Compared to the full-length metastin protein, the N-terminally truncated peptide metastin (45–54) has 3–10 times higher receptor affinity and selectivity for KISS1R receptors.

Kisspeptin is a member of the RFamide neuropeptide family that is expressed in the hypothalamic GnRH neurons.1 In turn, GnRH activates pituitary release of luteinizing hormone (LH) and follicle stimulating hormone (FSH) into the circulation to regulate testicular testosterone levels.

Continuous subcutaneous administration of KISS1R agonists induces a transient increase in plasma testosterone, followed by sustained (up to 4 weeks) reduction of plasma testosterone to castrate levels in a manner that is more rapid and profound than those induced by the GnRH agonist analogue leuprolide.4

KISS1R receptor agonists and antagonists have been explored to investigate the biology of targeting the KISS1 receptor. Reported metastin (45–54) analogues with higher agonist activity and improved metabolic stability suppresses plasma testosterone in male rats with continuous subcutaneous administration.4 In addition, a KISS1R agonist has reached phase 1 clinical testing.

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Kisspeptin is a member of the RFamide neuropeptide family that is implicated in gonadotropin secretion. KISS1 expression in the brain has a prognostic relevance in prostate cancer. Further studies are in progress to evaluate the lead KISS1R agonist peptides in multiple indications.

**References**