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^{99m}Tc-Duramycin

Duramycin is a natural antibiotic with 19-amino acids. Duramycin recognizes apoptotic and necrotic cells by binding to phosphatidyethanolamine (PE) with high affinity and specificity. The overall structure of Duramycin assumes a compact cyclic configuration, with a single binding pocket that specifically interacts with PE. Stabilized by 3 internal thioether linkages, Duramycin is the smallest known polypeptide that has a defined 3-dimensional binding site.

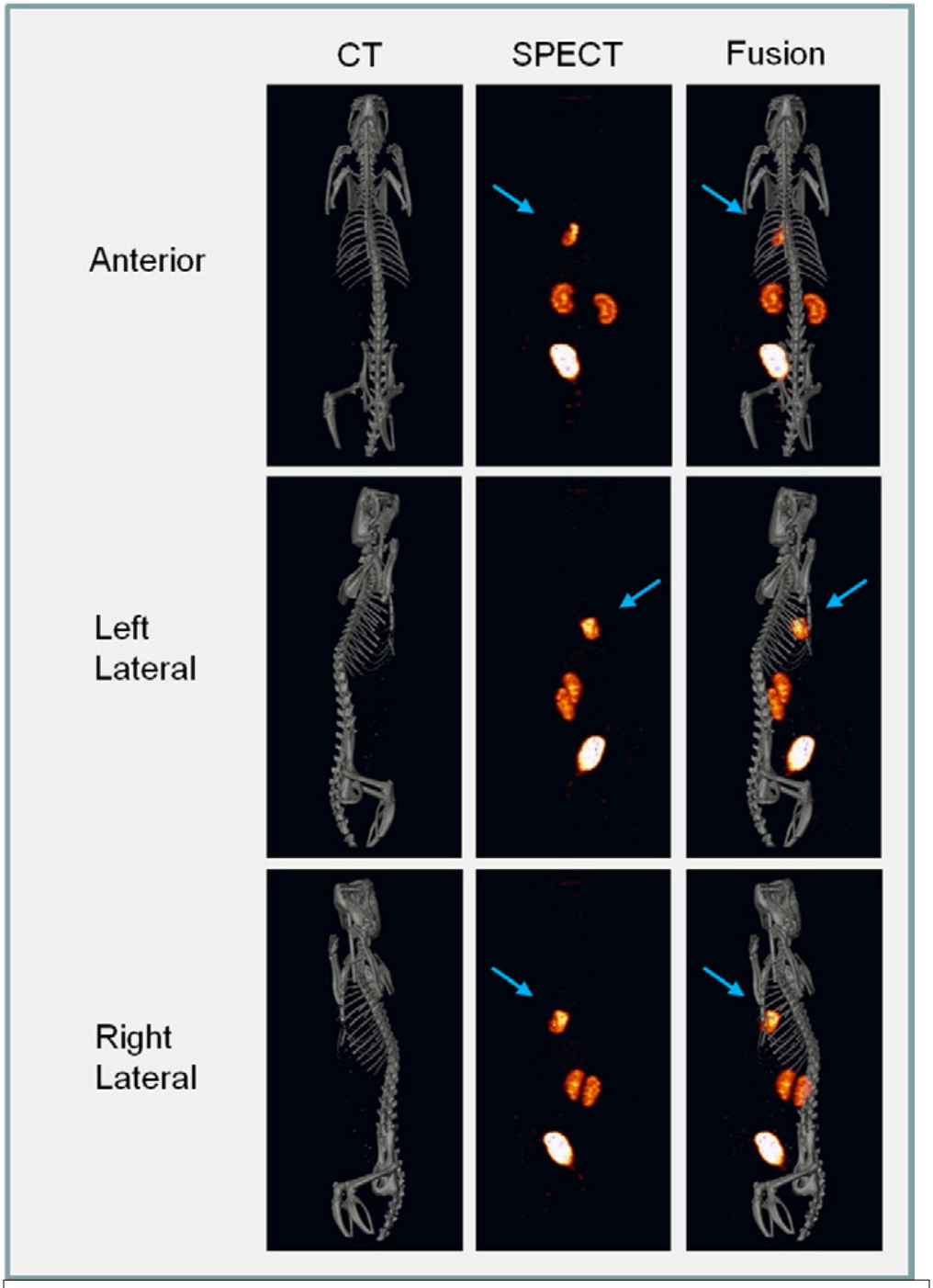
Duramycin has a number of unique structural features that are important for an ideal imaging agent. *i)* The small molecular size translates into a fast renal clearance and prompt blood clearance; *ii)* Duramycin is stabilized by extensive intramolecular cross-linking, with no free peptidic termini. As a result, the molecule is resistant to proteolytic degradation; *iii)* the presence of primary amines at the N-terminal provides convenient sites for covalent modification and radiolabeling; *iv)* Duramycin is readily modified with HYNIC for ^{99m}Tc labeling through coupling at the distal end, away from the binding pocket, thus not interfering with the binding activities of Duramycin.

Attributes of ^{99m}Tc-Duramycin as an Imaging Agent

- ^{99m}Tc-Duramycin retains its PE binding activity after radiolabeling and is highly stable in vivo.
- Binds apoptotic and necrotic cells with high affinity
- Rapid blood clearance with half-life of ~2-4 minutes
- Rapid renal clearance and low hepatic retention
- Ischemic/necrotic myocardium can be detected within 10-20 minutes post iv injection in animal AMI models
- Little washout from infarcted myocardium over time
- Infarcted tissue is detectable at least 48 hours post infarction but no uptake in older infarcts
- No toxicity expected with the current dosage

^{99m}Tc-Duramycin has been studied successfully in animal models for the imaging of myocardial infarct, stroke, atherosclerotic plaque, cardiotoxicity and cancer. Recently exquisite SPECT/CT images from a rat model of cardiac ischemia/reperfusion were published showing excellent focal infarct uptake and coupled with low systemic background and rapid renal/urinary clearance (*Audi et al./ Nuclear Medicine and Biology 39 (2012), 821-825. Figure on next page.)*

MTTI has licensed from the Medical College of Wisconsin rights to an allowed US patent covering the synthesis and characterization of ^{99m}Tc-HYNIC-Duramycin for the non-invasive imaging of phosphatidylethanolamine (PE) residues as well as HYNIC modification of Duramycin and its radiolabelling. Additionally, two other CIPs are pending, which include PET imaging with F-18 and Ga-68 labeled Duramycin.



Representative SPECT/CT images of ^{99m}Tc-Duramycin uptake in ischemically damaged cardiac tissue in vivo. The CT, SPECT and SPECT/CT fusion images are shown in the left, middle and right columns, respectively. Radioactivity uptake in the left ventricular free wall is highlighted with an arrow in the tomographic images.
(*Images courtesy of Dr. Ming Zhao, Northwestern University*.)