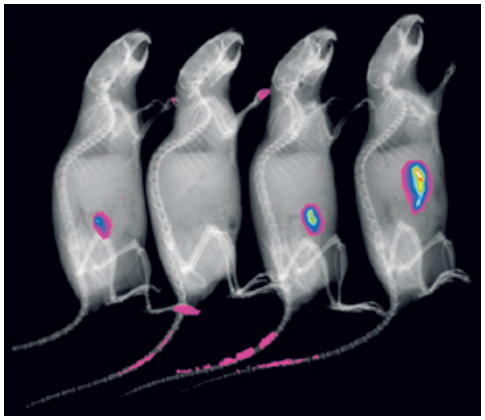
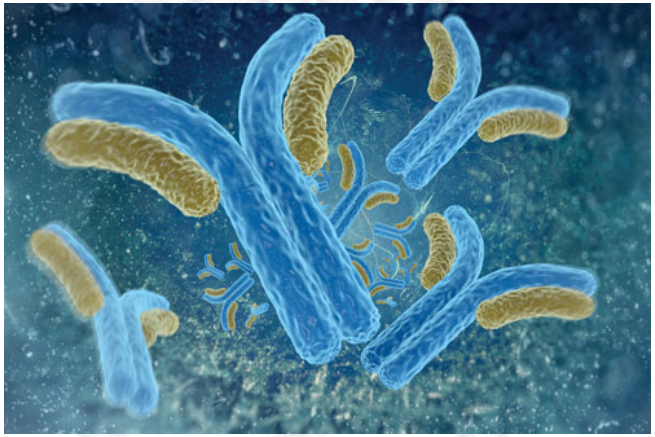
Memorial Sloan Kettering Cancer Center

Molecular Imaging of Ovarian Cancer



http://www.nature.com/nmeth/journal/v6/n6/images/nmeth0609-465-I2.jpg

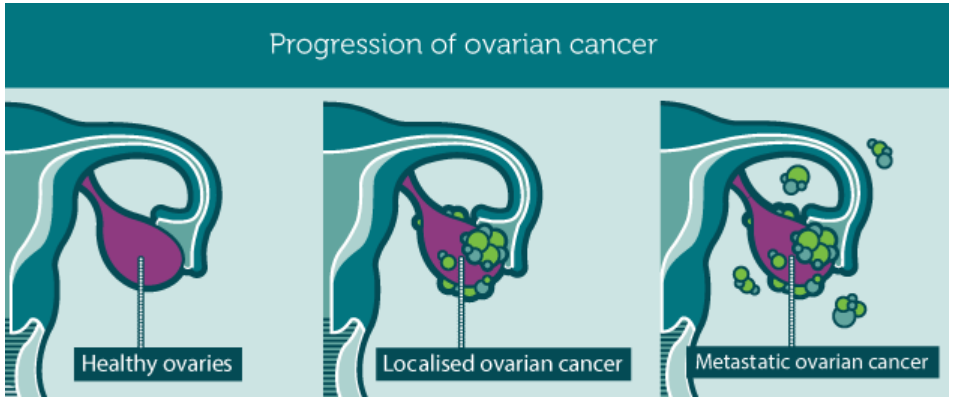
Robert Kimelman
Secaucus High School – Secaucus, NJ
Summer Student Intern
Lewis Lab Group Meeting
August 26, 2016



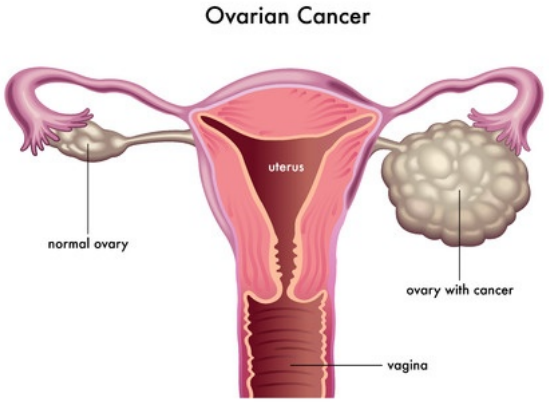
http://www.genengnews.com/gen-articles/the-antibody-dilemma/5550/

Background Information

- Symptoms: very subtle and non-specific
- Most fatal gynecologic malignancy
- Molecular signature of L1CAM antigen
- Sought to noninvasively perceive L1CAM in SKOV3 cell lines via PET/CT



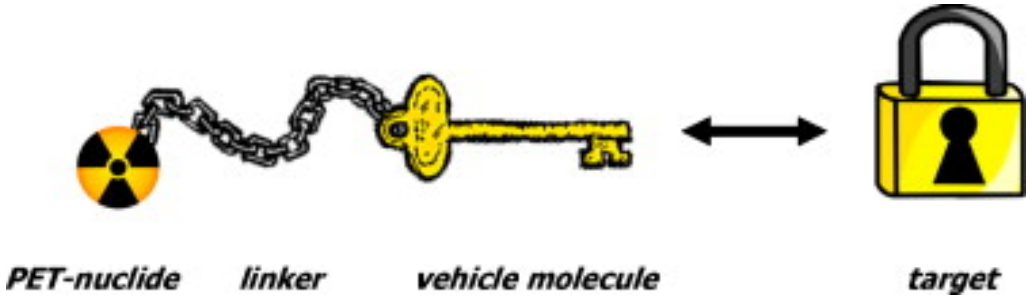
http://ovariancancerday.org/about-ovarian/

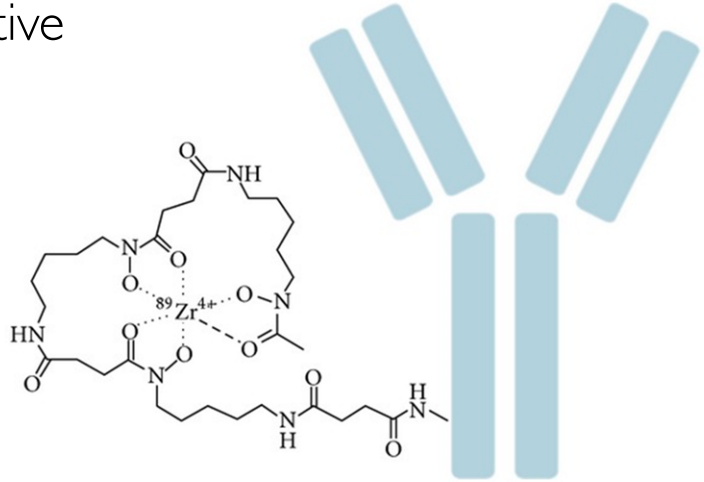


http://www.dallas-obgyn.com/gynecology/ovarian-cancer/

Background Information

- Positron emission tomography is at forefront of cancer "theranostics"
- Detects gamma rays emitted by isotopes to visualize radioactivity
- PET radiopharmaceuticals consist of:
  - A molecular structure
  - A positron emitting radionuclide
- Zirconium-89 labeling is favorable for PET
- Use of desferrioxamine (DFO) is very effective

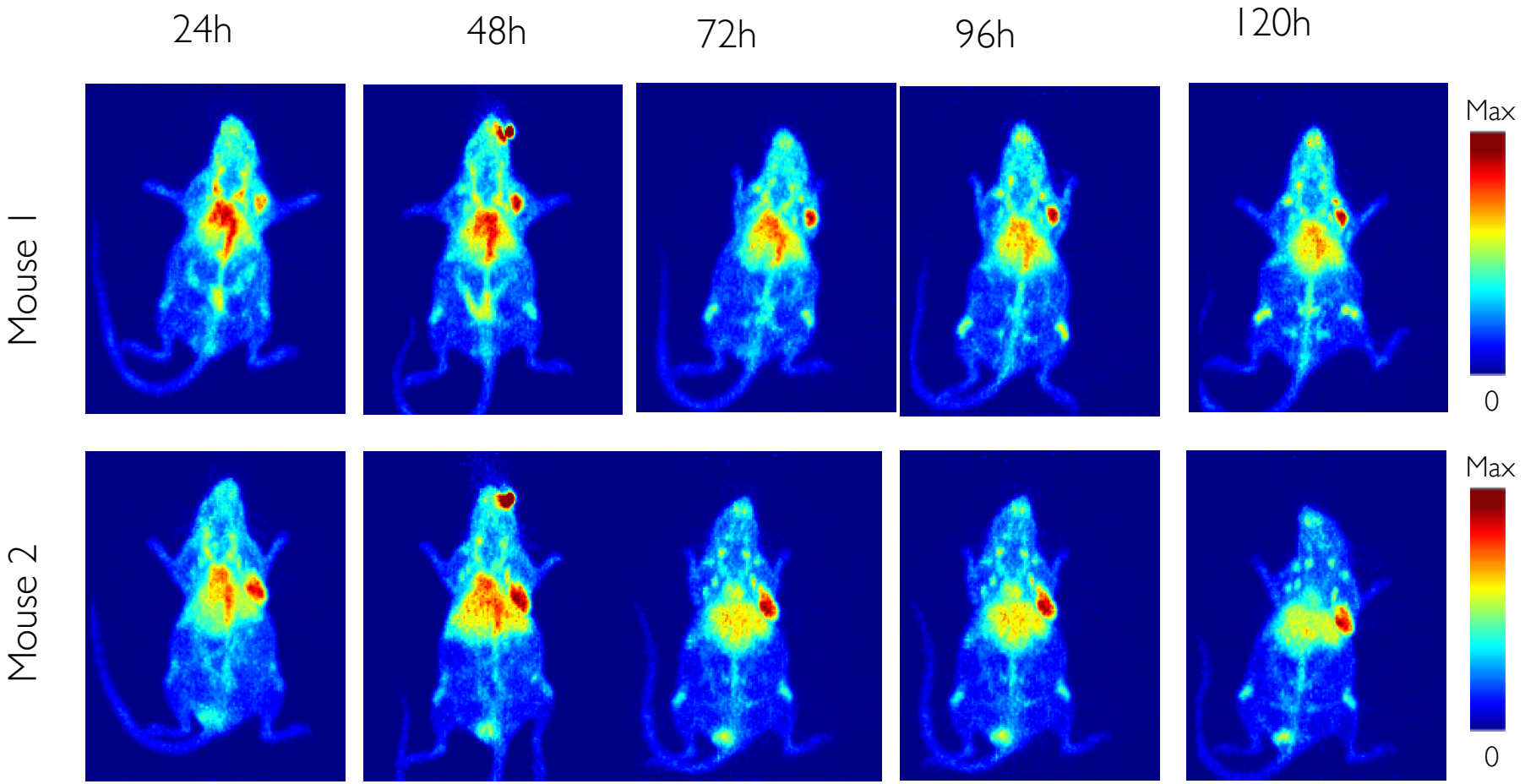


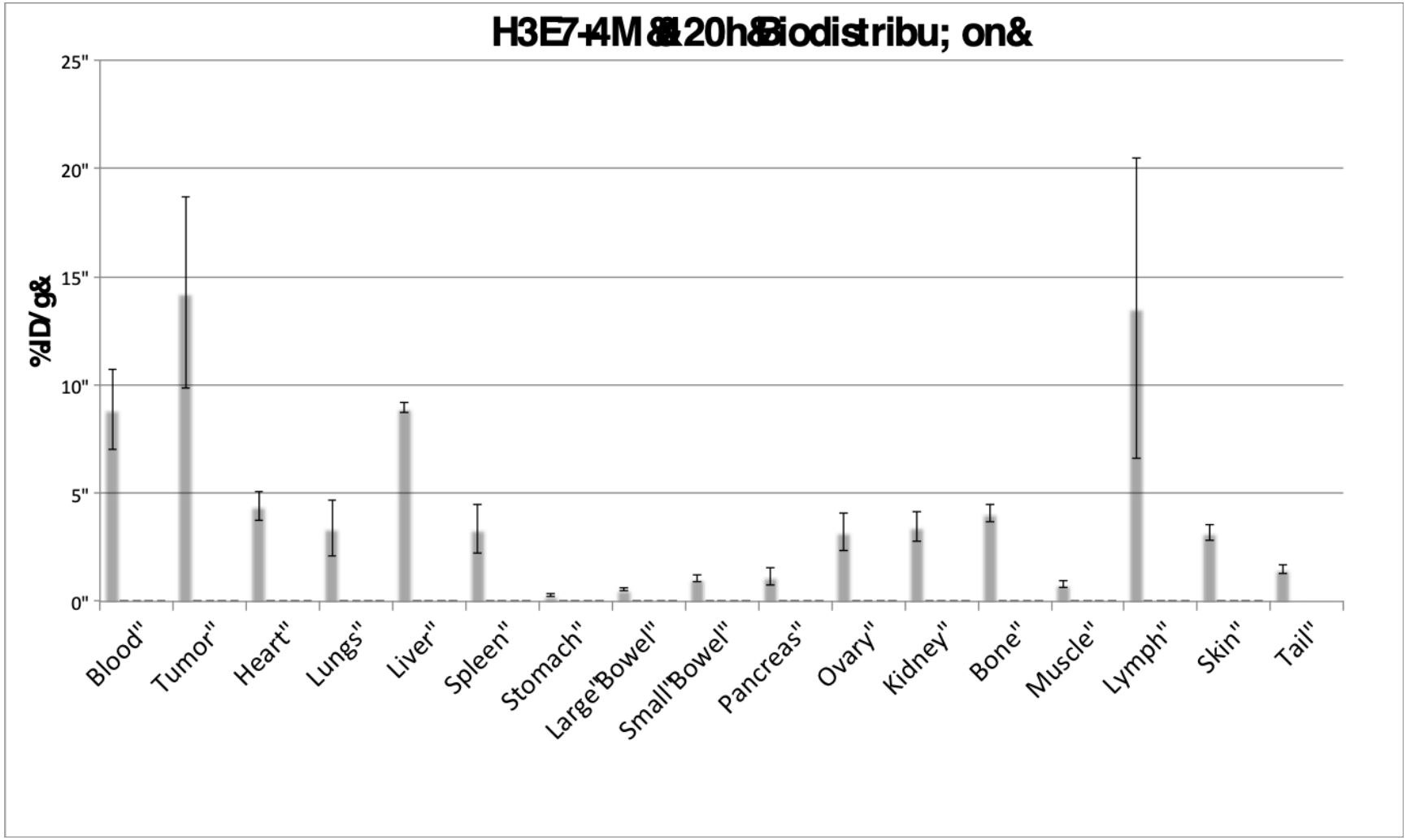


https://www.researchgate.net/figure/262763777_fig1_Schematic-overview-of-89Zr-labeled-antibody-using-DFO-as-chelator

http://www.sciencedirect.com/science/article/pii/S0720048X09006913

^{89}Zr-DFO-H3E7 IgG4 Mutated




H3E7+4M&&20h&Biodistribu;on&
%ID/g&
25"
20"
15"
10"
5"
0"
Blood"
Tumor"
Heart"
Lungs"
Liver"
Spleen"
Stomach"
Large'Bowel"
Small'Bowel"
Pancreas"
Ovary"
Kidney"
Bone"
Muscle"
Lymph"
Skin"
Tail"

Conjugation/Labeling Conditions

H3E7-4M DFO Conjugation

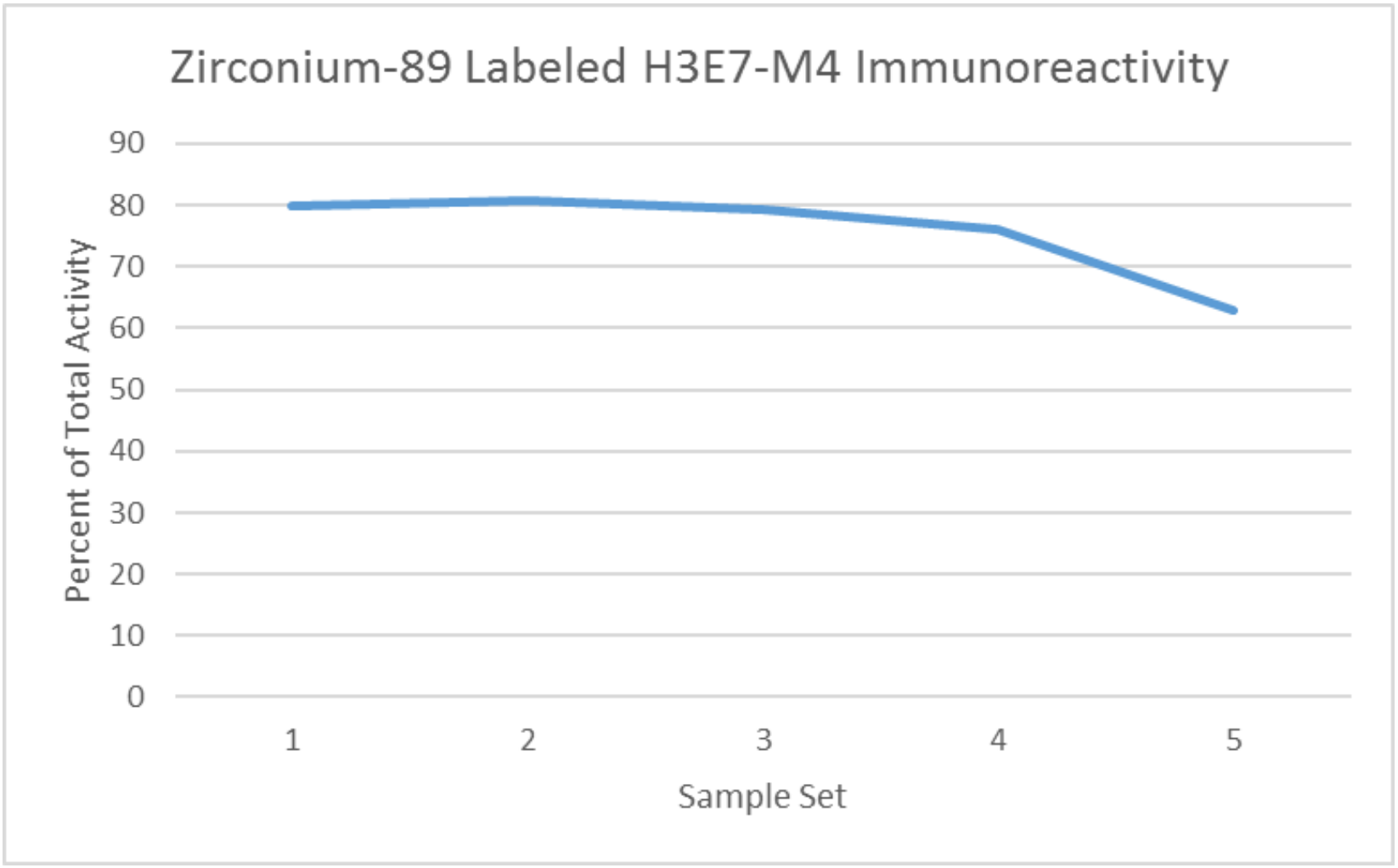
- 500 ug antibody
- DFO-antibody molar ratio – 20:1
- pH 9, 37 °C for 60 minutes in 1 mL

^{89}ZrDFO-H3E7-4M Labeling

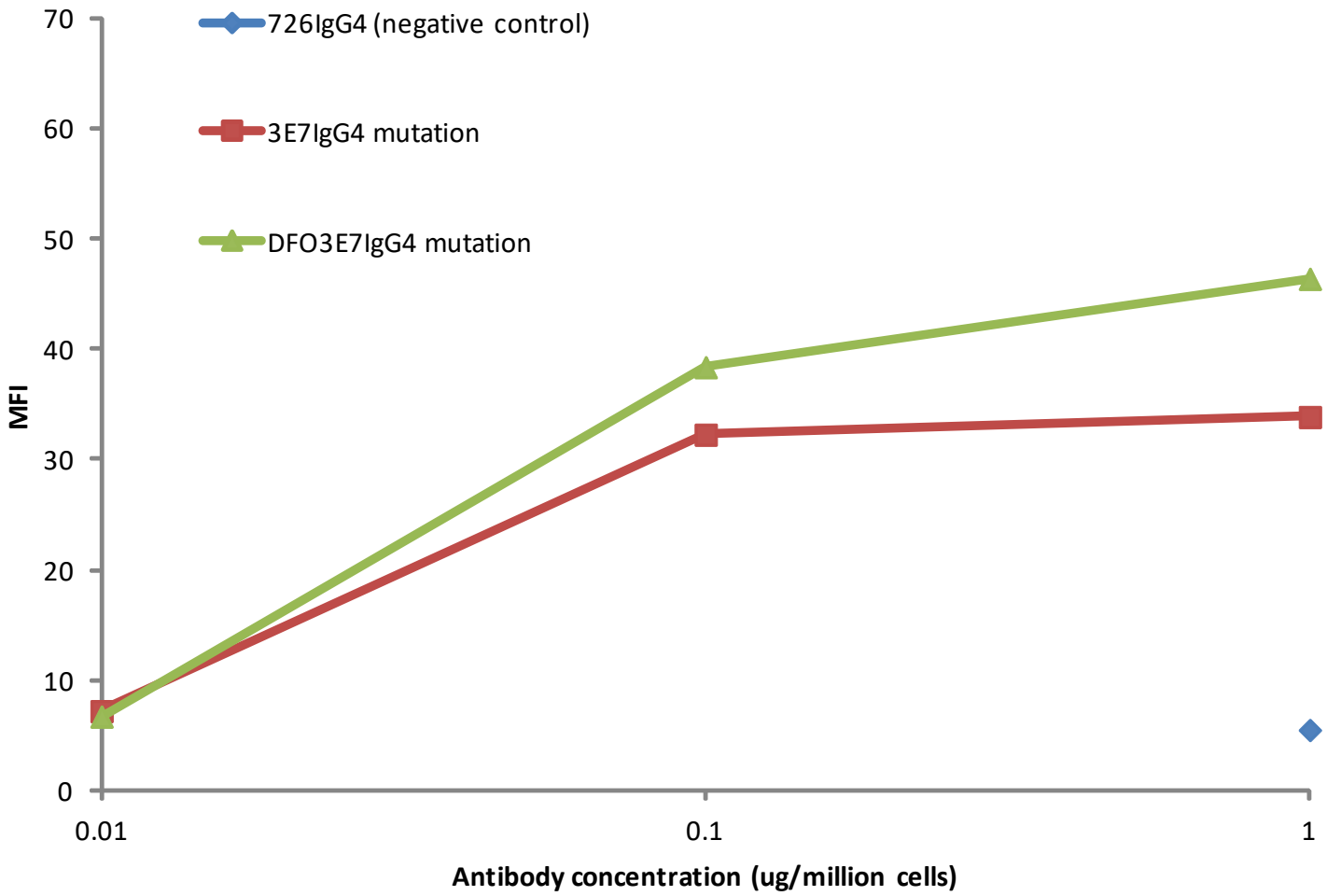
- 236 ug antibody, 650 uCi Zr
- pH 7.4, RT for 60 minutes
- **Crude RCY: 95% RCP: 99% SA: 2.75 uCi/ug**

Serum Stability

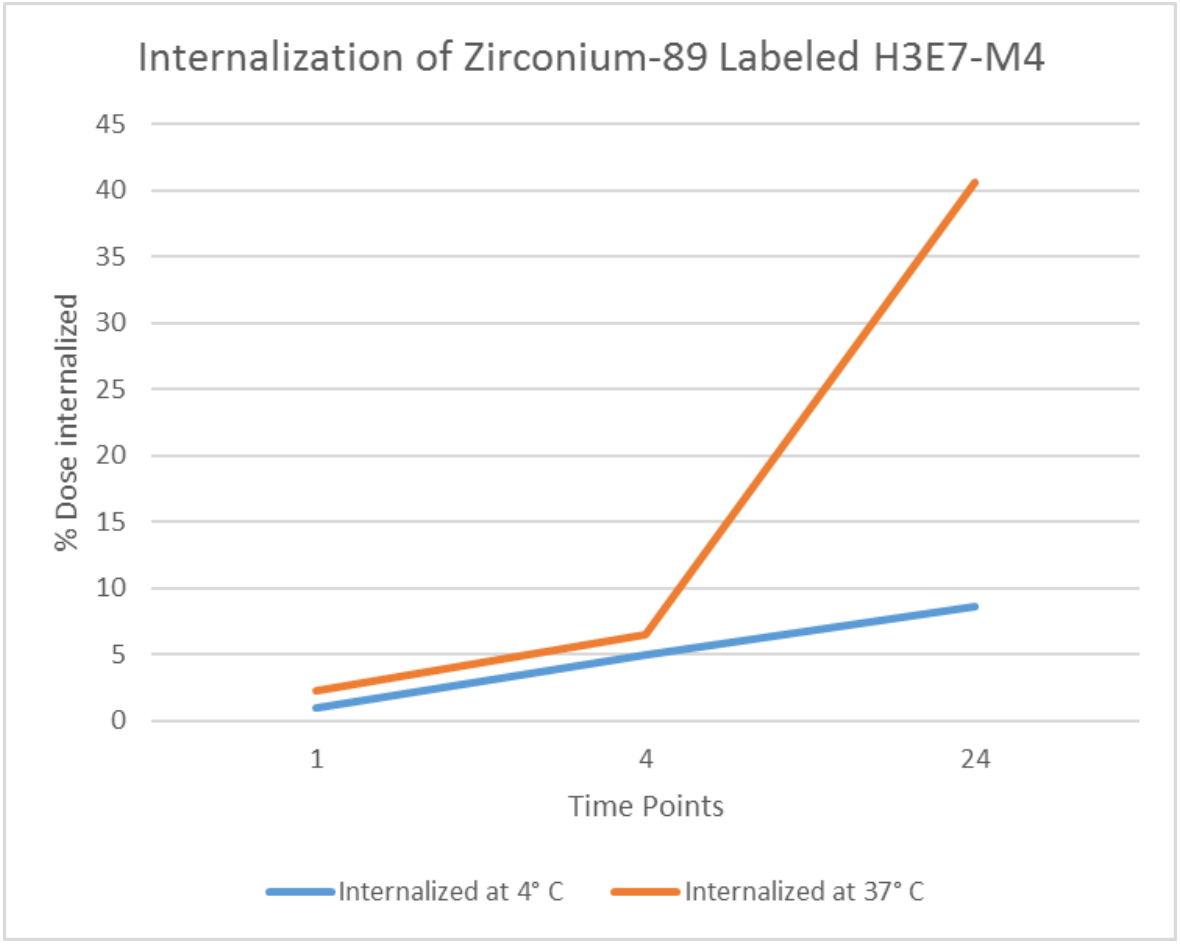
Immunoreactivity



FACS (cell line: IMR32-Luc)



Zirconium-89 Labeled H3E7-4M Internalization Assay



Conclusions and Future Work

- Minimal uptake of Zirconium-89 labeled H3E7-4M seen in kidneys
- Significant tumor uptake of Zirconium-89 labeled H3E7-4M
- SKOV3+ cells are actively internalizing Zirconium-89 labeled H3E7-4M
- Zirconium-89 labeled H3E7-4M is about 80% immunoreactive

- Future Work:
- Images with higher specific activity and biodistribution

Techniques I've Learned

- Cell Culture
- Pipetting
- PET/CT Imaging
- HPLC
- Western Blotting
- Antibody Conjugation
- Radiolabeling
- Biodistribution
- RARC Certified
- Tube Weighing
- Mouse Subcutaneous Xenografting
- Mouse Intravenous Tail Injections
- Immunoreactivity Cell Assay
- Internalization Cell Assay
- Zirconium-89 Preparation
- Orthotopic (Mouse) Surgery

Acknowledgements

- Brandon Nemieboka
- Dr. Jason Lewis
- The Lewis Lab