

pophysal portal blood (27) at the same concentrations (10^{-9} to $10^{-8}M$) that we find release TSH; AVP is located in the external zone of the median eminence in high concentrations (28), as are other releasing factors; AVP receptors are present in the anterior pituitary (29); and experimental (12) and human (13) hypothyroidism results in elevated basal plasma AVP. These observations provide additional support for the hypothesis that AVP is an important, but overlooked, TSH-releasing factor.

Finally, the fact that centrally administered AVP lowers plasma TSH (Fig. 4) but not other hormones is consistent with our observations that hypothalamic-releasing (14) or -inhibiting (30) factors, at the appropriate ventricular dose, produce effects that oppose their direct actions on their respective target cells of the adenohypophysis. Others (31) have supported this concept of negative ultrashort-loop feedback for hypothalamic releasing and inhibiting factors in vitro.

Thus, AVP at physiological concentrations acts specifically on anterior pituitary cells to enhance the release of TSH. The finding that AVP is equipotent with TRH in stimulating TSH release strongly suggests that AVP may indeed be a physiological regulator of TSH secretion. In the hypothalamus, however, AVP may function as a negative autofeedback agent to regulate signals for TSH release.

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32. Supported by NIH grant HD-09988.

21 July 1986; accepted 16 December 1986

Technical Comments

Trans-activator Gene of HTLV-II: Interpretation

We wish to inform the readership of *Science* of a problem in interpretation of our studies of the *trans*-activator gene (*tat*-II) of human T-lymphotropic virus type II (HTLV-II) described in (1). In recent studies of cell surface antigen expression, DNA polymorphisms of the DR- β class II major histocompatibility gene complex, and rearrangements of the T-cell receptor β -chain gene locus, we have determined that the sense *tat*-II gene was not introduced into Jurkat T cells, but rather into another T-cell line, probably HUT 78. We cannot detect either interleukin-2 (IL-2) receptor or IL-2 gene expression in the uninfected HUT 78 T-cell line carried in the Dana-Farber laboratory. Thus, the original conclusion that the *tat*-II gene induced the expression of these cellular genes may be correct. However, we have also demonstrated that this HUT 78 T-cell line, while monoclonal at the DR- β gene locus, is a polyclonal population of cells as judged by the presence of multiple T-cell receptor β -chain gene rearrangements. Therefore, it is possible that the expression of the IL-2 receptor and IL-2 genes observed in the four *tat*-II clones studied could reflect the outgrowth of undetectable subpopulations of cells that express these cellular gene products independent of the presence of the *tat*-II gene. However, in support of a specific effect of the *tat*-II protein, the National Cancer Institute and Dana-Farber laboratories have observed that this gene product induces the IL-2 receptor promoter and partially activates the IL-2 promoter in transient cotransfection assays

in Jurkat T cells. In addition, using Jurkat on HSB-2 T cells, Inoue and colleagues have described activation of both the IL-2 receptor and IL-2 genes by the *tat*-I gene isolated from HTLV-I (2), which shares similar structural and functional properties with the *tat*-II gene. Each of our three laboratories has also confirmed activation of the IL-2 receptor promoter by the *tat*-I gene product. The reintroduction of the *tat*-II gene into Jurkat T cells is currently being attempted.

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2 February 1987; accepted 4 February 1987

Trans-activator gene of HTLV-II: interpretation

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Science **235** (4792), 1073.

DOI: 10.1126/science.3029865

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