

KISSPEPTIN: A CENTRAL REGULATOR OF REPRODUCTION IN THE BITCH

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Kisspeptin (KISS1) and its receptor (KISS1R) are essential for normal reproductive function in many species. However, the role of KISS1-KISS1R signaling in the dog is unknown. Aims of this study were to identify the canine *KISS1* and *KISS1R* genes and to characterize the amino acid sequences of KISS1 and KISS1R. Subsequently the effect of kisspeptin on the hypothalamic-pituitary-gonadal axis in the dog was studied by performing KP10 (shortest biological active form of kisspeptin) stimulation tests using different doses of KP10.

Canine *KISS1* and *KISS1R* genes were localized by comparing the reference dog genome build 2.2, with the relevant human cDNA sequences using BLASTn software. The predicted mRNA of preprokisspeptin encodes a peptide of 111 amino acids. The amino acid sequence of canine KP10 differs at positions 5 and 10 from human KP10. The predicted mRNA for the canine KISS1R encodes a protein of 382 amino acid residues. The amino acid sequences of the canine and the human kisspeptin receptor were 75% identical.

Canine KP10 was administered intravenously at weekly intervals to 6 adult Beagle bitches during anestrus using the following doses: 0 (control, NaCl 0.9%), 1, 5, 10, 30, 50, and 100 $\mu\text{g}/\text{kg}$ per stimulation test. Blood samples were collected at -40 and 0 min before, and 10, 20, 30, 40, 60, 90 and 120 min after canine KP10 administration, for measurement of the plasma LH concentration. There was a significant increase in plasma LH concentrations after all administered canine KP10 doses, (Figure 1). There was no significant difference in LH response between the doses.

In conclusion, the *KISS1* and *KISS1R* genes are present in the canine genome and intravenous administration of canine KP10 results in increased LH secretion. This strongly suggests that KISS1-KISS1R signaling plays a key regulation role in canine reproduction.

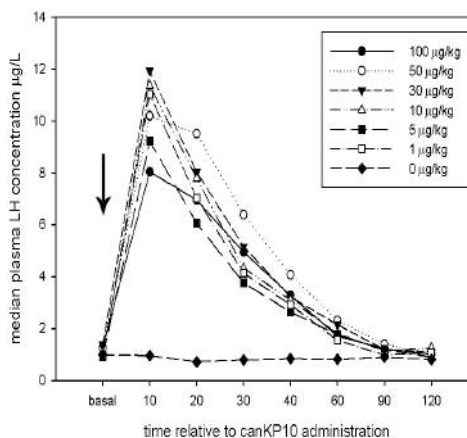


Figure 1. Median plasma LH concentrations after different dosages of KP10 administration (arrow).