

City of Hope experience with ^{67}Cu

- Iotron medical Inc. (Steve Sugden)
- ANL/ORNL/NIDC (Dave Rotsch, Karen Sikes, Jack McCollister)
- Radiopharmacy/COH (Kofi Poku)
- Animal studies (Megan Minnix)

⁶⁷Cu labeling of a DOTA peptide and antibody

Date	mCi	mCi/mg	peptide	antibody	IR	source
9/18/14	5.7	10	-	99%	100%	Idaho state
10/26/18	1.3	10	-	<3%	NA	ANL
10/26/18	1.2	100	<3%			ANL
10/24/19	1.3	100	98%			ANL
10/24/19	1.4	10		97%	96%	ANL
1/23/20	1.1	10		98%	96%	ANL
1/23/20	1.1	100	99%			ANL
2/20/20	0.75	10		97%	96%	ANL
2/20/20	0.75	100	99%			ANL
3/19/20	1.29	10		99%	95%	ANL
3/19/20	1.5	100	99%			ANL
8/6/20	12.5	250	100%			ANL

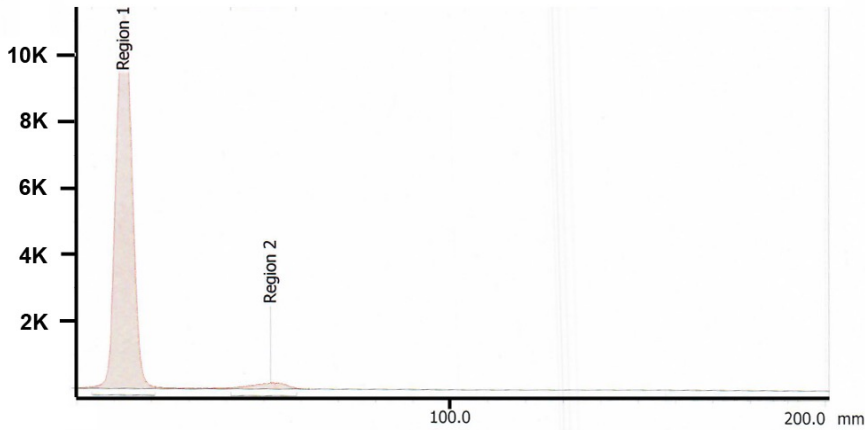
Peptide: 200 uCi/2 ug
100 uCi/nmole

Antibody: 1 mCi/100 ug

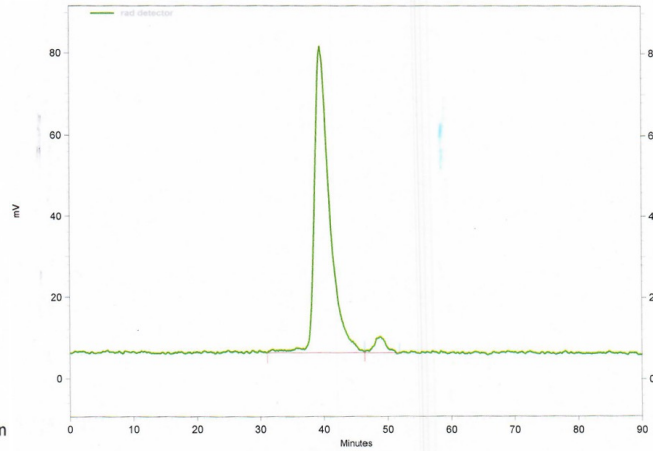
Peptide labeling ITLC and HPLC
Antibody labeling ITLC and SEC

Radionuclide was added to 20 ug peptide or 100 ug of antibody in 0.1 mL of 2.5 mM AmAcetate pH 5.5, 30 min at 43 deg

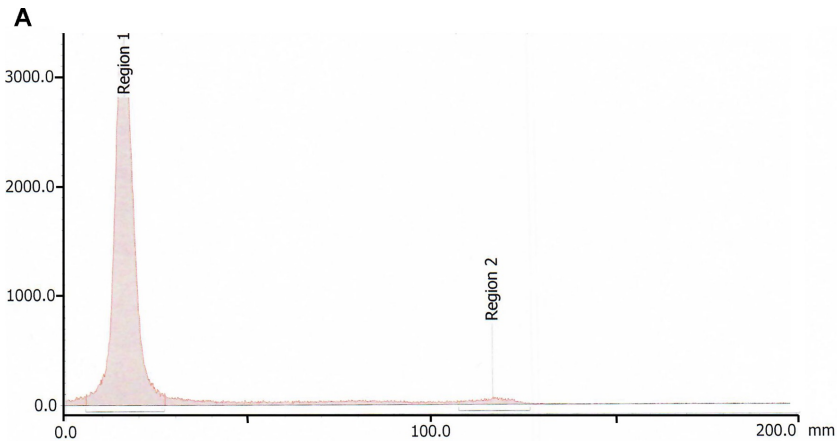
Lot #	Cu67-3-2020-0313-A	
Radiolabeling Efficiencies, at time of labeling		
Chelate	Test Result	Assay Date/Time (mm/dd/yy; hhmm)
TETA (M.W. = 650.38 g/mol)	<u>4.51</u> mCi/nmole	<u>3/18/2020</u> ; <u>10:45</u> CT
DOTA (M.W. = 404.42 g/mol)	<u>2.33</u> mCi/nmole	<u>3/18/2020</u> ; <u>11:30</u> CT
MeCOSar (M.W. = 427.58 g/mol)	<u>4.47</u> mCi/nmole	<u>3/18/2020</u> ; <u>13:30</u> CT
Chemical Purity (ppm) of stock solution. Stock solution volume: <u>1.0</u> mL		
Element Analyzed	Test Result	Assay Date/Time
Ca	15.1 ppm	<u>3/17/2020</u> ; CT
Co	0.03 ppm	
Fe	<2.2 ppm	
Ni	<0.02 ppm	
Cu*	0.26 ppm	
⁶⁸ Zn	0.20 ppm	
^{Nat} Zn	0.75 ppm	
Sn	0.16 ppm	
Pb	0.03 ppm	



Example of ITLC of ^{67}Cu -DOTA-M5A
Chased with 10 mM DTPA



Example of SEC of ^{67}Cu -DOTA-M5A



Example of ITLC of ^{67}Cu -(DOTA)₂-Lys-NT(6-13)
Chased with 10 mM DTPA

Peptide: 200 uCi/2 ug
100 uCi/nmole

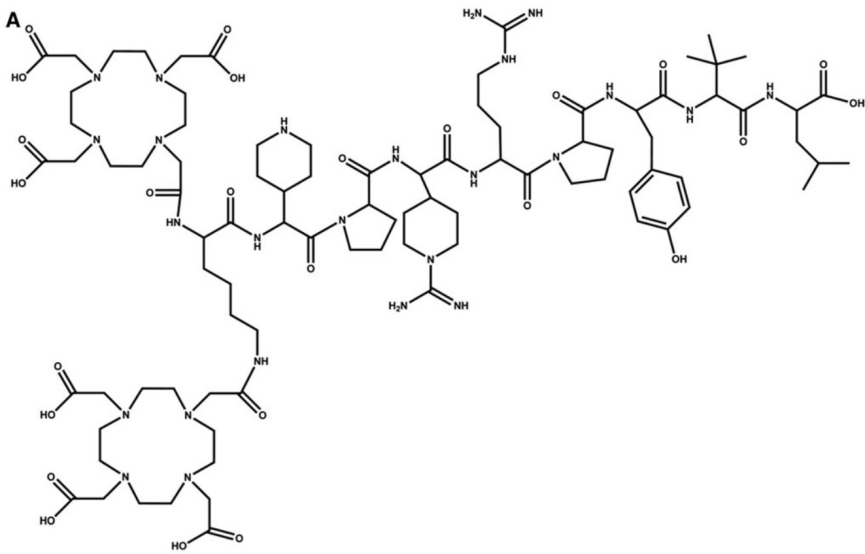
Antibody: 1 mCi/100 ug

Peptide labeling ITLC and HPLC
Antibody labeling ITLC and SEC

Radionuclide was added to 20 ug
peptide or 100 ug of antibody in
0.1 mL of 2.5 mM AmAcetate
pH 5.5, 30 min at 43 deg

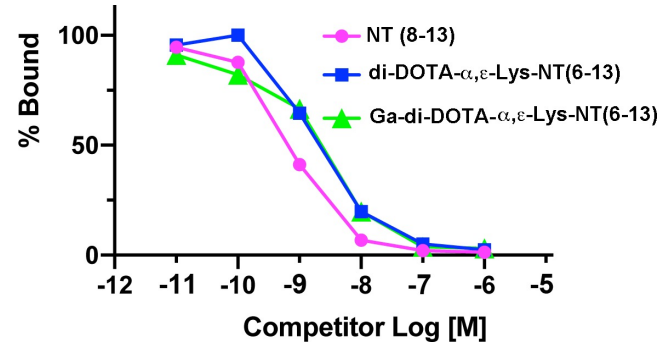
Neurotensin targeted imaging and therapy of NTRS1 tumors

(DOTA)₂ Lys-NT(6-13)

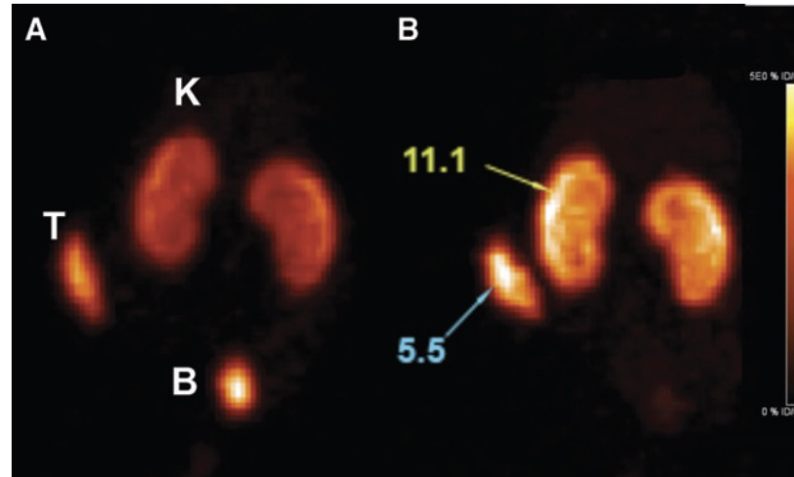


Amino acid derivatives to prolong serum half life

Li et al. Cancer Biother Biopharma 2020

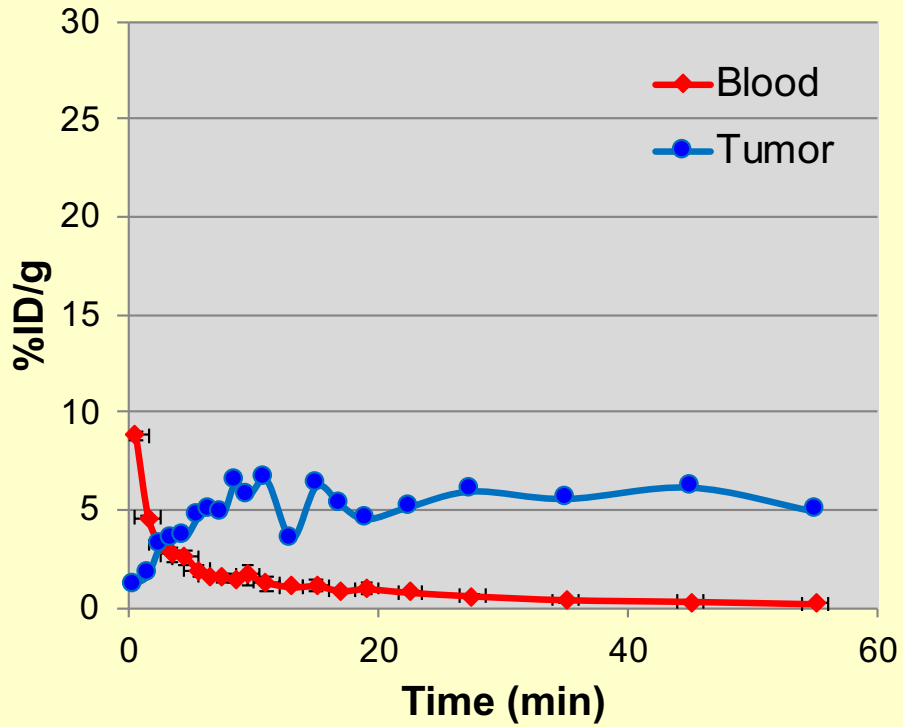


⁶⁴Cu PET image at 2hr and 4 hr (PC3.NTSR1)

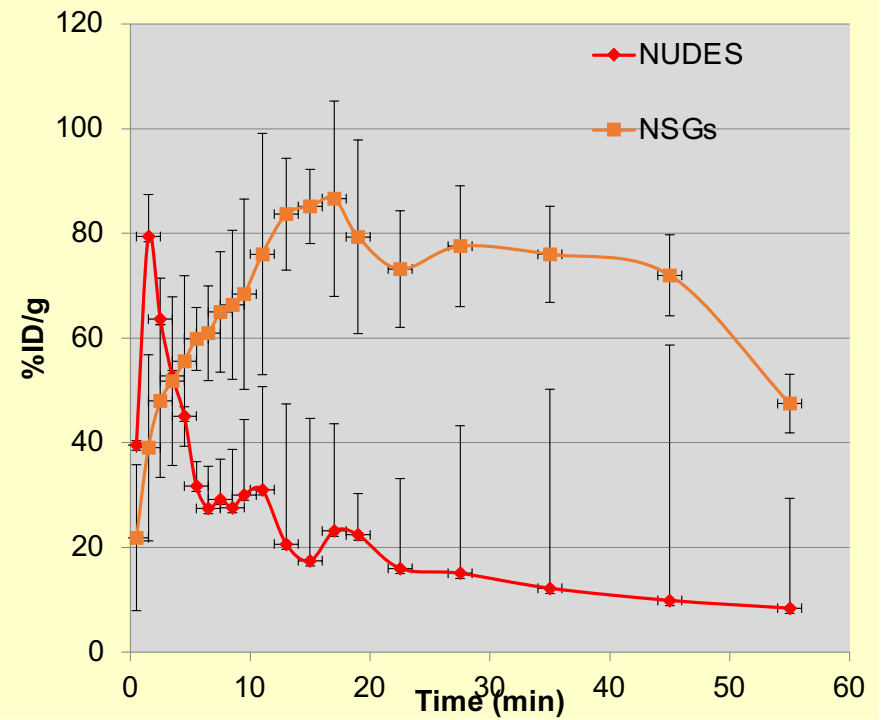


Time activity curves

Nudes: BLOOD & TUMOR



KIDNEY



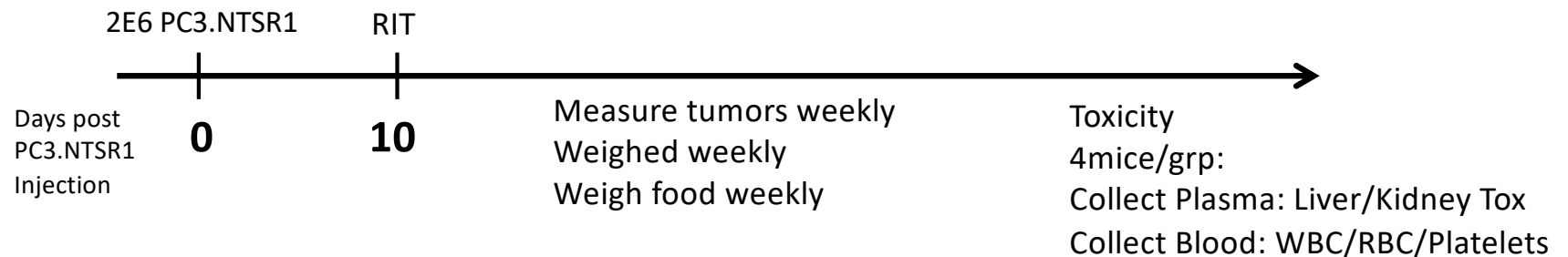
(DOTA)₂Neurotensin(6-13)-⁶⁷Cu treated PC3.NTSR1

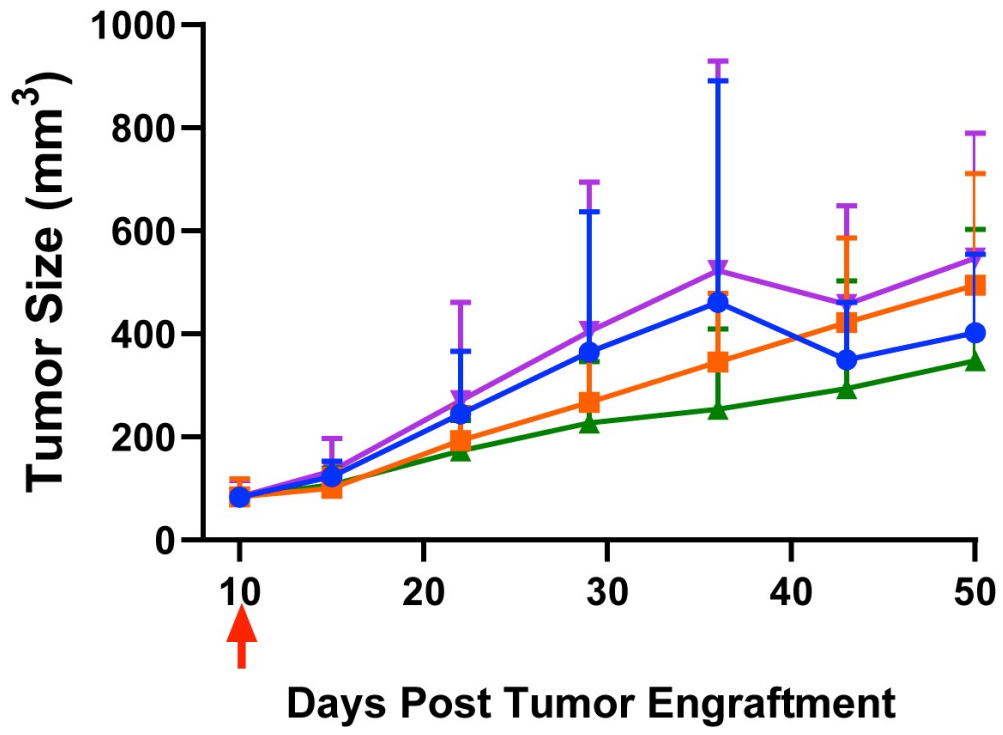
- Prostate Cancer; SQ
- Male Athymic
- ⁶⁷Cu half life: 2.6 days

2.0 ug DOTA₂NT(6-13)

Groups: (8/gr)

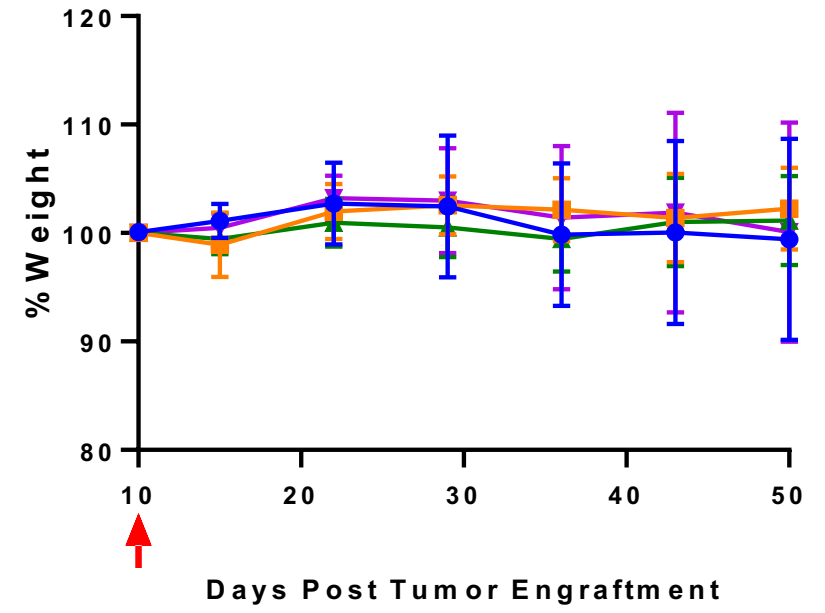
1. Saline
2. 125μCi NT-Cu67
3. 250μCi NT-Cu67
4. 500μCi NT-Cu67





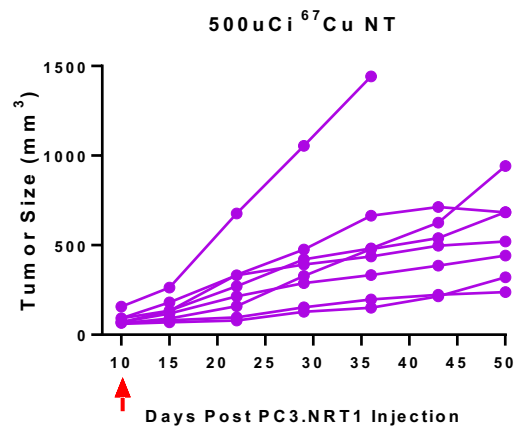
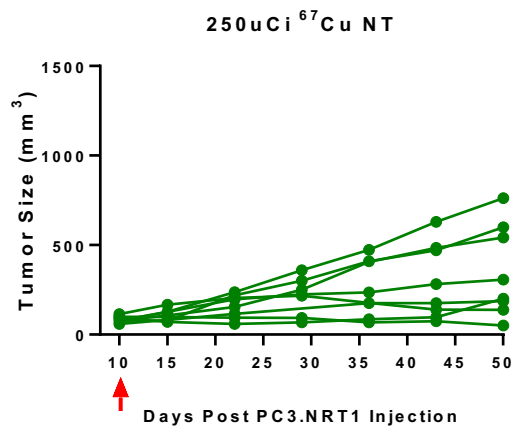
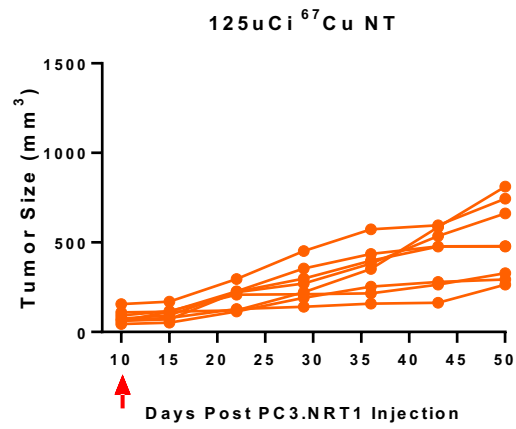
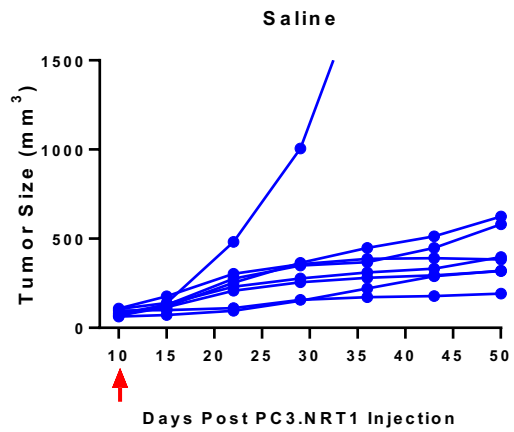
No Sig. Difference compared to Saline

- Vehicle Control
- 125uCi NT-Cu67 4.62 MBq
- ▲ 250uCi NT-Cu67 9.25 MBq
- ▼ 500uCi NT-Cu67 18.5 MBq



No evidence of whole body toxicity

Individual mouse curves



Conclusions, future directions

1. ANL production of Cu-67 reliable, high specific activity, >98% labeling for DOTA-peptide and DOTA-antibody
2. Preliminary dose study with peptide was not successful
3. Same model with Ac-225 labeled peptide (below) gave a dose response
4. Future: peptide studies will be focused on imaging and dosimetry before decision is made on therapy

Ac225 RIT in Athymic mice engrafted with PC3.NTR1

