

IMMORTALIZED LHRH NEURONS CONTAIN TRANSCRIPTS AND ACTIVITIES FOR MULTIPLE DEGRADATIVE ENZYMES

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Hypothalamic LHRH is secreted into the blood to regulate gonadotropin release from pituitary and it is also known to exert actions in brain. Termination of these activities is thought to occur through degradation of the decapeptide. *In vitro* LHRH is degraded by angiotensin-converting enzyme (ACE), neutral endopeptidase (NEP), metalloendopeptidase (MEP), and prolyl endopeptidase (PEP). To determine whether the immortalized LHRH neurons express these genes, Northern blots were run. Single hybridizing bands of 2.6 and 3.0 kb were seen for MEP and PEP, respectively; while two species were each discerned for ACE (2.3 and 4.15 kb) and NEP (2.4 and 4.4 kb). Preliminary studies reveal that forskolin increases NEP expression within 30 min, while it is reduced from 4-24 h with chronic treatment. Phorbol ester exerts little effect. To evaluate actions on enzyme activity, GT1 cells were treated with drugs, cell extracts were incubated with [³H]-LHRH, and products were separated by TLC. Five products were identified: LHRH-[1-2], [1-3], -[1-4], -[1-5], and -[1-6]. Only phorbol ester treatment, not forskolin, affected their production. The differential drug effects on gene expression and activity indicate that these processes are regulated independently in the GT1 neurons. Moreover, since some LHRH degradative products have bioactivities on their own, these findings suggest that LHRH and its fragments may be able to regulate multiple signaling cascades through autocrine, paracrine, and endocrine actions.

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