

Neuropeptide Y (NPY) mediator of feeding

Introduction

Neuropeptide Y (NPY), a peptide with 36 amino acid residues, is one of the most abundant neuropeptides in both the peripheral and the central nervous systems. It belongs to the pancreatic polypeptide family of peptides. (Fig. 1) Like its relatives, peptide YY (PYY) and pancreatic polypeptide (PP), NPY is bent into hairpin configuration that is important in bringing the free ends of the molecule together for binding to the receptors.

Structure of Pancreatic Polypeptide family

NPY, human	YPSKP	DNPGE	D	A	PA	E	DMAR	Y	YSA	LR	H	Y	I	N	L	I	TR	Q	R	Y-amide
PYY, human	YPIKP	EAPGE	D	A	SP	E	ELNR	Y	YAS	LR	H	Y	L	N	L	V	TR	Q	R	Y-amide
PP, human	APLEP	VYPGD	N	A	TP	E	QMAQ	Y	AAD	LR	R	Y	I	N	M	L	TR	P	R	Y-amide

Several receptor subtypes for the NPY-family peptides have been described pharmacologically using organ preparations from different species. The best characterized are Y1 and Y2 receptors, both of which bind to NYP as well as PYY. The Y3 receptor has preference for NPY over PYY, whereas a separate subtype binds most strongly to PYY. (Table 1) Also, PP has been reported to have a distinct receptor with unique properties. The feeding response seems to be mediated by a receptor with unique properties.

Ligands	NPY receptor sub-types
NPY(1-36)	Y1, Y2, Y3
PYY(1-36)	Y1, (Y2)
[Pro34] NPY(1-36)	Y1
NPY(2-36)	Y2
NPY(3-36)	Y2
NPY(13-36)	Y2
[Leu31, Pro34]NPY(1-36)	Y1, (Y3)
N-Ac-[Leu28,31]NPY(24-36)	Y2

NPY exerts a wide range of effects in the central nervous system (CNS) and the periphery. Its CNS actions include major effects on feeding and energy expenditure, and alterations in heart rate, blood pressure, arousal and mood. In the periphery, NPY causes vasoconstriction and hypertension; it is also found in the gastrointestinal and urogenital tract, implicating its functions by action upon gastrointestinal and renal targets. In recent studies, hypothalamic NPY has been

found to play a fundamental role in developing the features of obesity, it is a major transducer in the pathways signaling body fat to the hypothalamus, and in regulating body fat content. Leptin, an obese gene product, has been found to decrease NPY gene expression in obese (*ob/ob*) mice. Insulin and corticosteroids are also involved in the regulation of hypothalamic NPY synthesis, with insulin decreasing and corticosteroids increasing NPY expression.

In the past few years, several peptide and nonpeptide NPY receptor antagonists have been developed. Among them, BIBP3226 (Fig. 2), a nonpeptide compound with low molecular weight, is the most widely studied Y1 receptor antagonist.

Other peptide antagonists (e.g., 1229U91) also show very interesting Y1 receptor antagonist properties. (Fig. 3) It is, however, unclear whether these antagonists will specifically inhibit NPY-evoked feeding (Fig. 3). It seems increasingly likely, with the significance of NPY system, that it will provide the significant therapeutic potential for treatment of obesity and other diseases.

American Peptide Company, Inc.

Headquarters

777 East Evelyn Ave.
Sunnyvale, CA 94086
USA

Phone: (408)733-7604

Fax: (408)733-7603

cGMP Manufacturing

1271 Avenida Chelsea
Vista, CA 92081
USA

Phone: (760) 597-8820

Fax: (760) 597-8816

Toll free: phone/ (800) 926-8272 fax/ (888) 670-0070

Email: sales@americanpeptide.com,

URL: www.americanpeptide.com