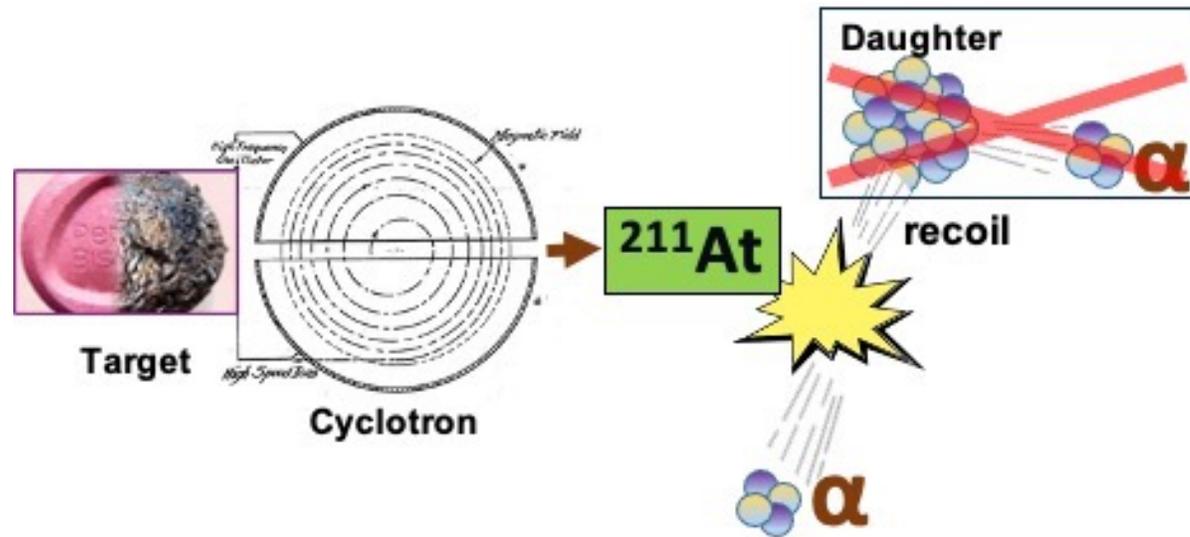


Production* and Applications of ^{211}At at Duke University



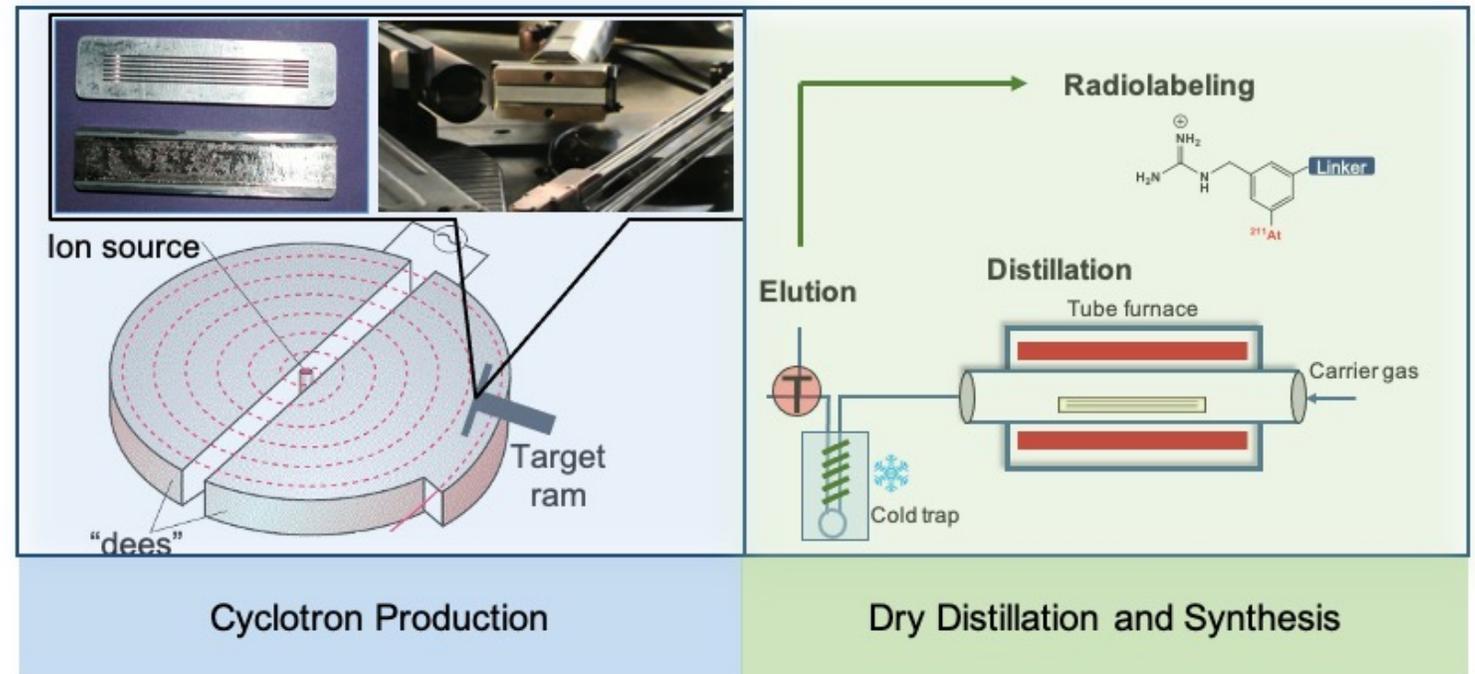
**Nucl. Med Biol.* 2021

DOI: [10.1016/j.nucmedbio.2021.05.007](https://doi.org/10.1016/j.nucmedbio.2021.05.007)

Astatine-211 Production: Current Status

- Internal target
- 28.0 MeV α -particles
- About 1 production run per week
- Max produced: 9.3 GBq
- Typical run: 3 h @ 48 μ Ap provides ~6.8 GBq EOB

CS-30 Cyclotron



MIT-1 internal target designed by George Hendry
4.7° grazing angle configuration
Graphite leading- and trailing edge beam current monitors

CS-30 has been reliable but is now >35 years old!



Cyclotron Subsystem Updates*

- Under direction of John Vincent – Ionetix
- Completed tasks (selected):
 - replaced air compressor drying system
 - rebuilt existing large cyclotron vacuum valve
 - address cooling water issues
 - obtain spare ion source power supply
 - design new rack for housing power supplies for ion source, deflector dee bias, harmonic trim coils

**Funded by DOE DE-SC0020218*

Updates that are in Progress*

- Design/install PLC-based control system with beam current readout
- Design/build new Knob/Meter
- Design/build console control power distribution panel



**Funded by DOE DE-SC0020218*

Next Steps and Potential Implications

- Increase α -particle beam energy to 29.0 MeV
 - radionuclidic purity evaluation by TUNL
- Evaluate alternative target geometry
 - head-to-head comparison with current target

Potential Patient Dose Production levels

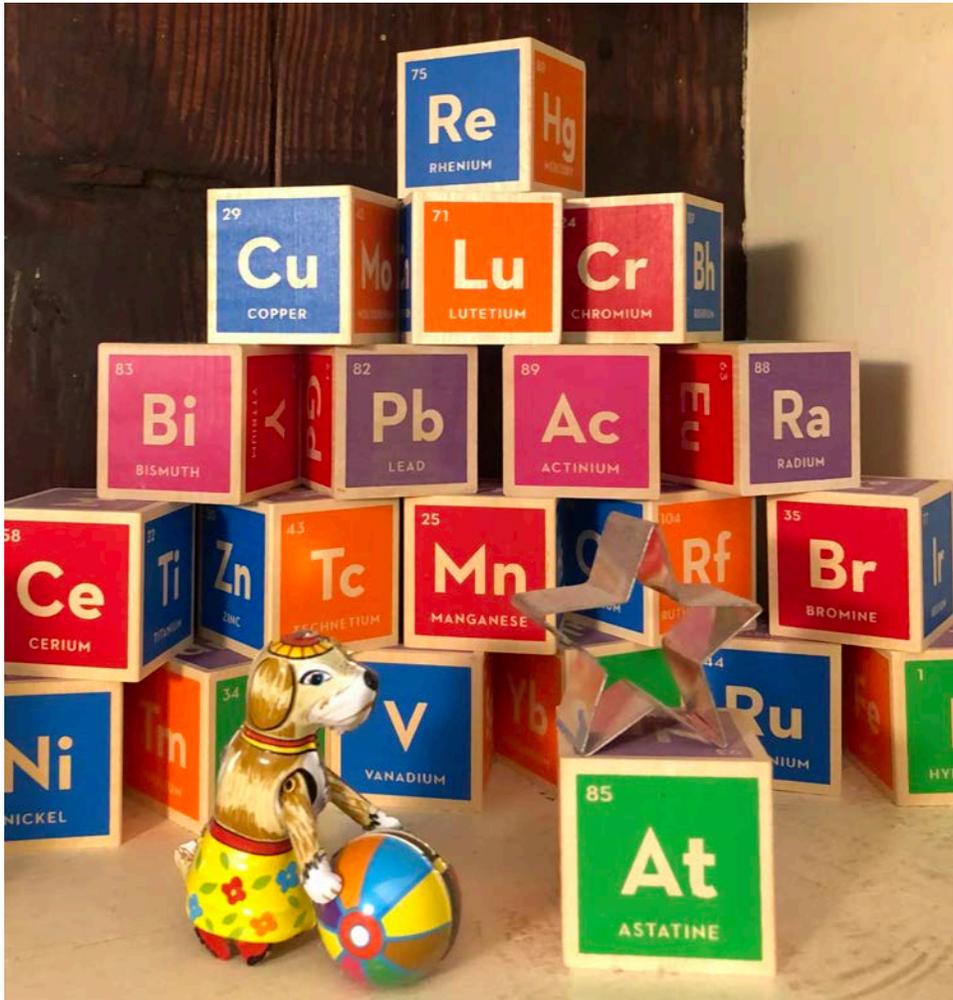
Assumptions:

1. 3 h@28 MeV = 6.8 GBq; @29 MeV = 14 GBq
2. Automated module: 89% yield purification; 75% yield for synthesis; 1 h total purification/production time = 607 MBq ^{211}At -TAT agent per GBq ^{211}At in target
3. Typical patient dose = 370 MBq

Then 3-h run @29 MeV could produce 23 patient doses

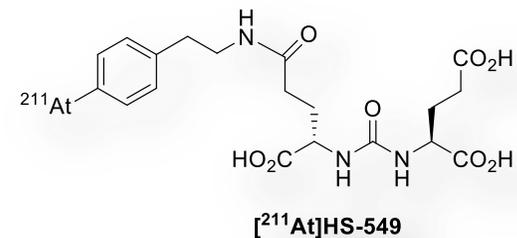
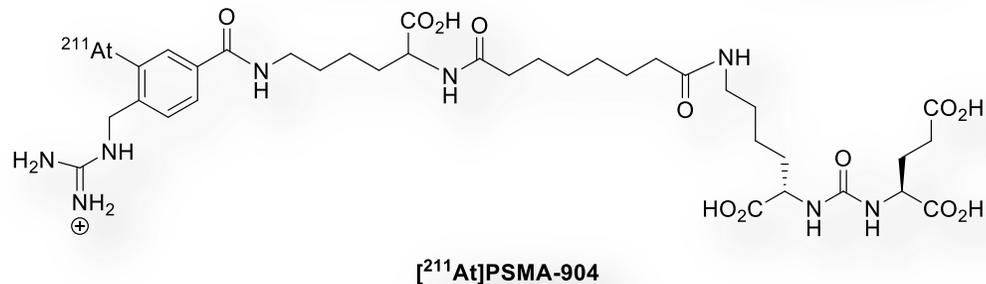
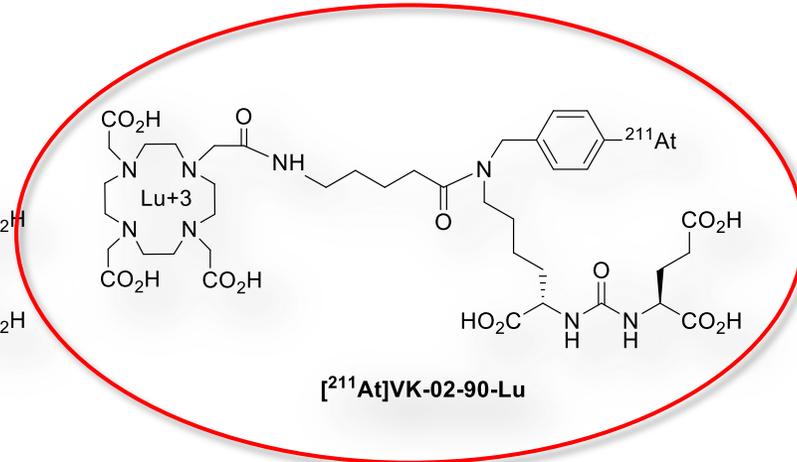
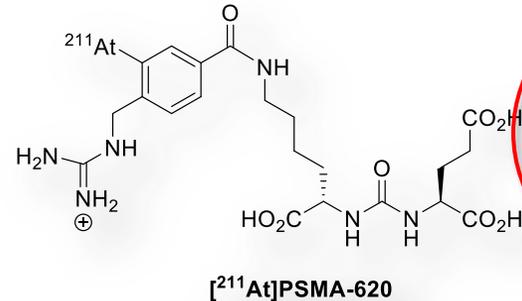
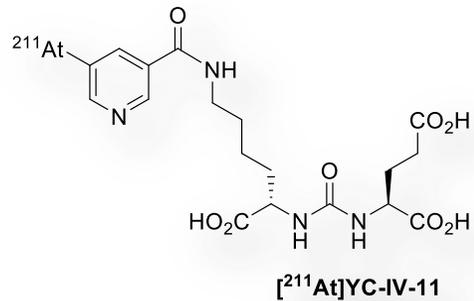
Two runs/day, 5 days/week x 50 weeks/year *could provide 11,500 patient doses per year*

Astatine-211 Projects at Duke



- PSMA inhibitors
- PARP inhibitors
- Gold nanostars
- VHH (nanobodies)
- Next generation labeling technologies

^{211}At -Labeled PSMA Inhibitors



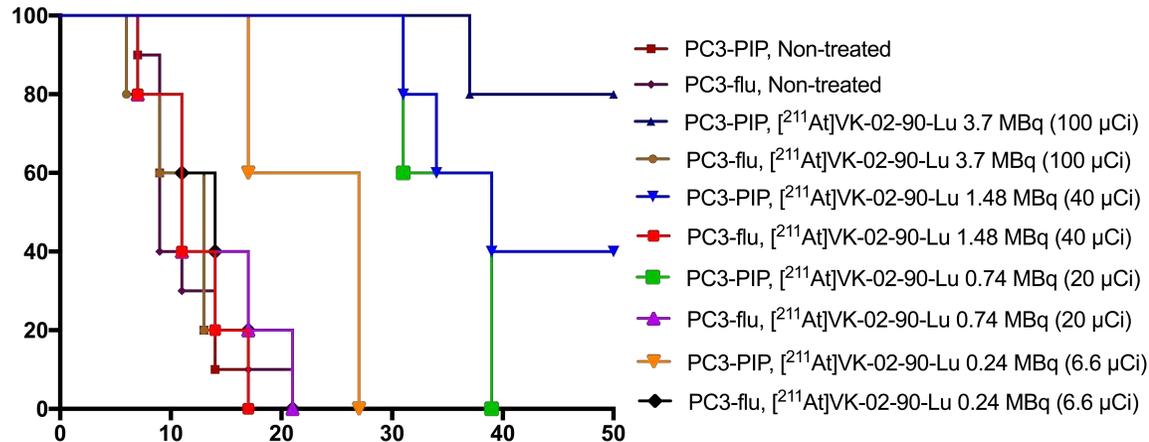
Tissue	Percentage of injected dose per gram (%ID/g)									
	$[^{211}\text{At}]\text{YC-IV-11}$		$[^{211}\text{At}]\text{PSMA-620}$		$[^{211}\text{At}]\text{HS-549}$		$[^{211}\text{At}]\text{PSMA-904}$		$[^{211}\text{At}]\text{VK-02-90-Lu}$	
	1 h	18 h	1 h	21 h	1 h	21 h	1 h	21 h	1 h	4 h
Tumor	17.9±3.0	31.1±9.8	16.5±4.8	13.6±3.3	43.2±9.8	10.6±9.9	22.7±5.4	12.1±5.0	30.6±4.8	17.1±5.2
Kidneys	72±12	57±7	103±24	7.5±1.8	47±8	2.6±0.8	87±16	4.4±3.5	90±43	2.1±0.6
Stomach	10.1±1.7	9.4±3.0	2.0±0.4	1.9±1.0	7.1±2.2	12.6±6.2	1.6±0.6	9.4±2.2	0.39±0.1	0.34±0.2

[²¹¹At]VK-02-90 Single Dose Efficacy Studies

Subcutaneous Model

PSMA+ PC3-PIP

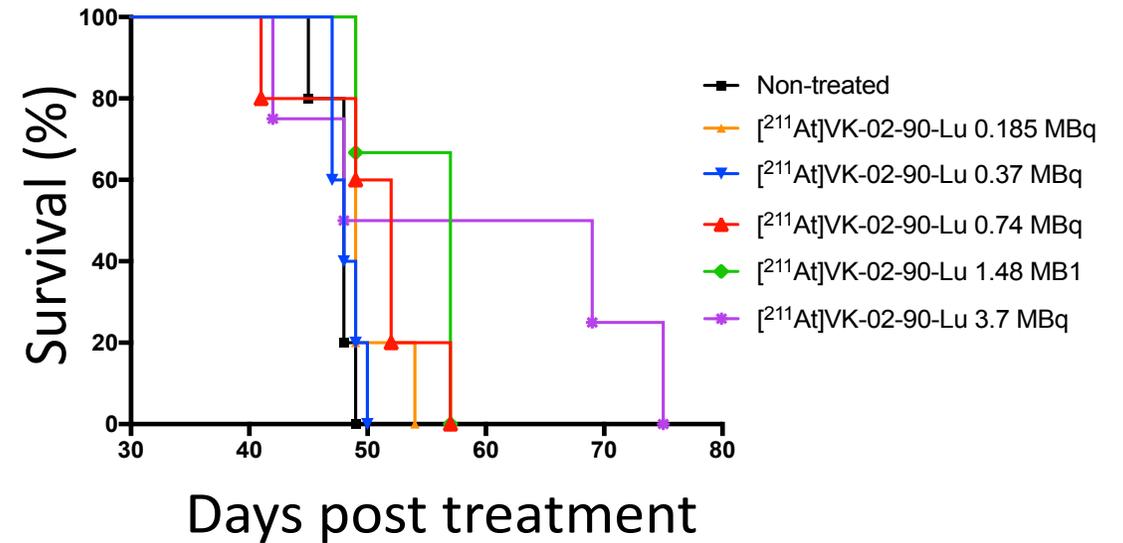
PSMA- PC3 flu



Metastatic Model

PC3-ML-Luc

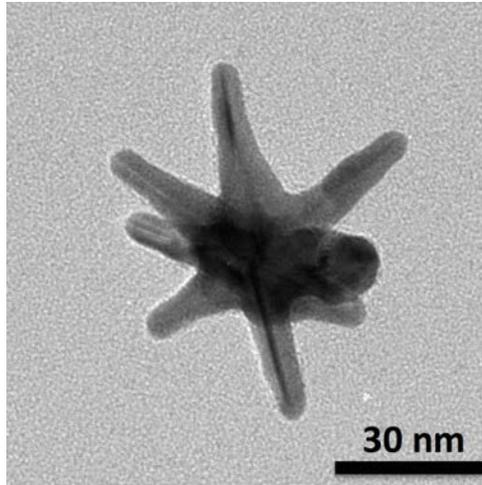
Monitored by BLI imaging



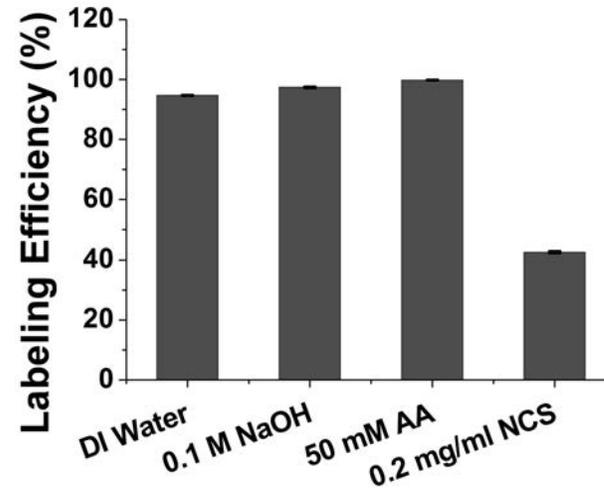
No toxicities observed in 13-month MTD study with CD-1 mice at therapeutic dose doses

Gold Nanostars for ^{211}At Delivery

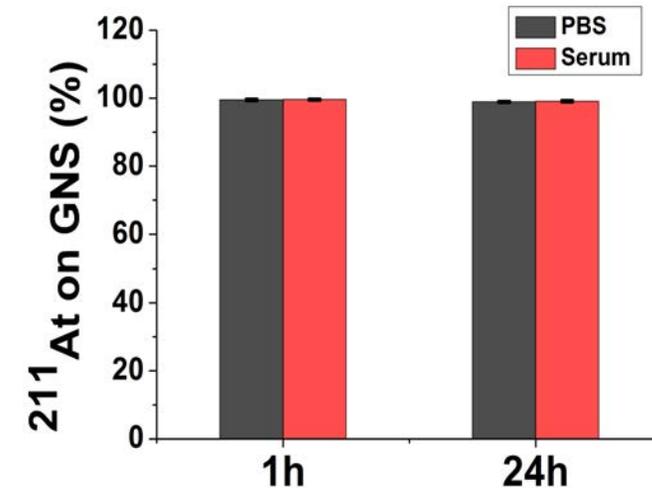
(A)



(B)

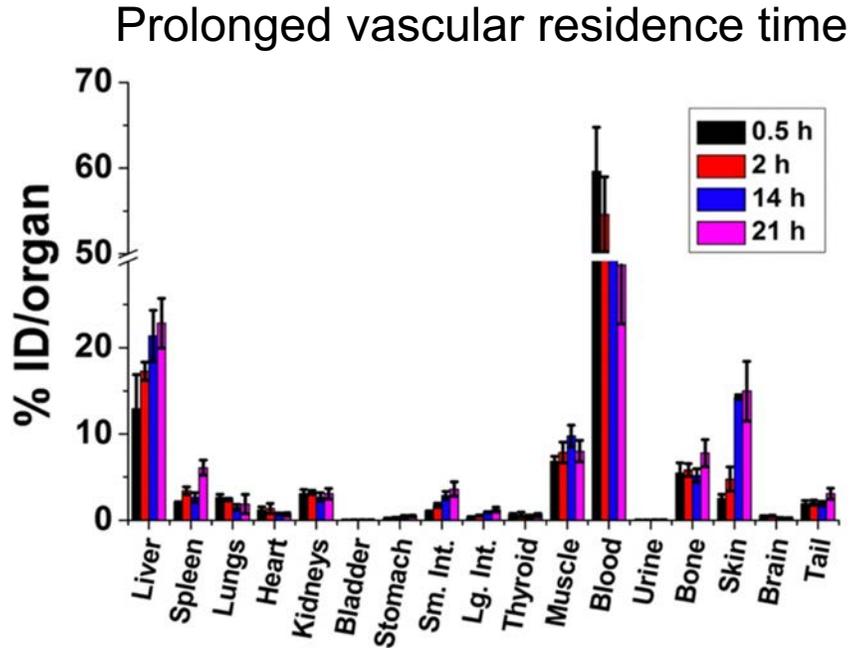


(C)



We have used star-shaped gold nanoparticles, gold nanostars (GNS), as a new strategy for ^{211}At delivery. Experiment results demonstrated that the ^{211}At labeling on GNS can be achieved with high efficiency in a short time. In addition, labeled ^{211}At on GNS has high stability with minimal dissociation when incubated in PBS or serum up to 24 h at 37 °C.

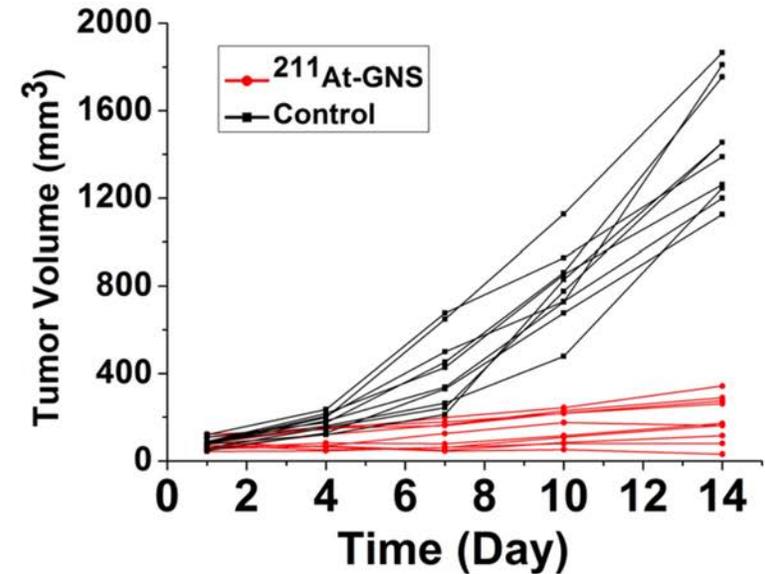
^{211}At -GNS: In Vivo Results



Low deastatination in vivo

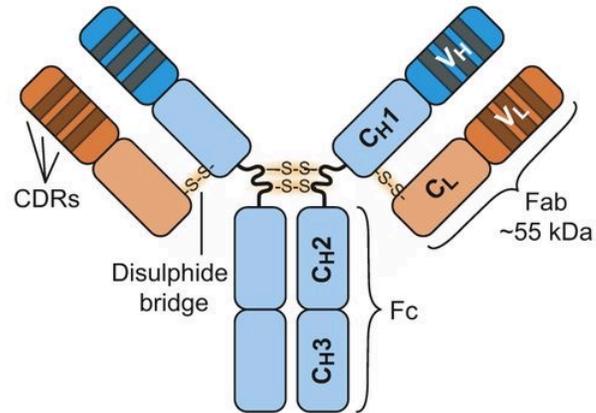
Tissue	%ID 30 min	% ID 2 h	%ID 14 h	%ID 21 h
Thyroid	0.61 ± 0.21	0.64 ± 0.28	0.44 ± 0.18	0.61 ± 0.21
Stomach	0.21 ± 0.06	0.28 ± 0.08	0.43 ± 0.14	0.49 ± 0.10

IT therapy in U87MG glioma model
(n=10) @ 1.11 MBq dose

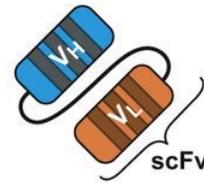


Nanobody™/VHH/sdAb

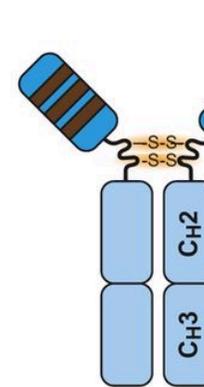
A Human IgG (~150 kDa)



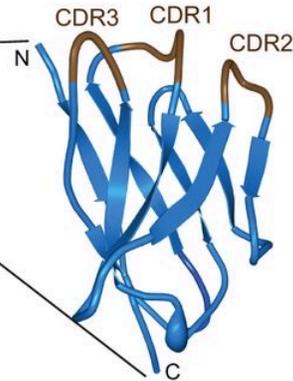
B scFv (~28 kDa)



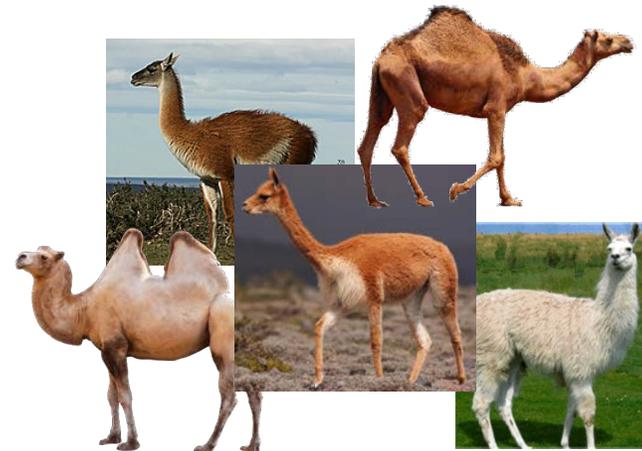
C Camelid HcAB (~96 kDa)



D Nanobody (~12-15 kDa)

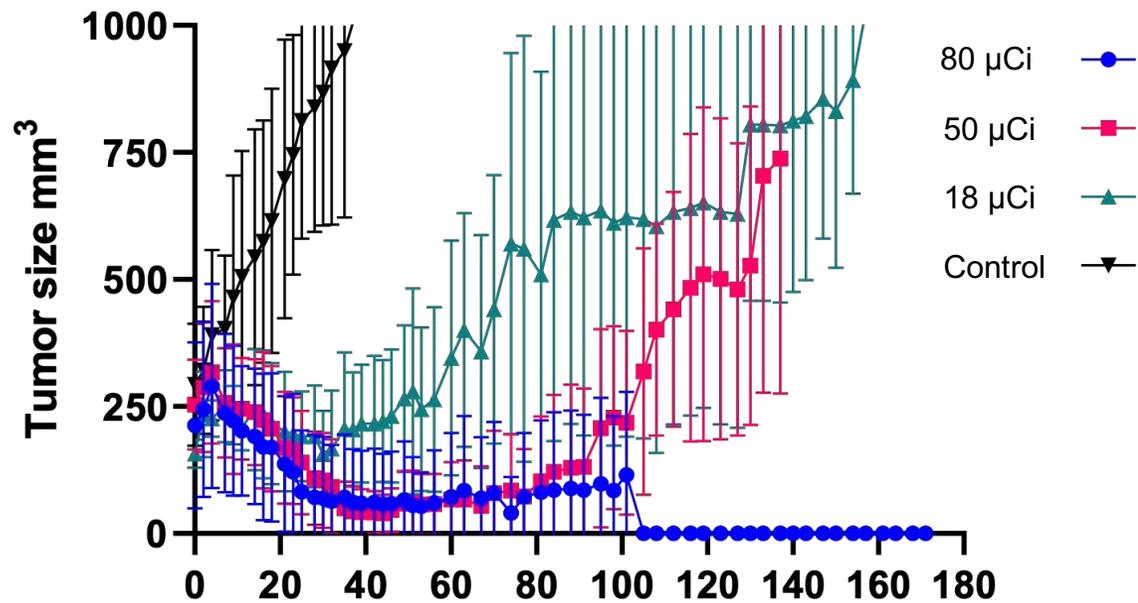


- *Derived from camelids*
- *Smallest fully functional fragment from a natural single chain Ab*

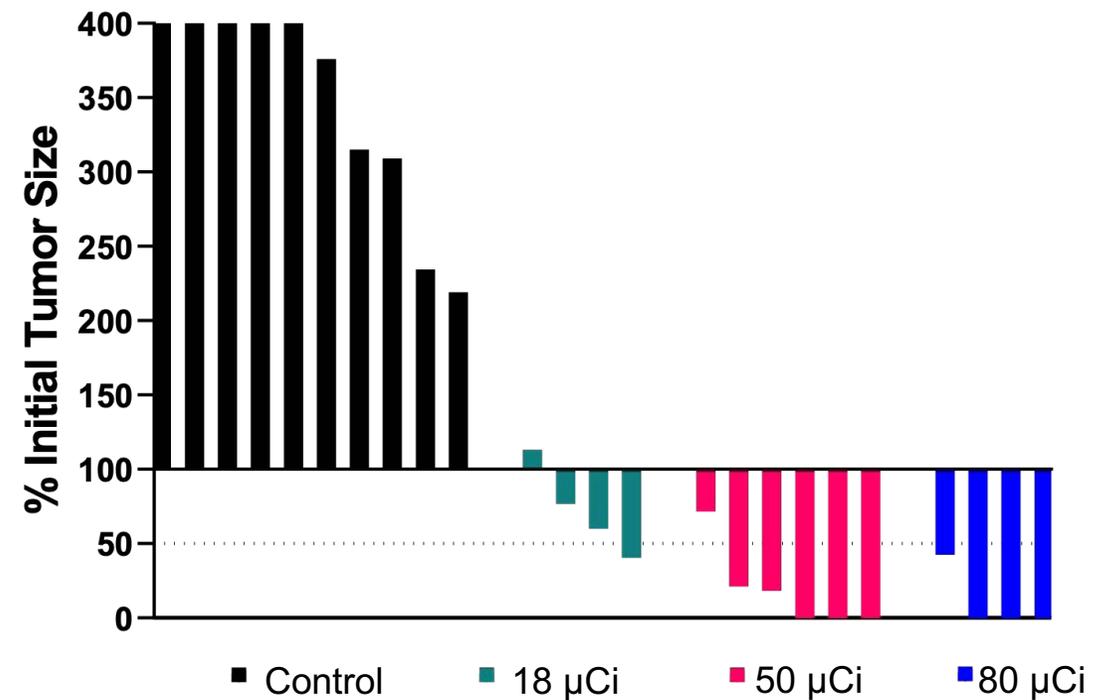


Treatment of BT-474 Breast Carcinoma Xenografts with Single Dose *iso*-[²¹¹At]SAGMB-5F7 VHH

Average Tumor Size



Maximum Tumor Response Waterfall



Acknowledgements

- Radiopharmaceutical Chemistry Lab
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