ROLE OF HYPOTHALAMIC AND PINEAL POLYPEPTIDE FACTORS IN REGULATION OF FUNCTION OF STEM CELL PRECURSORS OF GRANULO-MONOCYTOPOIESIS

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The role of hypothalamic and pineal polypeptides in the regulation of hematopoiesis has virtually not been studied. For a long time the view was held that the hypothalamic region of the brain influences hematopoietic organs only indirectly [3, 5, 6, 8]. It was later shown that some parts of the hypothalamus contain physiologically active substances of polypeptide nature which have both a stimulating and an inhibitory action on leuko-, thrombo-, and erythrocytopoiesis [1].

The aim of this investigation was to study the effect of hypothalamic and pineal polypeptide factors on function of stem cells which are precursors of granulo-monocytopoiesis.

EXPERIMENTAL METHOD

Hypothalamic and pineal polypeptide factors were obtained from the corresponding parts of the bovine brain by the method described previously [2]. The investigation was conducted with hematopoietic bone marrow cells obtained by sternal puncture from 29 clinically healthy persons.

A bilayer agar system [7] with certain modifications [6] was used. Hematopoietic cells from each bone marrow were cultured in an agar bilayer system in three series of experiments; I) control, II) with addition of hypothalamic polypeptide factor to the top agar layer (1 μg per 10^5 explanted cells), III) with the addition of pineal polypeptide factor to the top agar layer (1 μg per 10^5 explanted bone marrow monocytes). Hematopoietic cells from each bone marrow (10^5 cells) also were cultured in a monolayer agar system (without feeder) as a control of possible spontaneous colony formation. The results were read on the 8th day of culture under the microscope. The colony-forming ability (CFA) of the bone marrow cells was determined as the number of colonies, and the cluster-forming ability (ClFA) as the number of clusters per 10^5 explanted cells. Aggregates containing more than 20 cells were taken as colonies, those containing from 3 to 20 cells as clusters. The colonies were subdivided into small (20-40 cells), medium (40-100 cells), and large (over 100 cells).

TABLE 1. Effect of Hypothalamic and Pineal Polypeptide Factors on ClFA and CFA of Precursor Cells of Granulo-Monocytopoiesis in Human Bone Marrow (M ± m)

Experimental conditions	n	ClFA per 10^5 bone marrow monocytes	CFA per 10^5 bone marrow monocytes	Number of colonies of different sizes		
				20-40 cells	40-100 cells	over 100 cells
Control	29	141,8±10,5	52,6±3,6	24,9±1,8	22,0±1,7	6,4±0,5
Addition of hypothalamic polypeptide factor	11	319,9±53,4*	71,4±3,5*	30,8±2,6	26,7±0,9*	13,6±1,5*
Addition of pineal polypeptide factor	10	130,0±10,2	40,9±2,3*	20,2±1,96	16,9±2,7	4,0±0,9*

Legend. *P < 0.05 compared with control.

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EXPERIMENTAL RESULTS

Unlike bilayer agar cultures, growth of colonies was not found in a single monolayer agar system. Consequently, clonal growth of granulo-monocytic precursor cells depends on the quantity of colony-stimulating factor in the nutrient layer (feeder). In the presence of hypothalamic polypeptide factor both ClFA and CFA of the granulo-monocytopoietic precursor cells were increased; the number of medium and large colonies was significantly increased in this case (Table 1).

During culture of hematopoietic cells with pineal polypeptide factor a moderate decrease in CFA of the precursor cells of granulo-monocytopoiesis was found, mainly on account of precursor cells forming large colonies. Polypeptides isolated from the hypothalamus and pineal gland thus differ in their regulating effect on precursor cells of granulo-monocytopoiesis.

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ACTION OF HEPATIC CHALONES ON HEPATOCYTE PROLIFERATION IN THE INTACT AND DENERVATED LIVER

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A central place in the problem of constancy of cell composition of organs and tissues is currently occupied by the question of interaction between regulatory factors at different levels — from tissue to organism. The proliferative program of a tissue and the initiation and completion of reparative regeneration also are evidently the integrative result of interaction between various factors and the reacting tissue. A matter of great importance in this context is elucidation of the role of the nervous factor in the regulation of cell proliferation and, in particular, its interaction with endogenous tissue regulators of cell divison. The basis for this approach to the problem is formed by data on intensification of proliferative activity of cells in organs with disturbed innervation [1, 5, 9]. However, the mechanisms of this phenomenon are not yet clear.

Accordingly, in the investigation described below, it was decided to study the action of tissue-specific inhibitors of cell proliferation (chalones) on DNA synthesis and mitotic activity in the regenerating denervated animal liver.

EXPERIMENTAL METHOD

Male Wistar rats with an average weight of 140-160 g were used. The rats were divided into two groups: the animals of group 1 served as the control, those of group 2 were subjected to subdiaphragmatic vagotomy 1 week before the experiment. Two-thirds of the liver

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