chorionic gonadotropin, luteinizing hormone, and growth hormone (Smith et al., 1983, 1986; Emanuele et al., 1990; Weigent and Blalock, 1990; Harbour-McMenamin et al., 1986). Since all these hormones can also function as immunomodulators, it is proposed that cells in the immune system are able to produce neuroendocrine hormones, which can in turn have autocrine or paracrine effects on the immunocytes themselves.

In the past two decades, increasing evidence has pointed to the theory that growth hormone (GH) not only is an essential neuroendocrine hormone but also plays an important role in the immune system. GH has been found to have influences on the thymus, the lymphocytes, and the macrophages, both in vitro and in vivo (Kelley, 1990). Recently, production of immunoreactive growth hormone (irGH) by human peripheral blood lymphocytes (PBL) has been reported (Weigent et al., 1988; Hattori et al., 1990). Characterization of lymphocyte-derived irGH molecules indicate that they have molecular weight and bioactivity similar to their pituitary counterpart. Quantitation using a highly sensitive immunoassay showed that PBL secreted irGH at picogram level (Hattori et al., 1990). Furthermore, irGH molecules have been shown to be able to stimulate lymphocyte proliferation, suggesting that irGH may play an autocrine/paracrine role in lymphocyte replications (Weigent et al., 1991).

The use of primary cell cultures for study of irGH production results in an inability to obtain a large, homogeneous cell population and adds difficulty to studies on regulation of irGH secretion. Development of model systems using lymphocyte cell lines could be one way to solve the problem. Similar systems have been developed for TSH and prolactin (Harbour et al., 1989; DiMattia et al., 1988). Previous study suggested that both T and B lymphocytes secrete irGH (Hattori et al., 1990). In the present study, we report identification of a T-cell and a B-cell lymphocyte cell lines which produce irGH molecules as well as their characterization.

**MATERIALS AND METHODS**

**Cell Cultures**

IM9 cells were obtained from the laboratory of Dr E. Brad Thompson, and H9 cells from Dr Miles W. Cloyd, both at the University of Texas Medical Branch in Galveston. The cells were cultured in RPMI 1640 supplemented with either 5% fetal calf serum (GCS) or insulin–transferrin–sodium selenite medium supplement (Sigma). Nb2 cells were provided by Dr Li Yu-Lee of Baylor College of Medicine. GH3 cells were provided by Dr Scott Supowit of University of Texas Medical Branch in Galveston.