



U.S. DEPARTMENT OF
ENERGY

Lawrence Berkeley National Laboratory

A Murine Melanoma Growth Suppression Case Study for Pb-212

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Elements with Isotopes of Interest for Targeted Alpha-Therapy

Considerations:

- Half life
- Radiation type
- Activity & daughters
- Chemical properties
- Availability

Periodic Table of the Elements

1 H Hydrogen 1.008	2 He Helium 4.003																
3 Li Lithium 6.941	4 Be Beryllium 9.012											5 B Boron 10.811	6 C Carbon 12.011	7 N Nitrogen 14.007	8 O Oxygen 15.999	9 F Fluorine 18.998	10 Ne Neon 20.180
11 Na Sodium 22.990	12 Mg Magnesium 24.305	13 Al Aluminum 26.982	14 Si Silicon 28.086	15 P Phosphorus 30.974	16 S Sulfur 32.066	17 Cl Chlorine 35.453	18 Ar Argon 39.948										
19 K Potassium 39.098	20 Ca Calcium 40.078	21 Sc Scandium 44.956	22 Ti Titanium 47.867	23 V Vanadium 50.942	24 Cr Chromium 51.996	25 Mn Manganese 54.938	26 Fe Iron 55.845	27 Co Cobalt 58.933	28 Ni Nickel 58.693	29 Cu Copper 63.546	30 Zn Zinc 65.38	31 Ga Gallium 69.723	32 Ge Germanium 72.631	33 As Arsenic 74.922	34 Se Selenium 78.971	35 Br Bromine 79.904	36 Kr Krypton 83.796
37 Rb Rubidium 85.468	38 Sr Strontium 87.62	39 Y Yttrium 88.906	40 Zr Zirconium 91.224	41 Nb Niobium 92.906	42 Mo Molybdenum 95.95	43 Tc Technetium 98.907	44 Ru Ruthenium 101.07	45 Rh Rhodium 102.906	46 Pd Palladium 106.42	47 Ag Silver 107.868	48 Cd Cadmium 112.414	49 In Indium 114.818	50 Sn Tin 118.711	51 Sb Antimony 121.760	52 Te Tellurium 127.6	53 I Iodine 126.904	54 Xe Xenon 131.294
55 Cs Cesium 132.905	56 Ba Barium 137.328	57-71 Lanthanide Series	72 Hf Hafnium 178.49	73 Ta Tantalum 180.948	74 W Tungsten 183.84	75 Re Rhenium 186.207	76 Os Osmium 190.23	77 Ir Iridium 192.217	78 Pt Platinum 195.085	79 Au Gold 196.967	80 Hg Mercury 200.592	81 Tl Thallium 204.383	82 Pb Lead 207.2	83 Bi Bismuth 208.980	84 Po Polonium [208.982]	85 At Astatine 209.987	86 Rn Radon 222.018
87 Fr Francium 223.020	88 Ra Radium 226.025	89-103 Actinide Series	104 Rf Rutherfordium [261]	105 Db Dubnium [262]	106 Sg Seaborgium [266]	107 Bh Bohrium [264]	108 Hs Hassium [269]	109 Mt Meitnerium [278]	110 Ds Darmstadtium [281]	111 Rg Roentgenium [280]	112 Cn Copernicium [285]	113 Nh Nihonium [286]	114 Fl Flerovium [289]	115 Mc Moscovium [289]	116 Lv Livermorium [293]	117 Ts Tennessine [294]	118 Og Oganesson [294]

57 La Lanthanum 138.905	58 Ce Cerium 140.116	59 Pr Praseodymium 140.908	60 Nd Neodymium 144.243	61 Pm Promethium 144.913	62 Sm Samarium 150.36	63 Eu Europium 151.964	64 Gd Gadolinium 157.25	65 Tb Terbium 158.925	66 Dy Dysprosium 162.500	67 Ho Holmium 164.930	68 Er Erbium 167.259	69 Tm Thulium 168.934	70 Yb Ytterbium 173.055	71 Lu Lutetium 174.967
89 Ac Actinium 227.028	90 Th Thorium 232.038	91 Pa Protactinium 231.036	92 U Uranium 238.029	93 Np Neptunium 237.048	94 Pu Plutonium 244.064	95 Am Americium 243.061	96 Cm Curium 247.070	97 Bk Berkelium 247.070	98 Cf Californium 251.080	99 Es Einsteinium [254]	100 Fm Fermium 257.095	101 Md Mendelevium 258.1	102 No Nobelium 259.101	103 Lr Lawrencium [262]

U-230 (20 d)

Th-227 (18 d)

Ac-225 (10 d)

Ra-223 (11 d)

Pb-212 (10.6 h)

At-211 (7.2 h)

Bi-213 (46 min)

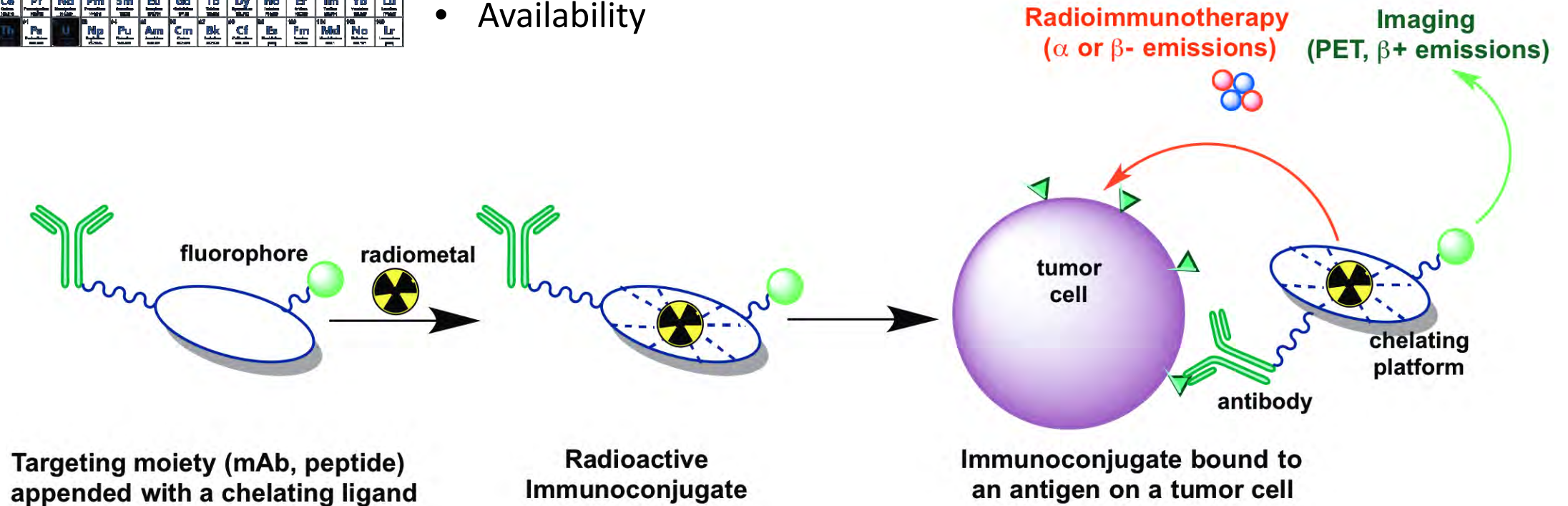
Radiolabeling Biological Molecules with Radiometals

Periodic Table of the Elements

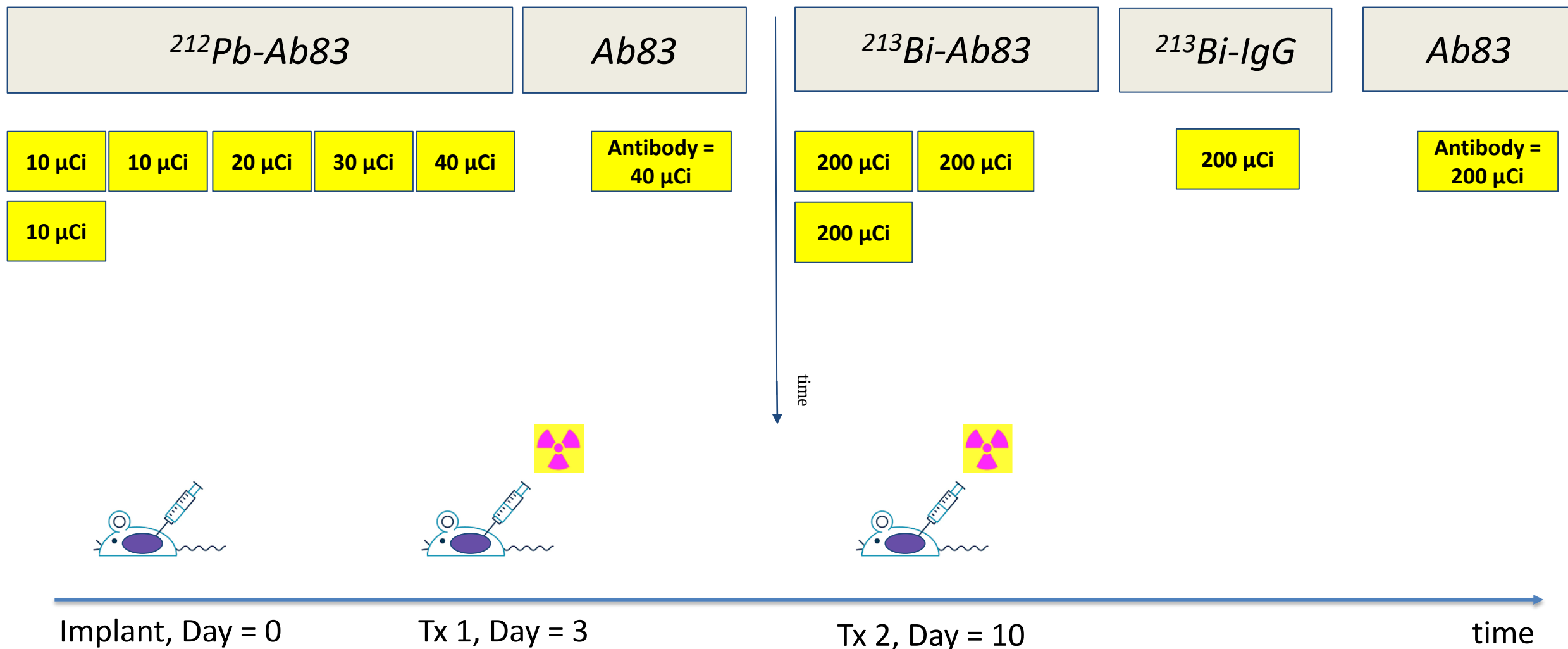
The periodic table shows elements from Hydrogen (H) to Oganesson (Og). Radiometals, which are radioactive isotopes of metals, are highlighted in black. These include: ²¹²Pb, ²¹³Pb, ²¹⁴Pb, ²¹⁵Pb, ²¹⁶Pb, ²¹⁷Pb, ²¹⁸Pb, ²¹⁹Pb, ²²⁰Pb, ²²¹Pb, ²²²Pb, ²²³Pb, ²²⁴Pb, ²²⁵Pb, ²²⁶Pb, ²²⁷Pb, ²²⁸Pb, ²²⁹Pb, ²³⁰Pb, ²³¹Pb, ²³²Pb, ²³³Pb, ²³⁴Pb, ²³⁵Pb, ²³⁶Pb, ²³⁷Pb, ²³⁸Pb, ²³⁹Pb, ²⁴⁰Pb, ²⁴¹Pb, ²⁴²Pb, ²⁴³Pb, ²⁴⁴Pb, ²⁴⁵Pb, ²⁴⁶Pb, ²⁴⁷Pb, ²⁴⁸Pb, ²⁴⁹Pb, ²⁵⁰Pb, ²⁵¹Pb, ²⁵²Pb, ²⁵³Pb, ²⁵⁴Pb, ²⁵⁵Pb, ²⁵⁶Pb, ²⁵⁷Pb, ²⁵⁸Pb, ²⁵⁹Pb, ²⁶⁰Pb, ²⁶¹Pb, ²⁶²Pb, ²⁶³Pb, ²⁶⁴Pb, ²⁶⁵Pb, ²⁶⁶Pb, ²⁶⁷Pb, ²⁶⁸Pb, ²⁶⁹Pb, ²⁷⁰Pb, ²⁷¹Pb, ²⁷²Pb, ²⁷³Pb, ²⁷⁴Pb, ²⁷⁵Pb, ²⁷⁶Pb, ²⁷⁷Pb, ²⁷⁸Pb, ²⁷⁹Pb, ²⁸⁰Pb, ²⁸¹Pb, ²⁸²Pb, ²⁸³Pb, ²⁸⁴Pb, ²⁸⁵Pb, ²⁸⁶Pb, ²⁸⁷Pb, ²⁸⁸Pb, ²⁸⁹Pb, ²⁹⁰Pb, ²⁹¹Pb, ²⁹²Pb, ²⁹³Pb, ²⁹⁴Pb, ²⁹⁵Pb, ²⁹⁶Pb, ²⁹⁷Pb, ²⁹⁸Pb, ²⁹⁹Pb, ³⁰⁰Pb, ³⁰¹Pb, ³⁰²Pb, ³⁰³Pb, ³⁰⁴Pb, ³⁰⁵Pb, ³⁰⁶Pb, ³⁰⁷Pb, ³⁰⁸Pb, ³⁰⁹Pb, ³¹⁰Pb, ³¹¹Pb, ³¹²Pb, ³¹³Pb, ³¹⁴Pb, ³¹⁵Pb, ³¹⁶Pb, ³¹⁷Pb, ³¹⁸Pb, ³¹⁹Pb, ³²⁰Pb, ³²¹Pb, ³²²Pb, ³²³Pb, ³²⁴Pb, ³²⁵Pb, ³²⁶Pb, ³²⁷Pb, ³²⁸Pb, ³²⁹Pb, ³³⁰Pb, ³³¹Pb, ³³²Pb, ³³³Pb, ³³⁴Pb, ³³⁵Pb, ³³⁶Pb, ³³⁷Pb, ³³⁸Pb, ³³⁹Pb, ³⁴⁰Pb, ³⁴¹Pb, ³⁴²Pb, ³⁴³Pb, ³⁴⁴Pb, ³⁴⁵Pb, ³⁴⁶Pb, ³⁴⁷Pb, ³⁴⁸Pb, ³⁴⁹Pb, ³⁵⁰Pb, ³⁵¹Pb, 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Considerations:

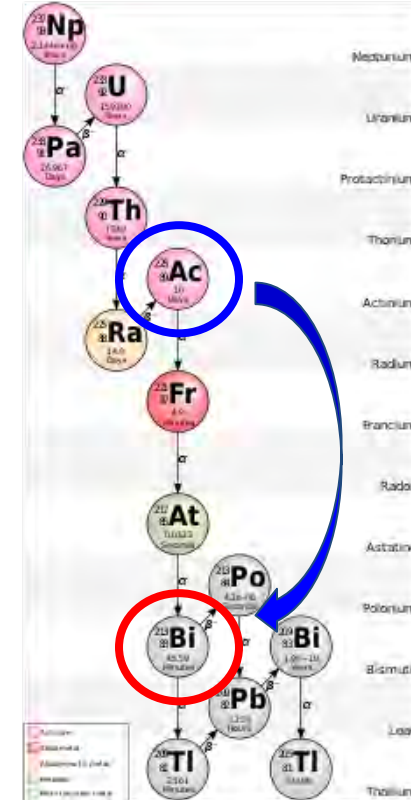
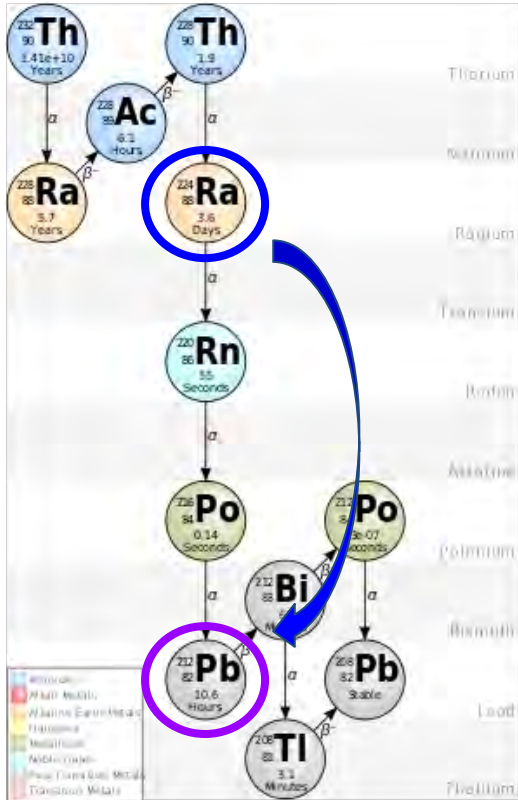
- Half life
- Radiation type
- Activity & daughters
- Chemical properties
- Availability



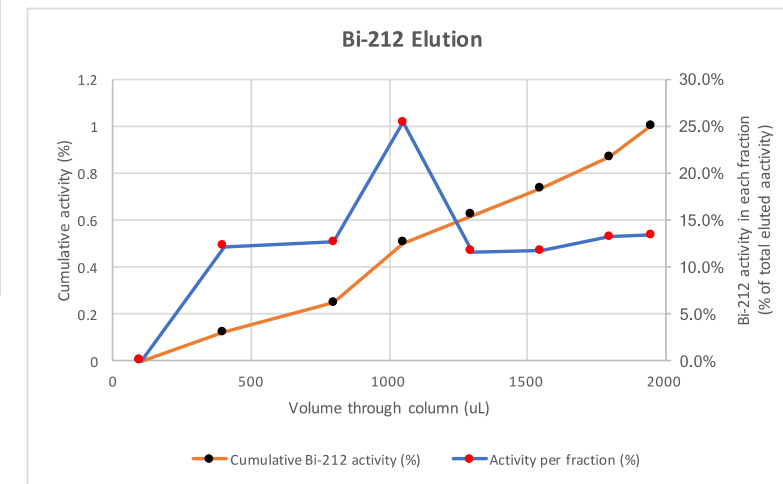
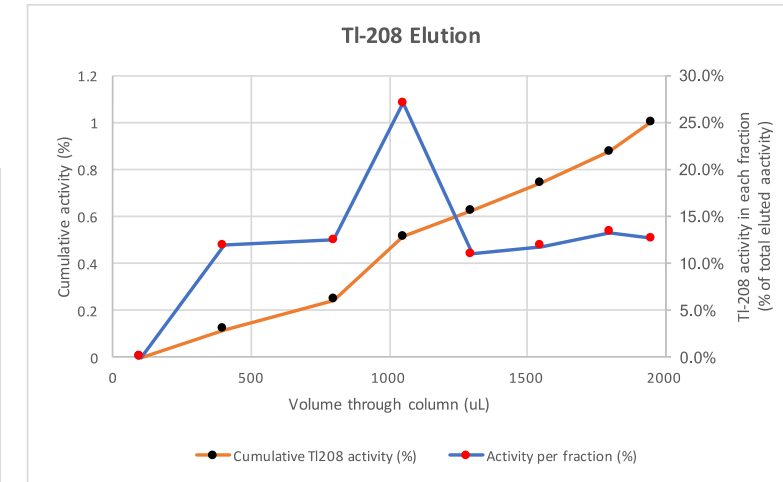
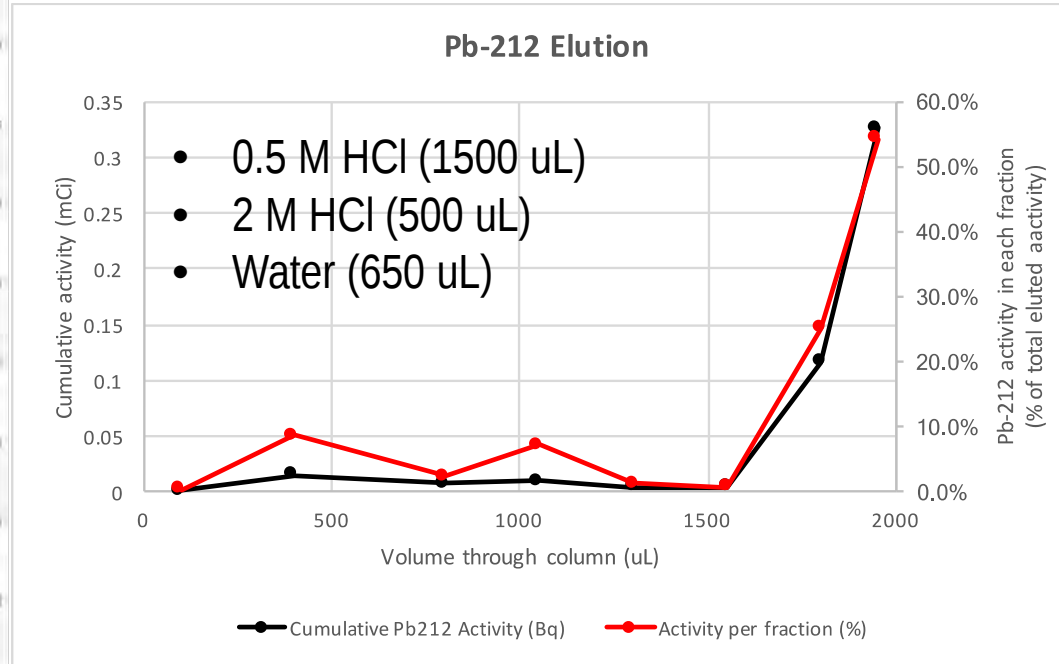
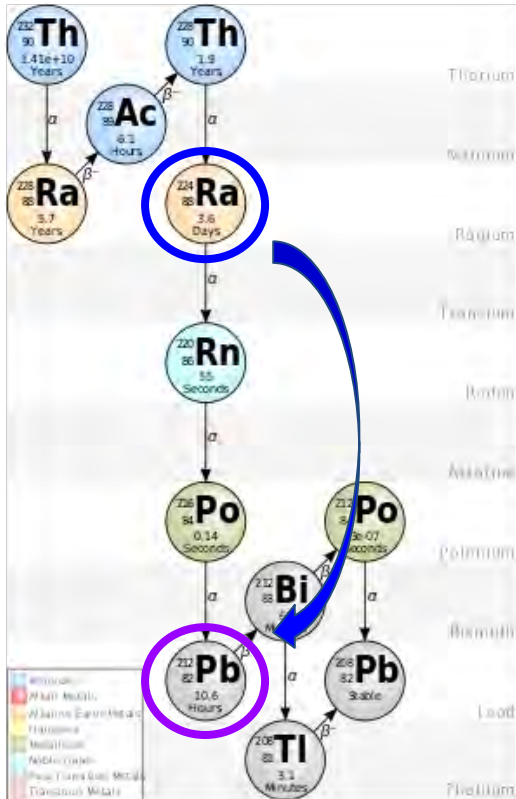
Murine Melanoma Growth Suppression Study Design – Bi-213 vs Pb-212



Different Radiometals $\leftrightarrow$ Different Generators

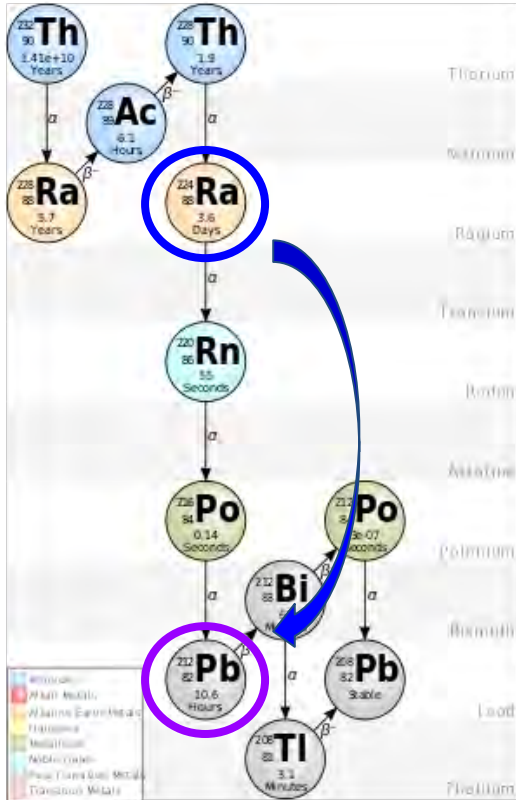


Different Radiometals $\leftrightarrow$ Different Generators

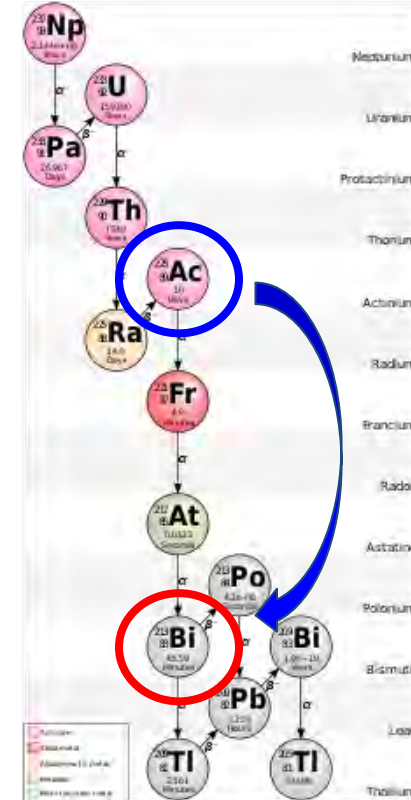
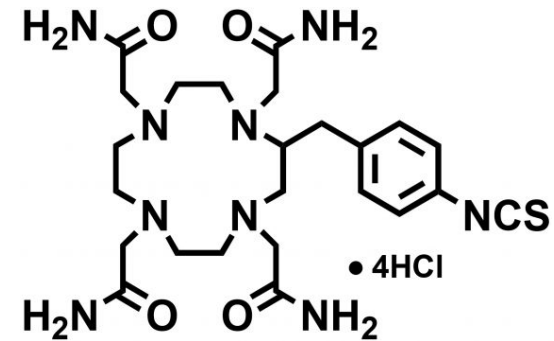


- Is matrix exchange necessary?

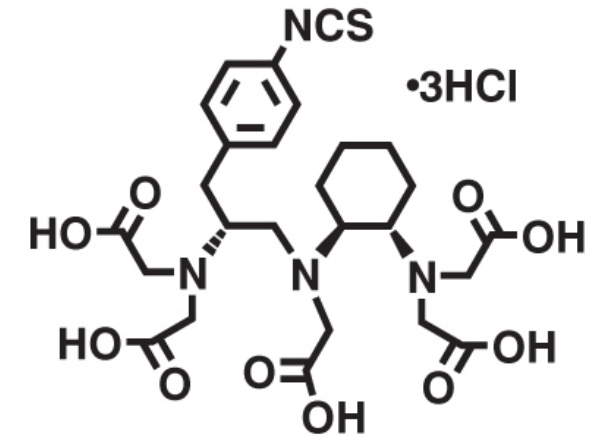
Different Radiometals $\leftrightarrow$ Different Chelators



p-SCN-Bn-TCMC



p-SCN-Bn-CHX-A''-DTPA



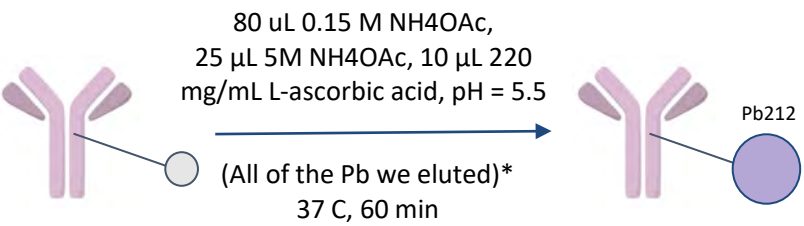
Antibody Labeling

CAR +/- sd

Ab83-CHX-A'	1.86 +/- 0.38
Ab83-TCMC	3.039 +/- 0.45
IgG-CHX-A'	2.058 +/- 0.15

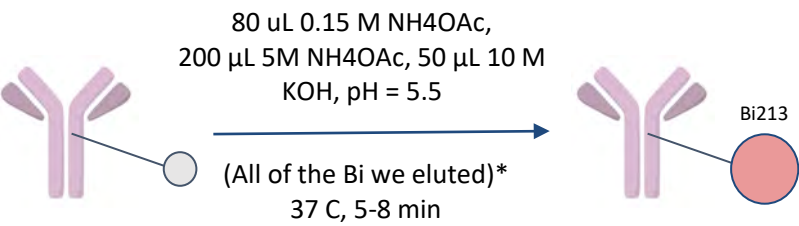
Pb-212
Radiolabeling

Date	RadioPurity (%)
5/7	92.93
5/8	87.94
5/14	61.06
5/15	81.76
5/20	30.26
5/20	28.11

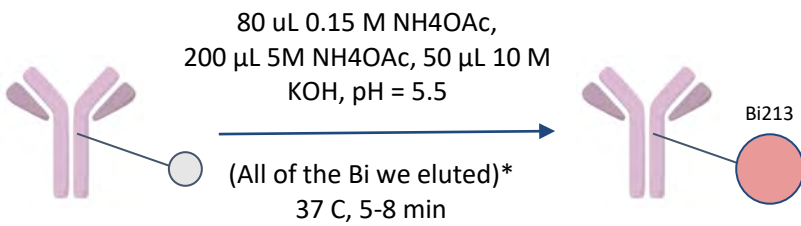


*H8C3-TCMC concentration was 4 mg/mL for radiolabeling.

²¹²Pb-Ab83

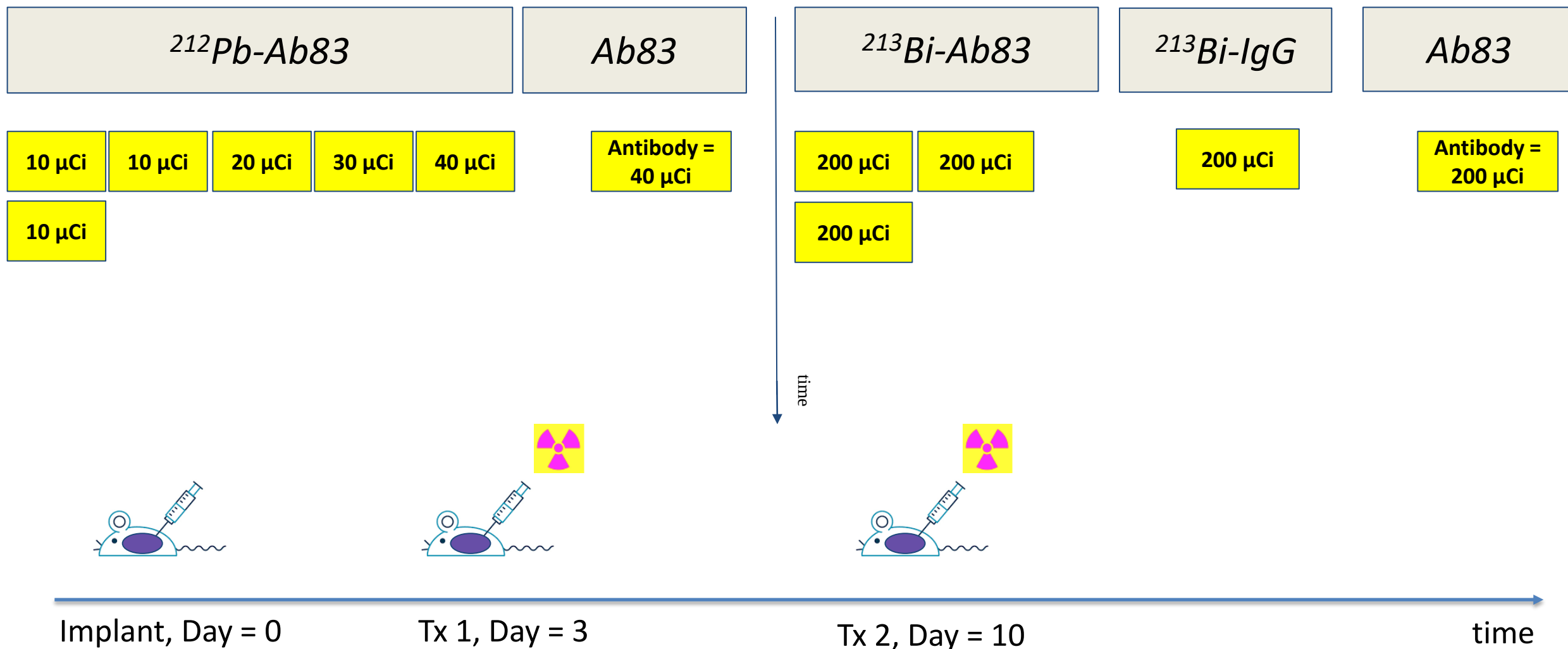


²¹³Bi-Ab83

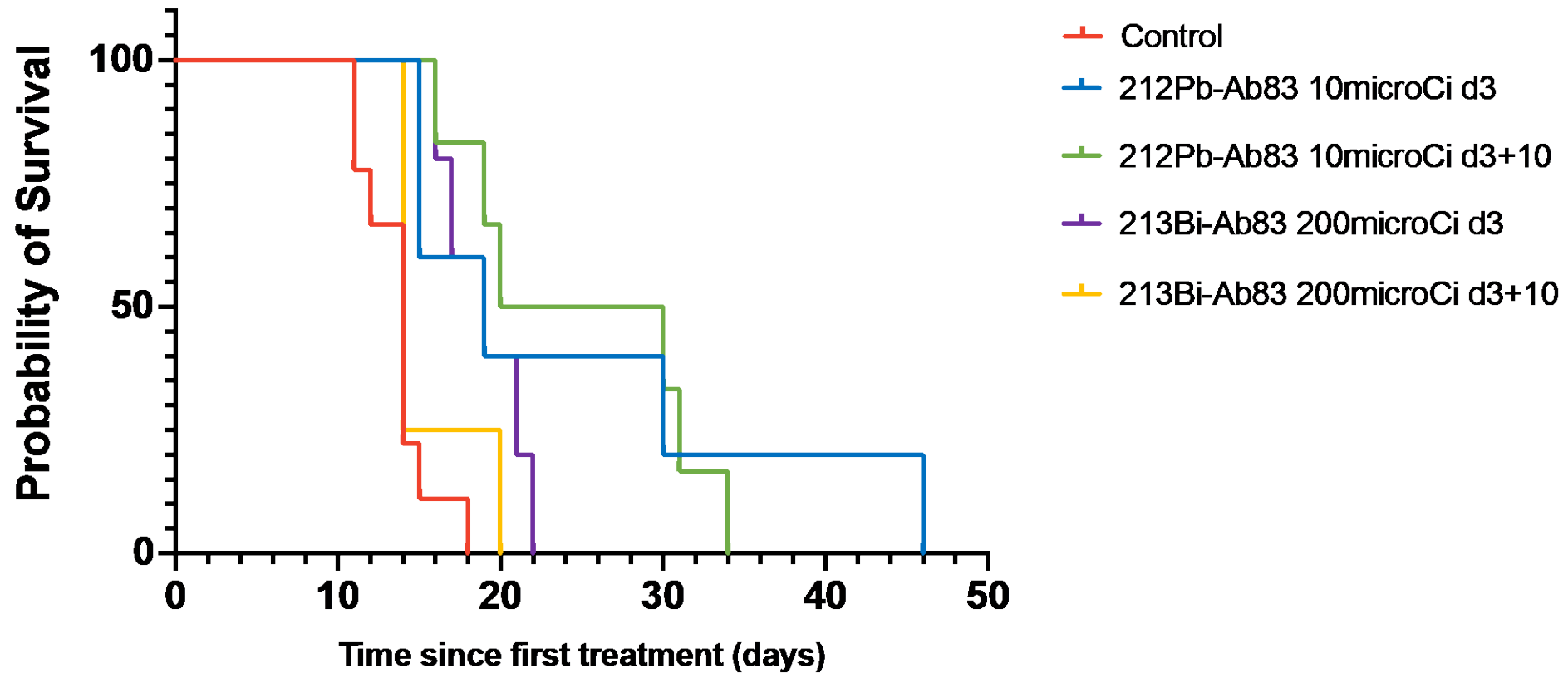


²¹³Bi-IgG

Murine Melanoma Growth Suppression Study Design



Murine Melanoma Growth Suppression Study – ^{213}Bi vs ^{212}Pb



Median survivals: 14d, 19d, 25d, 19d, 14d (Log-rank test $P = 0.0001$)

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LBNL Radiation Protection

