

## New Product Highlights

### [cPP<sup>1-7</sup>,NPY<sup>19-23</sup>,Ala<sup>31</sup>,Aib<sup>32</sup>,Gln<sup>34</sup>]-Pancreatic Polypeptide (human): An agonist for the Y<sub>5</sub> neuropeptide Y receptor

Neuropeptide Y (NPY; Prod. Nos. [N 5017](#), [N 3266](#)) is the most abundant neuropeptide in brain. It consists of 36 amino acid residues that share high sequence homology with pancreatic polypeptide (PP; Prod. Nos. [P 9903](#), [P 6410](#)) and peptide YY (PYY; Prod. No. [P 1306](#)). The various biological effects of NPY and its homologs are mediated by the activation of at least five types of G protein-coupled receptors, designated as Y<sub>1</sub> (Prod. No. [N-186](#)), Y<sub>2</sub>, Y<sub>4</sub>, Y<sub>5</sub> and y<sub>6</sub>. There has been particular interest in the Y<sub>1</sub> and Y<sub>5</sub> receptors, since they have been associated with the stimulatory effects of NPY on food intake [1,2].

Sigma-RBI is pleased to introduce the first potent and selective agonist for the Y<sub>5</sub> neuropeptide Y receptor, [cPP<sup>1-7</sup>,NPY<sup>19-23</sup>,Ala<sup>31</sup>,Aib<sup>32</sup>,Gln<sup>34</sup>]-pancreatic polypeptide (human) (Prod. No. [P 4118](#)). This polypeptide exhibits high affinity for the human Y<sub>5</sub> neuropeptide Y receptor expressed in HEK-293 cells, possessing an

IC<sub>50</sub> value of 0.24 nM as compared with an IC<sub>50</sub> value of 0.6 nM obtained for NPY [3]. In contrast, the synthetic polypeptide exhibited IC<sub>50</sub> values of 530, >500 and 51 nM, respectively, versus human Y<sub>1</sub>, Y<sub>2</sub>, and Y<sub>4</sub> receptors expressed in BHK cells [3]. In *in vivo* experiments, [cPP<sup>1-7</sup>,NPY<sup>19-23</sup>,Ala<sup>31</sup>,Aib<sup>32</sup>,Gln<sup>34</sup>]-pancreatic polypeptide (human) induced long-term stimulation of food intake in rats when administered centrally, thereby supporting the hypothesis that the Y<sub>5</sub> receptor as an orexigenic receptor [3].

In summary, [cPP<sup>1-7</sup>,NPY<sup>19-23</sup>,Ala<sup>31</sup>,Aib<sup>32</sup>,Gln<sup>34</sup>]-Pancreatic Polypeptide (human) will serve as an important research tool for studying the Y<sub>5</sub> neuropeptide Y receptor and its role in regulating food intake.

#### References:

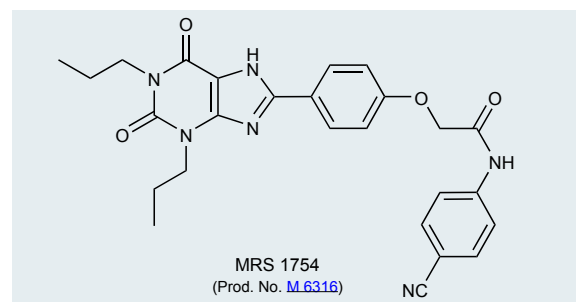
1. Lecklin, A., et al., *Br. J. Pharmacol.*, **135**, 2029-2037 (2002).
2. Pralong, F.P., et al., *FASEB J.*, **16**, 712-714 (2002).
3. Cabrele, C., et al., *J. Biol. Chem.*, **275**, 36043-36048 (2000).

### MRS 1754: A selective A<sub>2B</sub> adenosine receptor antagonist

Adenosine (Prod. No. [A 9251](#)) receptors have been implicated in the etiology of various cardiovascular, inflammatory and neurological diseases. Certain Alkylxanthine derivatives, such as caffeine (Prod. No. [C 8960](#)) and theophylline (Prod. No. [T 1633](#)), are antagonists at adenosine receptors with the latter compound having been used in the treatment of asthma. Four adenosine receptor subtypes have been identified and are referred to as A<sub>1</sub>, A<sub>2A</sub>, A<sub>2B</sub> and A<sub>3</sub>. A<sub>2B</sub> adenosine receptors stimulate adenylyl cyclase, increase intracellular calcium release and are involved in the control of vascular tone, cell growth and gene expression, mast cell degranulation and intestinal water secretion [1]. While A<sub>2B</sub> adenosine receptor antagonists such as ZM 241385 and I-ABOPX have been identified, these compounds are not selective and display significant interaction with other adenosine receptor subtypes.

Sigma-RBI is pleased to introduce MRS 1754 (Prod. No. [M 6316](#)), a selective, high-affinity A<sub>2B</sub> adenosine receptor antagonist. [<sup>3</sup>H]-MRS 1754 bound to human A<sub>2B</sub> and A<sub>2A</sub> adenosine receptors expressed in HEK-293 cells with K<sub>D</sub> values of 1.13 nM and >50 nM,

respectively [2]. In contrast, it did not bind to membranes expressing rat or human A<sub>1</sub> or A<sub>3</sub> receptors. MRS 1754 also displaced both [<sup>3</sup>H]-ZM 241385 and [<sup>125</sup>I]-I-ABOPX from human A<sub>2B</sub> adenosine receptors with K<sub>i</sub> values of 1.97 nM [2], in addition to displacing [<sup>3</sup>H]-MRS 1754 from the same receptors with a K<sub>i</sub> value of 1.45 nM [2]. MRS 1754, therefore, represents a highly selective tool with which to study the physiology of A<sub>2B</sub> adenosine receptors.



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1. Kim, Y-C., et al., *J. Med. Chem.*, **43**, 1165-1172 (2000).
2. Ji, X-D., et al., *Biochem. Pharmacol.*, **61**, 657-663 (2001).