spontaneous motor activity. As a neurotransmitter candidate, it modifies the rate of discharge of neurons and the secretion of monoamine analgesics, such as hypnotics, sedatives, and anticonvulsants.

This potent, but structurally simple, peptide was first isolated from hundreds of kilograms of brain extracts to yield only milligram quantities of peptide. Upon hydrolysis of the highly purified ovine and porcine extracts, only three amino acids were found in equimolar amounts. As an approach to TRF's characterization, all possible permutations of these three amino acids were synthesized and yielded six peptides, none of which was active. Upon cyclization of the N-terminus glutamic acid and amidation of the C-terminus proline in the sequence of Glu-His-Pro, a fully blocked tripeptide was obtained that had all of the characteristics of the natural hormone, including its biological activity. To date, innumerable syntheses have been reported which have included classical and solid-phase approaches. Several hundred analogues of TRF have been synthesized. Some of the analogues are more potent than others, while some are selective in action on the central nervous system.