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### **Carboxyl-terminal Parathyroid Hormone (CPTH); Prediction of Novel Functions, Structural Features and Potential receptor.**

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#### *Abstract:* Background:

Parathyroid hormone (PTH) is the major physiological regulator of blood calcium and phosphate, and it exerts potent effects upon cells in bone, cartilage, and kidney. The PTH1 receptor (PTH1R) recognizes the highly conserved amino (NH<sub>2</sub>)-terminal domain of PTH (and the homologous NH<sub>2</sub> terminus of PTHrP) and thus is fully activated by both PTH-(1-34) and the intact hormone, PTH-(1-84). Carboxyl (C) fragments of intact PTH-(1-84), such as PTH-(39-84) or PTH-(53-84), do not bind or activate the PTH1R. A possible physiological role for this region of the hormone is suggested by observations that the amino acid sequence of the COOH-terminal domain is highly homologous across species. Furthermore, direct physical evidence of a putative receptor, i.e., a carboxyl-terminal PTH receptor (CPTHR) with binding specificity for COOH-terminal PTH sequences, was obtained by cross-linking of <sup>125</sup>I-[Tyr<sup>34</sup>]-hPTH-(19-84) (which does not bind to the PTH1R) to 40-kDa and 90-kDa proteins in the ROS 17/2.8 rat osteosarcoma cell line.

#### Objectives:

To characterize CPTH functional and structural features using bioinformatic analytical tools. The premise is that such characterization would allow for future experimental examinations on the pathophysiology of diseases involving significant changes in CPTH expression levels or mode of function.

Methods: Several bioinformatic tools were utilized including Pfam, ELM, ProFun, PFP, Consensus Secondary Structure Prediction server and I-TASSER.

#### Results:

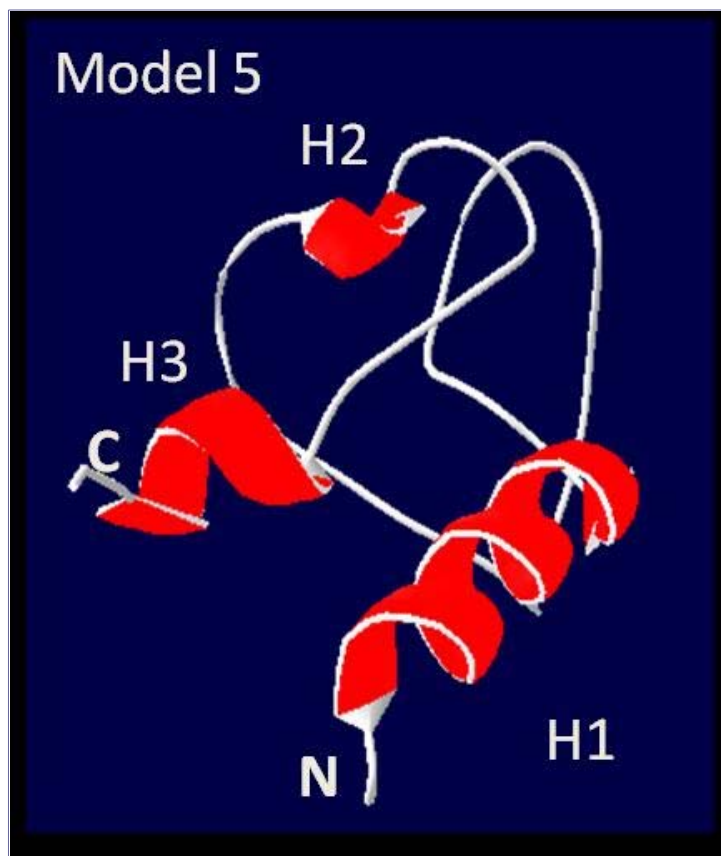
1- ELM predicted N-Arg dibasic convertase cleavage site at position 40-42, Casein Kinase II (CK2) phosphorylation site (71-74), Protein kinase C phosphorylation site (53-55).

2- Function prediction analysis suggested that CPTH may play a role in the following biological processes; cell proliferation (growth factor), cAMP metabolism, cell-cell signaling, calcium ion homeostasis, GTPase activity and GTP binding.

3-Secondary and Tertiary structure predictions suggested that CPTH has two helical domains on its termini at positions (23-35) and (74-83) as well as coils and sheets regions in the middle (36-73).

Conclusions:

CPTH bioinformatic analysis data provide useful resources for researchers to understand and manipulate CPTH



functions and to predict potential CPTH receptor(s).

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**Author Disclosure Information:** A.A. Selim, None.

**Category (Complete):** E. Growth Factors, Cytokines, Immunomodulators ; B. Osteocytes

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