

# PYY analogue - Y2 selective

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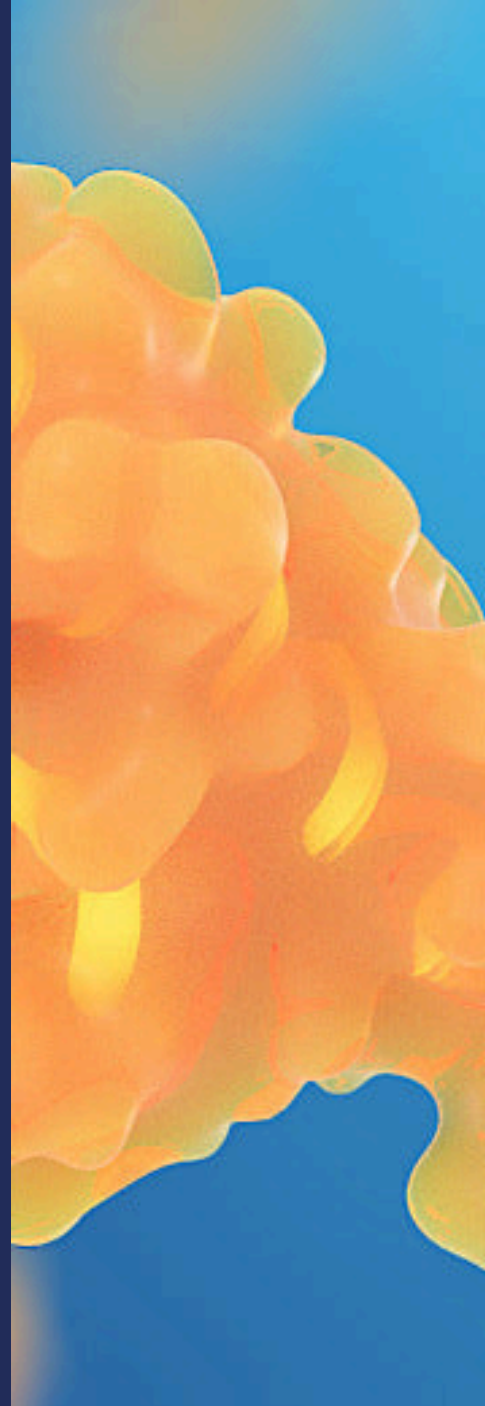
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# PYY analogue - Y2 selective

PYY is secreted from the L-cells in the intestine in response to a meal. The PYY1-36 is rapidly cleaved to PYY3-36 and this analogue bind and activate selectively the Y2 receptor. PYY3-36 is also quite rapidly degraded to the inactive version PYY3-34. The Y2 receptor belongs to a the NPY family of receptors that comprise four receptors Y1, Y2 Y4 and Y5. It is a satiety factor and lowers food intake as well as glucose regulation. In combination with GLP-1 which is also co-secreted from the L-cells the effects are potentiated.

NNC0165-1273 is a modified PYY3-36 analogue with increased selectivity for Y2 against Y1, Y4 and Y5 receptors. It is modified in the C-terminal position 35 where the arginine has been replaced with beta-homo-arginine and Leu30 has been replaced by Trp30. In the Østergaard *et al.* 2018 reference listed in the reference section, NNC0165-1273 is peptide **29**. The C-terminal modification results in a slightly lower Y2 activity, but much improved selectivity and it also stabilizes against C-terminal degradation.

Category	PYY
ID	NNC0165-1273
Amount pr. vial	1000 nmol

# Calculated properties

Property	NNC0165-1273	PYY3-36
MW (Da)	4163.5	4049.5
pI (calculated)	8.5	8.5
Seauence substitutions (compared to reference)	30 tryptophan and 35-beta-homo-arginine	-
Extinsion coefficient (calculated, 280nm)	11460	11460

Selected calculated properties for NNC0165-1273 and PYY3-36 (NNC0165-0020).

# Structural information



**Figure 1**



**Figure 2**

**Figure 1**

2D sketch of NNC0165-1273. Compared to native PYY, NNC0165-1273 has a beta-homo-arginine in position 35.

**Figure 2**

2D sketch of the sequence of native PYY (3-36)-NH<sub>2</sub>.

# *In vitro* data

NPY receptor scintillation proximity assays (SPA) were performed using cell membrane preparations from cell lines expressing one of the human Y1, Y2, Y4, or Y5 receptors. Reduction of cyclic adenosine monophosphate (cAMP) through Gi-coupled Y receptor activation was measured using human embryonic kidney (HEK) 293 cells stably expressing one of the human Y1, Y2, Y4, or Y5 receptors and a cAMP-sensitive calcium channel. See the Østergaard *et al.* 2018 reference listed in the reference list for further data and details on the experimental setup of the *in vitro* assays.

Receptor binding data ( $K_i$ , nM)				
Compound	Y1	Y2	Y4	Y5
PYY3-36	40	0.40	13	3.2
NNC0165-1273	1000	2.0	2500	1300

Potency data (EC50, nM)				
Compound	Y1	Y2	Y4	Y5
PYY3-36	16	1.0	>30	7.9
NNC0165-1273	>1000	5.0	>1000	790

Y1, Y2, Y4, Y5 are NPY receptor subtype 1,2,4, and 5, respectively

# *In vivo* data

For *in vivo* data, please see the Jones *et al.* 2019 reference listed in the reference section.

# Reference Compound

The reference compound to NNC0165-1273 is PYY3-36 (NNC0165-0020). Please indicate (with a check mark at 'Please add the reference compound if available) during your compound request if you would like to have PYY3-36 (NNC0165-0020) included in your shipment

# Compound handling instructions

The PYY peptides are easily dissolved in MilliQ water or DMSO. Avoid stock solutions at neutral pH since this is close to pI. Peptides and proteins have a tendency to adhere to glass and plastic surfaces. This may at low concentration impact the actual amount in solution. To minimize this unspecific adherence, adding detergents or inert proteins like e. g., ovalbumin or other serum albumins to the solution can minimize this phenomenon. In case albumins are added to peptide/protein solutions, ensure that the albumins are free of any proteases, but be aware that it will affect the apparent potency and affinity in in vitro assays in case a fatty acid is attached to the compound.

# References

- 1. Østergaard S et al.**  
Design of Y2 Receptor Selective and Proteolytically Stable PYY336 Analogues  
*J Med Chem.* 2018;61(23):10519-10530
- 2. Jones ES et al.**  
Modified peptide YY molecule attenuates the activity of NPY/AgRP neurons and reduces food intake in male mice  
*Endocrinology.* 2019;160(11):2737-2747