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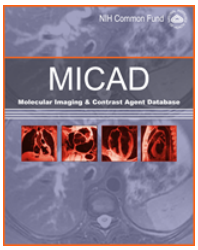

^{99m}Tc-Human β-defensin-3

^{99m}Tc-HBD-3

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Chemical name:	^{99m}Tc-Human β-defensin-3	
Abbreviated name:	^{99m}Tc-HBD-3	
Synonym:		
Agent category:	Peptide	
Target:	Microbial membrane	
Target category:	Bacteria	
Method of detection:	Single-photon emission computed tomography (SPECT), gamma planar imaging	
Source of signal\contrast:	^{99m}Tc	
Activation:	No	
Studies:	• *In vitro* • Rodents	Click on protein, nucleotide (RefSeq), and gene for more information about human β-defensin-3.

Background

[PubMed]

Antimicrobial peptides are small, cationic, amphiphilic peptides of 12–50 amino acids with microbicidal activity against both bacteria and fungi (1). The mammalian defensins can be subdivided into three main classes according to their structural differences: α-defensins, β-defensins, and theta-defensins. Mammalian α-defensins are predominantly found in neutrophils and in small intestinal epithelial cells, whereas mammalian β-defensins have been isolated from both leukocytes and epithelial cells. Recently, two novel human β-defensins (human β-defensin-3 (HBD-3) and human β-defensin-4 (HBD-4)) have been identified. Similar to HBD-1 and HBD-2, HBD-3 has microbicidal activity toward the Gram-negative bacteria (e.g., *Pseudomonas aeruginosa*, *Escherichia coli*) and yeasts. In addition, HBD-3 kills Gram-positive bacteria such as *Streptococcus pyogenes* or *Staphylococcus aureus*, including multi-resistant *S. aureus* strains. In contrast to HBD-1 and HBD-2, significant expression of HBD-3 has been demonstrated in non-epithelial tissues such as leukocytes, heart, and skeletal muscle. HBD-4 is expressed in certain epithelial cells and in neutrophils.

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A variety of radiolabeled compounds, including ^{67}Ga-citrate, ^{99m}Tc-ciprofloxacin, ^{18}F-FDG, and ^{111}In- or ^{99m}Tc-labeled antibodies that interact with specific receptors on the infiltrating leukocytes, and peptides have been evaluated for the detection of infections (2, 3). However, because they accumulate in both infected and inflamed areas of the body, these radiopharmaceuticals are nonspecific and cannot distinguish between infection and inflammation. In an effort to identify and develop radioactive compounds that are specific for the detection of infections, various investigators have evaluated the use of antimicrobial peptides that are found naturally in most multicellular organisms (4). Such peptides bind specifically to microbes, presumably through cationic domains that interact with anionic regions of the microbial membrane, and have been shown to distinguish infected tissue from inflamed tissue (5). Liberatore et al. (6) radiolabeled HBD-3 with ^{99m}Tc for single-photon emission computed tomography imaging of infected tissue.

Synthesis

[PubMed]

A solution $Na^{99m}TcO_4$ (74–148 MBq (2–4 mCi)) and sodium borohydride in the presence of carbon monoxide was heated for 20 min at 100°C in a vial (6). A solution of HBD-3 (0.020–0.0040 mg) was added to the reaction vial and incubated for 60 min at room temperature (7). ^{99m}Tc-HBD-3 was purified with PD-10 column chromatography. The specific activity of the purified product was 2–6 GBq/mg (0.054–0.162 Ci/mg) with a radiolabeling efficiency of 40–50%.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

S. aureus and *E. coli* suspensions were incubated with 2.5–5.0 μg/ml ^{99m}Tc-HBD-3, which exhibited ~3-fold higher inhibition of the growth of *S. aureus* than *E. coli* (6).

Animal Studies

Rodents

[PubMed]

Liberatore et al. (6) performed *ex vivo* biodistribution studies of 1.6–3.3 μg ^{99m}Tc-HBD-3 in rats with *S. aureus* infection in the right foreleg and sterile inflammation in the left foreleg (n = 3/group) at 1, 3, and 5 h after injection. Accumulation of radioactivity at the infection sites was 0.053% injected dose/g (ID/g) at 1 h, 0.080% ID/g at 3 h, and 0.083% ID/g at 5 h. Accumulation of radioactivity at the inflammation sites was 0.064% ID/g at 1 h, 0.032% ID/g at 3 h, and 0.033% ID/g at 5 h. Therefore, there was 1.5-fold higher ^{99m}Tc-HBD-3 accumulation at the infection sites than at the inflammation sites at 3 h and 5 h after injection. Accumulation in the normal muscle was 0.030–0.036% ID/g at these time points. No blocking experiment was performed. Concentration levels of ^{99m}Tc-HBD-3 in blood from mice with infection and inflammation were not reported.

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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