COMPOUND DETAILS NNC9204-1702

Partial glucagonR agonist

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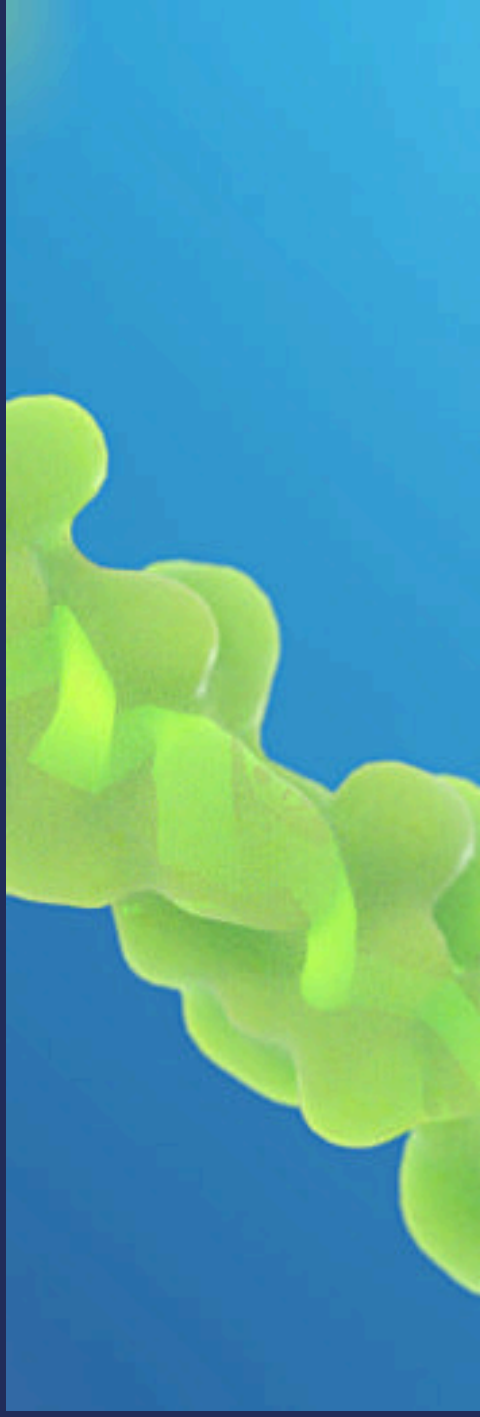
Content



Partial glucagonR agonist

Glucagon is s a 29 amino acid residue peptide hormone produced by the alpha-cells in the pancreas. Together with insulin it regulates blood glucose levels. It stimulates release of glucose from the liver at low blood glucose levels by increasing gluconeogenesis and glycogenolysis, and by suppressing glycolysis. Glucagon is used to treat insulin-induced severe hypoglycemia.

NNC9204-1702 is a partial glucagon receptor agonist.

Category	Glucagon
ID	NNC9204-1702
Amount pr. vial	1000 nmol

Calculated properties

Property	NNC9204-1702	Glucagon
MW (Da)	3900.1	3482.7
pI (calculated)	3.7	6.4
Sequence substitutions (compared to rerefence);	desHis1, Glu9, Lys24(4xgGlu-Ac)	-
Extinction coefficient (calculated, 280 nm)	8480	8840

Structural information

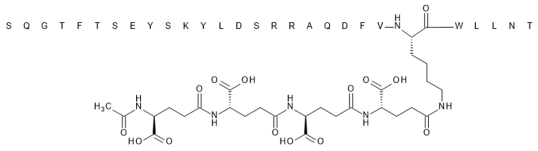


Figure 1

H S Q G T F T S D Y S K Y L D S R R A Q D F V Q W L M N T

Figure 2

Figure 1

2D sketch of the structure of NNC9204-1702. Compared to native glucagon, the N-terminal histine has been removed, a glutamic acid is present in position 9 and Ac-4xgGlu has been attached to the lysine in position 24. A crystal structure of GCGR-NNC9204-1702 complex is shown in the Zhang et al 2018 reference.

Figure 2

2D sketch of the sequence of native glucagon.

In vitro data

The binding affinity to human GCGR was measured by the ability of the compounds to displace 125-iodine-labelled glucagon from baby hamster kidney (BHK) cell plasma membranes stably expressing the human GCGR in a scintiallation proximity assay (SPA) setup. The *in vitro* potencies were determined by luciferase assays using BHK cells stably transfected with the human GCGR and CRE luciferase. Please see the Zhang *et al.* 2018 reference listed in the reference section for further details on the experimental setup of the *in vitro* assays.

Compound	Affinity (IC50, nM ± SEM)	Potency (EC50, nM ± SEM)
NNC9204-1702	12.8 ± 6.6	16.2 ± 8.4
Glucagon	1.2 ± 0.5	22.8 ± 18.2

BHK: baby hamster kidney; GCGR: glucagon receptor; SPA: scintillation proximity assay

Reference Compound

The reference compound to NNC9204-1702 is native glucagon (NNC0025-8000). Please indicate (with a check mark at ‘Please add the reference compound if available) during your compound request if you would like to have native glucagon (NNC0025-8000) included in your shipment.

Compound handling instructions

The freeze-dried material should be stored at -18C. NNC9204-1702 can be dosed in vivo in a formulation vehicle containing 50mM sodium phosphate, 145mM propylene glycol, (0.007% polysorbate 20 if concentrations are so low that adsorption to vials may affect the concentration), pH 7.4. Stability in aqueous media is poor thus formulations should be used fresh. For in vitro it is recommended to dissolve human glucagon in 100% DMSO (e.g at a concentration of 300 uM) and keep at max 5C. 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.

References

1. Zhang H et al.
Structure of the glucagon receptor in complex with a glucagon analogue

Nature. 2018;553(7686):106-110