Metastin

Phoenix kit detects levels in early pregnancy

p234: Kisspeptin Antagonist

Decreased plasma levels of metastin in early pregnancy are associated with small for gestational age neonates.

OBJECTIVE: To investigate whether pregnancies with small for gestational age (SGA) neonates, defined as customized birth weight below the 10th centile, are associated with altered levels of metastin in maternal plasma in the first trimester.
STUDY DESIGN: Maternal blood was obtained between 8 and 14 weeks of pregnancy. Levels of metastin were measured in pregnancies with (n = 31) or without SGA-neonates (n = 31), matched for gestational age at venipuncture. Measurement of beta-hCG was included to study the influence of gestational age and placental volume on plasma levels of the measured markers.
RESULTS: Metastin was significantly lower in SGA-pregnancies compared to an equal number of matched uneventful pregnancies (metastin: 1376 +/- 1317 pmol/L vs 2035 +/- 1260 pmol/L, p = 0.035; mean +/- standard deviation)(Cat. # : RK-048-56). beta-hCG levels were not different.
CONCLUSION: Metastin is significantly lower in maternal plasma in the first trimester, in pregnancies with SGA-neonates. It might therefore be used in combination with other markers for risk estimation of growth impairment in the first trimester.
Smets et al. Prenat Diagn. 2008 Apr;28(4):299-303.

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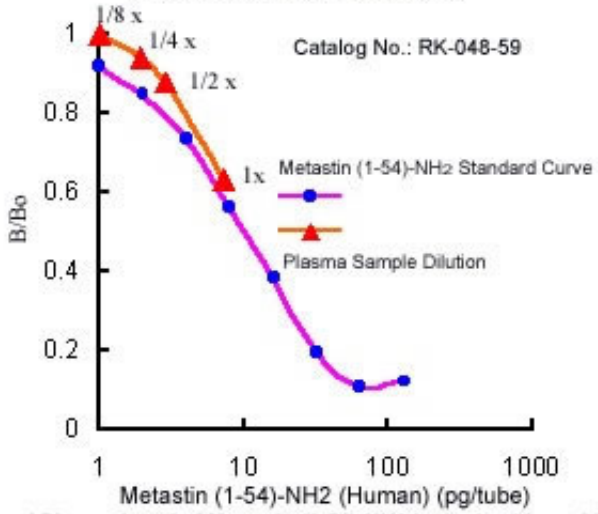
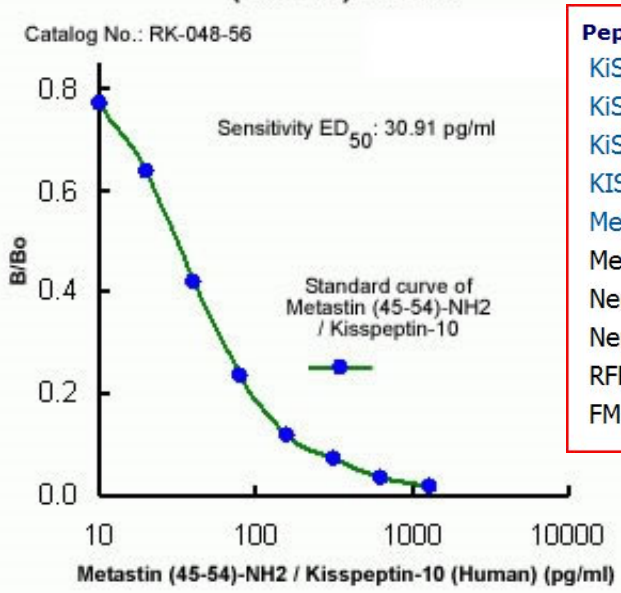
Detection of Metastin (1-54)-NH2 plasma level by Metastin (1-54)-NH2 RIA Kit



Normal Plasma Level of Metastin (1-54)-NH2 in the healthy subjects: 9 pg/ml (n=15)

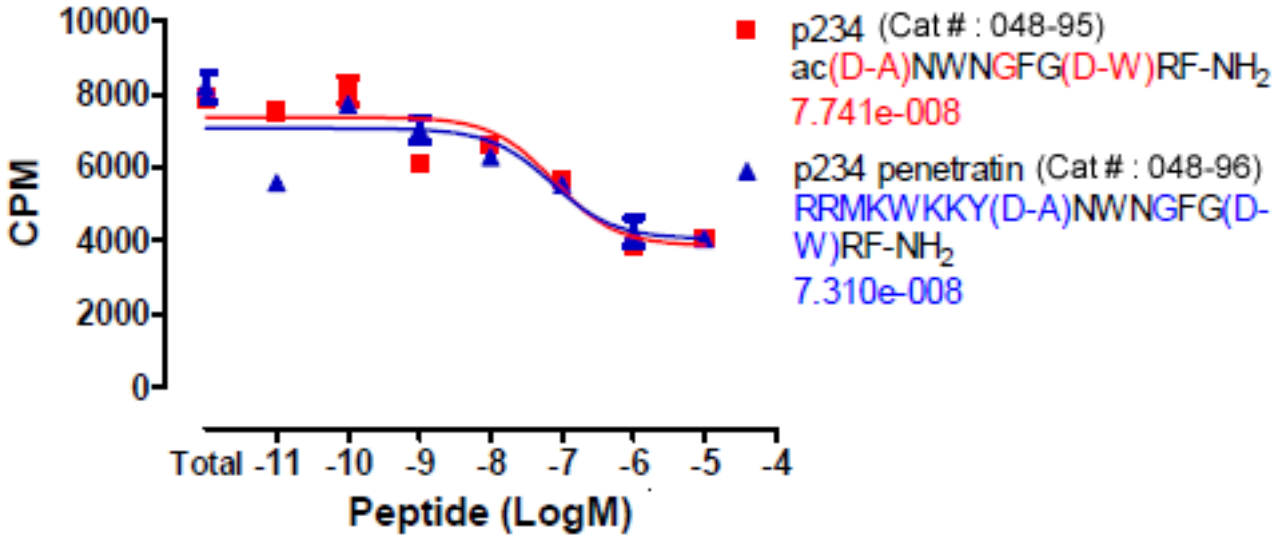
Peptide	% Cross-reactivity
KiSS-1 (112-121)/Metastin (45-54)-NH2 (Human)	100
KiSS-1 (68-121) Amide / Metastin (1-54) Amide (Human)	100
KiSS-1 (68-119) Amide (Mouse)	0
KISS-1, Prepro (20-65) (Mouse)	0
Metastin (Rat)	0
Metastin (26-54)-NH2, [pGlu26] (Human)	25
Neuropeptide AF (NPAF) (Human)	4
Neuropeptide FF (NPFF) (Human)	0
RFRP-3 (Human)	0
FMRF-NH2	0

Metastin (45-54)-NH2 / Kisspeptin-10 (Human) RIA Kit



Peptide	% Cross-reactivity
KiSS-1 (112-121)/Metastin (45-54)-NH2 (Human)	100
KiSS-1 (68-121) Amide / Metastin (1-54) Amide (Human)	100
KiSS-1 (68-119) Amide (Mouse)	0
KISS-1, Prepro (20-65) (Mouse)	0
Metastin (Rat)	0
Metastin (26-54)-NH2, [pGlu26] (Human)	25
Neuropeptide AF (NPAF) (Human)	4
Neuropeptide FF (NPFF) (Human)	0
RFRP-3 (Human)	0
FMRF-NH2	0

Comparison of binding for p234 vs. p234-penetratin in CHO cells stably expressing human GPR54



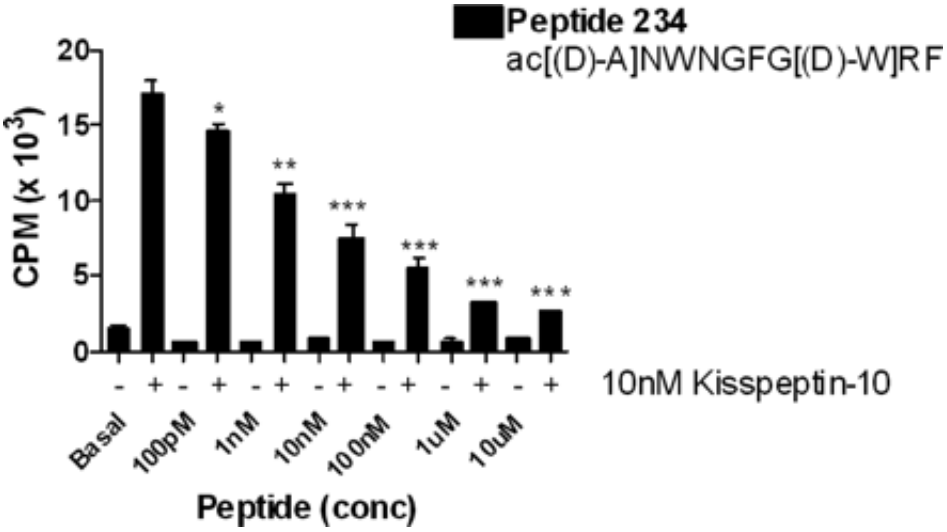
Critical roles of kisspeptins in female puberty and preovulatory gonadotropin surges as revealed by a novel antagonist.

Kisspeptins (Kp) have recently emerged as master regulators of the reproductive axis and among the most potent elicitors of GnRH-gonadotropin secretion. Despite their paramount importance in reproductive physiology and their potential therapeutic implications, development of Kp antagonists has remained elusive, and only recently has the first compound with the ability to block Kp actions in vitro and in vivo, namely p234, been reported. However, previous in vivo studies all used acute central injections, whereas characterization of the effects of the antagonist after continuous or systemic administration, which poses pharmacological challenges, is still pending. We report herein a comprehensive series of analyses on the impact of continuous intracerebroventricular infusion of p234 on puberty onset and the preovulatory surge of gonadotropins in the female rat. In addition, the effects of systemic (ip) administration of a tagged p234-penetratin, with a predicted higher permeability at the blood-brain barrier, on Kp-10 induced gonadotropin secretion were evaluated. Central infusion of p234 to pubertal females delayed vaginal opening and decreased uterine and ovarian weights at the expected time of puberty, without affecting body weight. Likewise, chronic intracerebroventricular administration of p234 for 4 d prevented the preovulatory surges of LH and FSH. In addition, systemic (ip) administration of p234-penetratin significantly attenuated acute LH and FSH responses to Kp-10, either after intracerebroventricular or ip injection of Kp. Our data document the validity of p234 for antagonizing Kp actions in vivo and provide direct experimental evidence for the important role of Kp signaling in the key events of female reproduction, such as puberty onset and the preovulatory surge of gonadotropins.
Pineda et al. Endocrinology. 2010 Feb;151(2):722-30.

Discovery of potent kisspeptin antagonists delineate physiological mechanisms of gonadotropin regulation.

Neurons that produce gonadotropin-releasing hormone (GnRH) are the final common pathway by which the brain regulates reproduction. GnRH neurons are regulated by an afferent network of kisspeptin-producing neurons. Kisspeptin binds to its cognate receptor on GnRH neurons and stimulates their activity, which in turn provides an obligatory signal for GnRH secretion, thus gating down-stream events supporting reproduction. We have developed kisspeptin antagonists to facilitate the direct determination of the role of kisspeptin neurons in the neuroendocrine regulation of reproduction. In vitro and in vivo studies of analogues of kisspeptin-10 with amino substitutions have identified several potent and specific antagonists. A selected antagonist was shown to inhibit the firing of GnRH neurons in the brain of the mouse and to reduce pulsatile GnRH secretion in female pubertal monkeys; the later supporting a key role of kisspeptin in puberty onset. This analog also inhibited the kisspeptin-induced release of luteinizing hormone (LH) in rats and mice and blocked the postcastration rise in LH in sheep, rats, and mice, suggesting that kisspeptin neurons mediate the negative feedback effect of sex steroids on gonadotropin secretion in mammals. The development of kisspeptin antagonists provides a valuable tool for investigating the physiological and pathophysiological roles of kisspeptin in the regulation of reproduction and could offer a unique therapeutic agent for treating hormone-dependent disorders of reproduction, including precocious puberty, endometriosis, and metastatic prostate cancer.
Roseweir et al. J Neurosci. 2009 Mar 25;29(12):3920-9.

Peptide 234 is a potent inhibitor of kisspeptin-10 stimulation of IP.



Substitution of Leu8 with D-Trp in combination with Ser5 substitution with Gly created potent antagonists (see supplemental Table S1, available at www.jneurosci.org as supplemental material). Additional substitution of Tyr1 with D-Ala (234 shown here) enhanced this (*p < 0.05, **p < 0.01, ***p < 0.001). Peptide 234 alone had no intrinsic IP stimulation. Bars show mean ± SEM of five experiments.
Roseweir et al. J Neurosci. 2009 Mar 25;29(12):3920-9.

Catalog No.	Name	Size
048-95	p234 - Kisspeptin Antagonist	200 µg
048-96	p234 penetratin - Kisspeptin Antagonist	200 µg
RK-048-59	KiSS-1 (68-121) Amide / Metastin (1-54) Amide (Human) - RIA Kit	1 kit
RK-048-56	KiSS-1 (112-121) Amide / Kisspeptin-10 / Metastin (45-54) Amide (Human) - RIA Kit	1 kit