MOLECULAR TARGETING TECHNOLOGIES, INC.

Duramycin Analogs	Probes Targeting Cell Death

Background
Duramycin is a 19-amino acid tetracyclic polypeptide (MW=2013 Daltons) that belongs to the type B lantibiotic group of bacteriocins produced by Streptoverticillium cinnamoneus. The peptide backbone is stabilized by three thioether crosslinks which provides rigidity and stability and a well-defined three dimensional binding pocket with high selectivity and affinity for binding to the headgroup of phosphatidylethanolamine (PE). Kd =4-10 nM at a 1:1 molar ratio.

What are the unique features of duramycin?

- able to recognize PE with protein-like specificity and affinity
- its low molecular weight warrants fast blood clearance and low background in molecular imaging
- exhibits improved tissue penetration compared to protein based probes
- extensive crosslinking warrants greater stability and resistance to proteolytic degradation by blood-borne proteases and peptidases

How do they work?
PE comprises 20-50% of total phospholipids on cell membranes. Upon apoptosis, PE is translocated from the inner leaflets to the outer leaflets of the cell membrane. The expression of PE at the cell surface is one of the most important “eat me” triggers that results in phagocytosis of apoptotic cells. Duramycin has been conjugated with commonly used chelators HYNIC, MAG3, NODAGA, DOTA and TCO to provide analogs for direct radiolabeling, and also with a range of common fluorescent probes such as fluorescein, Cy3, Cy5 and NIR dye, for detection of PE expression via nuclear or optical imaging respectively. Figure 1 below shows the use of Tc-99m duramycin imaging of early tumor response to targeted therapy *in vivo* and Figure 2 depicts the Cy5-duramycin for imaging apoptosis *in vitro*.

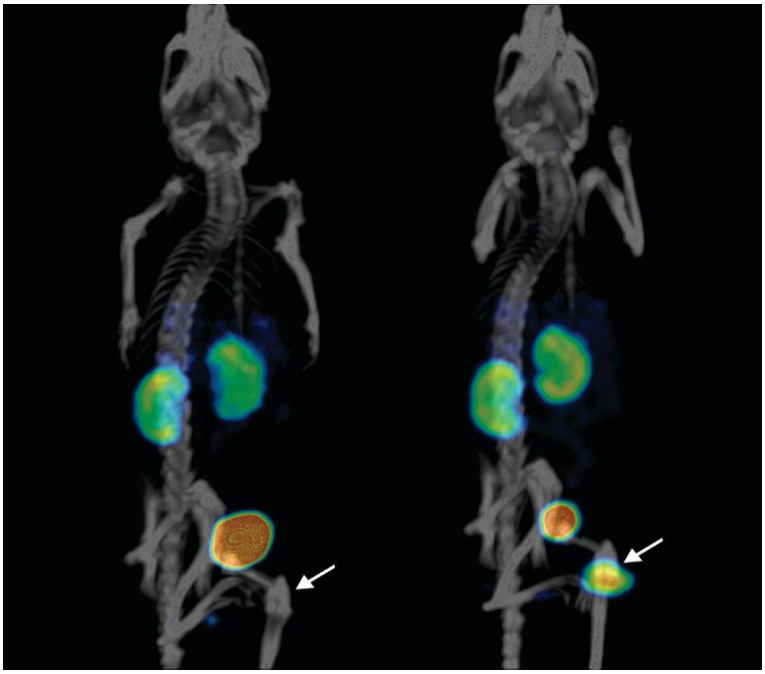
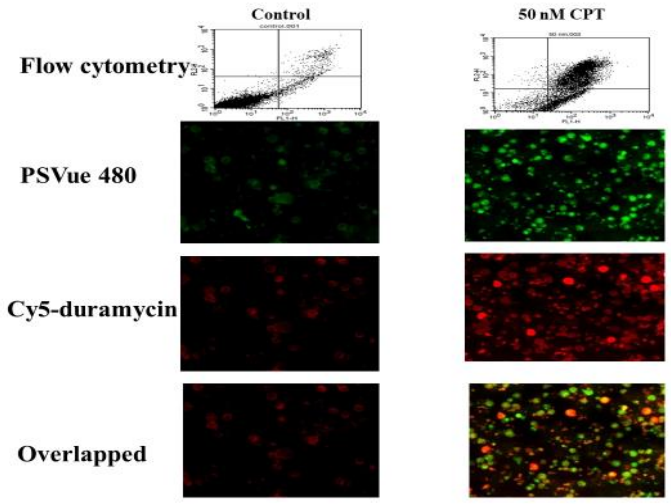


Figure 1: Colo 205 xenografts: TumorVue (Tc-99m Duramycin) uptake at the baseline was shown on the left and the arrow on the right side showed 7-fold increase 24 hour after Conatumumab treatment.

Courtesy of Professor Leonie wyffels and Dr. Filipe Elvas of University of Antwerp (Journal of Nuclear Medicine 2017, 58:665-670) and the picture won the **2017 MILabs Image of the Year award.**



Representative flow cytometry (top panel) and fluorescent microscopy images (bottom 3 rows). U937 cells were treated with CPT (0 and 50 nM) for 24 h and showed 7 and 89 % of apoptosis (early and late apoptosis) by flow cytometry. Flow cytometry was performed with a commercially available annexin V and PI kit. Cells were also co-stained with PSVue480 (a PS binding probe) and Cy5-duramycin for visualization by fluorescent microscope. Courtesy of Professor Chin Ng and Dr. Junling Li of University of Louisville.

Catalog Number	
D-1001	Duramycin-LC-Fluorescein
D-1002	Duramycin-Cy5-Conjugate
D-1003	Duramycin-LC-Biotin
D-1004	Duramycin-NIR790-Conjugate
D-1005	Duramycin (2 mg)
D-1006	Duramycin-Cy3 Fluorescent Conjugate
D-1007	Duramycin-HYNIC (15 ug) for Tc-99m labeling
D-1008	Duramycin-MAG3 (20 ug) for Tc-99m labeling
D-1009	Duramycin-NODAGA (20 ug) for Ga-68/Cu-64 labeling
D-1010	Duramycin-DOTA (20 ug) for Lu-177 labeling
D-1011	Duramycin-TCO (20 ug) for F-18 labeling

MTTI
833 Lincoln Ave., Unit 9
West Chester, PA 19380
P: 610.738.7938 F: 610.738.7928
Contact us: info@mtarget.com; www.mtarget.com