^{68}Ga-1,4,7-Triazacyclononane-1,4-diacetic acid-8-aminooctanoic acid-Gln-Trp-Ala-Val-Gly-His-Leu-Met-NH_2

^{68}Ga-NOTA-8-Aoc-BBN[7-14]NH_2

Kam Leung, PhD[1]

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Chemical name:	^{68}Ga-1,4,7-Triazacyclononane-1.4-diacetic acid-8-aminooctanoic acid-Gln-Trp-Ala-Val-Gly-His-Leu-Met-NH_2	
Abbreviated name:	^{68}Ga-NOTA-8-Aoc-BBN[7-14]NH_2	
Synonym:		
Agent category:	Peptide	
Target:	Gastrin-releasing peptide receptor (GRPR)	
Target category:	Receptor	
Method of detection:	Positron emission tomography (PET)	
Source of signal\contrast:	^{68}Ga	
Activation:	No	
Studies:	• *In vitro* • Rodents	Click on protein, nucleotide (RefSeq), and gene for more information about gastrin-releasing peptide receptor.

Background

[PubMed]

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The amphibian bombesin (BBN or BN, a peptide of 14 amino acids) is an analog of human gastrin-releasing peptide (GRP, a peptide of 27 amino acids) that binds to GRP receptors (GRPR) with high affinity and specificity (1, 2). Both GRP and BBN share an amidated C-terminus sequence homology of seven amino acids, Trp-Ala-Val-Gly-His-Leu-Met-NH_2. BBN-Like peptides have been shown to induce various biological responses in diverse tissues, including the central nervous system and the gastrointestinal system. They also act as potential growth factors for both normal and neoplastic tissues (3). Specific BBN receptors (BBN-R) have been identified on central nervous system and gastrointestinal tissues and on a number of tumor cell lines (4). The BBN-R superfamily includes at least four different subtypes, namely the GRPR subtype (BB2), the neuromedin B (NMB) receptor subtype (BB1), the BB3 subtype, and the BB4 subtype. The findings of GRPR overexpression in various human tumors, such as breast, prostate, lung, colon, ovarian, and pancreatic cancers, provide opportunities for tumor imaging by designing specific molecular imaging agents to target the GRPR (5, 6).

Various BBN analogs has been label with ^{99m}Tc and ^{111}In for single-photon emission computed tomography imaging studies (7) and ^{64}Cu, ^{68}Ga, and ^{86}Y for positron emission tomography imaging studies (8, 9). Dijkgraaf et al. (10) 1,4,7-triazacyclononane-1,4-7-triacetic acid (NOTA) as a bifunctional chelator for labeling 8-aminooctanoic acid-Gln-Trp-Ala-Val-Gly-His-Leu-Met-NH_2 (8-Aoc-BBN[7-14]NH_2) with ^{68}Ga. ^{68}Ga-NOTA-8-Aoc-BBN[7-14]NH_2 was evaluated as a PET imaging agent of GRPR in nude mice bearing human PC-3 prostate cancer cells.

Related Resource Links:

- Chapters in MICAD (GRPR, bombesin)
- Gene information in NCBI (GRPR, GRP)
- Articles in Online Mendelian Inheritance in Man (OMIM) (GRPR, GRP)
- Clinical trials (GRPR)

Synthesis

[PubMed]

8-Aoc-BBN[7-14]NH_2 was prepared with solid-phase peptide synthesis with subsequent addition of NOTA group to form NOTA-8-Aoc-BBN[7-14]NH_2 (10). $^{68}GaCl_3$ was added to a solution of NOTA-8-Aoc-BBN[7-14]NH_2 in sodium acetate buffer (pH 4.1). The mixture was heated for 10 min at 95°C. The product, ^{68}Ga-NOTA-8-Aoc-BBN[7-14]NH_2, was purified with cartridge chromatography with 50-90% yield and a radiochemical purity of >95%. The specific activity of ^{68}Ga-NOTA-8-Aoc-BBN[7-14]NH_2 was >10 MBq/nmol (0.27 mCi/nmol) at the end of synthesis. Total preparation time was ~45 min. ^{68}Ga-NOTA-8-Aoc-BBN[7-14]NH_2 exhibited a Log *P* value of -1.98 ± 0.03.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Dijkgraaf et al. (10) performed *in vitro* inhibition studies of NOTA-8-Aoc-BBN[7-14]NH_2 and ^{nat}Ga-NOTA-8-Aoc-BBN[7-14]NH_2 in cultured human prostate PC-3 tumor cells with ^{111}In-NOTA-8-Aoc-BBN[7-14]NH_2. The 50% inhibition concentration (IC_{50}) values for NOTA-8-Aoc-BBN[7-14]NH_2 and ^{nat}Ga-NOTA-8-Aoc-BBN[7-14]NH_2 were 0.37 ± 0.15 nM and 0.41 ± 0.15 nM, respectively.

Animal Studies

Rodents

[PubMed]

Dijkgraaf et al. (10) performed *ex vivo* biodistribution studies of ^{68}Ga-NOTA-8-Aoc-BBN[7-14]NH_2 (~0.3 nmol) in nude mice bearing PC-3 xenografts with (n = 6) or without (n = 3) coinjection of 100-fold excess unlabeled NOTA-8-Aoc-BBN[7-14]NH_2 at 1 h after injection. Tumor accumulation was 1.24 ± 0.26% injected dose per gram (ID/g). The organ with the highest accumulation was the pancreas (6% ID/g), followed by the colon (1% ID/g), small intestine (2% ID/g), liver (1% ID/g), kidney (1% ID/g), and stomach (0.5% ID/g). Little accumulation was observed in the spleen, lung, blood and muscle (<0.5% ID/g). NOTA-8-Aoc-BBN[7-14]NH_2 blocked tumor accumulation by 83%. Significant inhibition (>90%) was also observed in the pancreas, stomach and colon. PET imaging studies were not performed.

Other Non-Primate Mammals

[PubMed]

No publication is currently available.

Non-Human Primates

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

No publication is currently available.

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