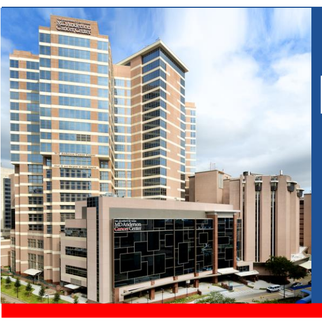

Radiolabeling of Radiopharmaceuticals for PET Imaging of Tumors

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Introduction

- Positron Emission Tomography (PET) is a non invasive diagnostic technique that employs positron-emitting radionuclides.
- [^{18}F]FDG is the most commonly used PET tracer for tumor diagnosis, and staging. It is less effective in more specific applications such as monitoring tumor response to treatment, or personalized therapy.
- **There is a need for new small molecules or antibody PET tracers**
- Small molecules have faster clearance and are usually radiolabeled via a covalent bond formation with a short-lived isotopes (ex: ^{18}F and ^{11}C).
- Monoclonal Antibody (mAb) have a slower clearance and are usually labeled via conjugation with chelator and metal complex formation with long-lived radiometals (ex: ^{64}Cu and ^{89}Zr)

Objectives

- Synthesis of a small molecule:
  - 4-[^{18}F]fluoronaphthol ([^{18}F]4FN) synthetic precursor
  - Automatic synthesis of [^{18}F]4FN on synthetic module GE-TRACERlab
- Antibody labeling
  - Conjugation of the monoclonal antibody (mAb) IgG2a with the ligand NOTA-CNS
  - Radiolabeling of IgG2a-NOTA with gallium-68 (^{68}Ga)
- Radiolabeling methodology
  - Comparison among ^{68}Ga-ligands NOTA, DOTA and ENBPI

References & Acknowledgements

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3) Sharma V, Sivapackiam J, Harpstrite SE, Prior JL, Gu H, Rath NP, Piwnica-Worms D. A generator-produced gallium-68 radiopharmaceutical for PET imaging of myocardial perfusion. PLoS One. 2014 Oct 29;9(10):e109361

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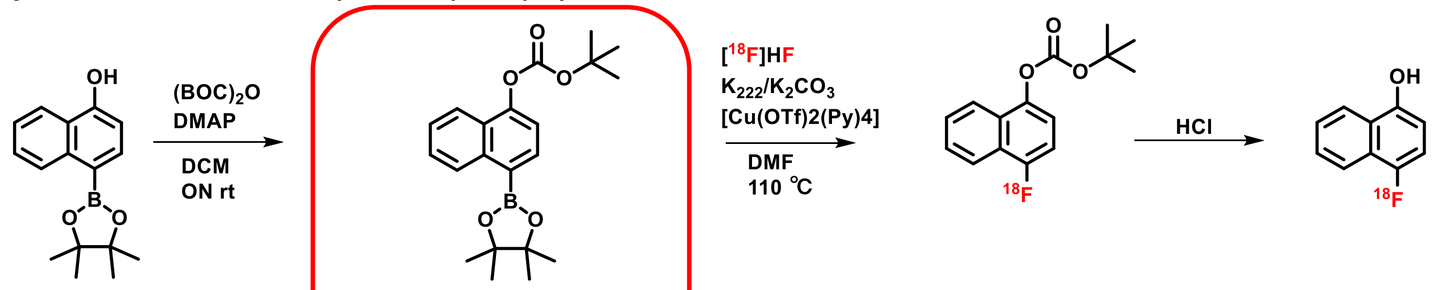
Synthesis of Small Molecules

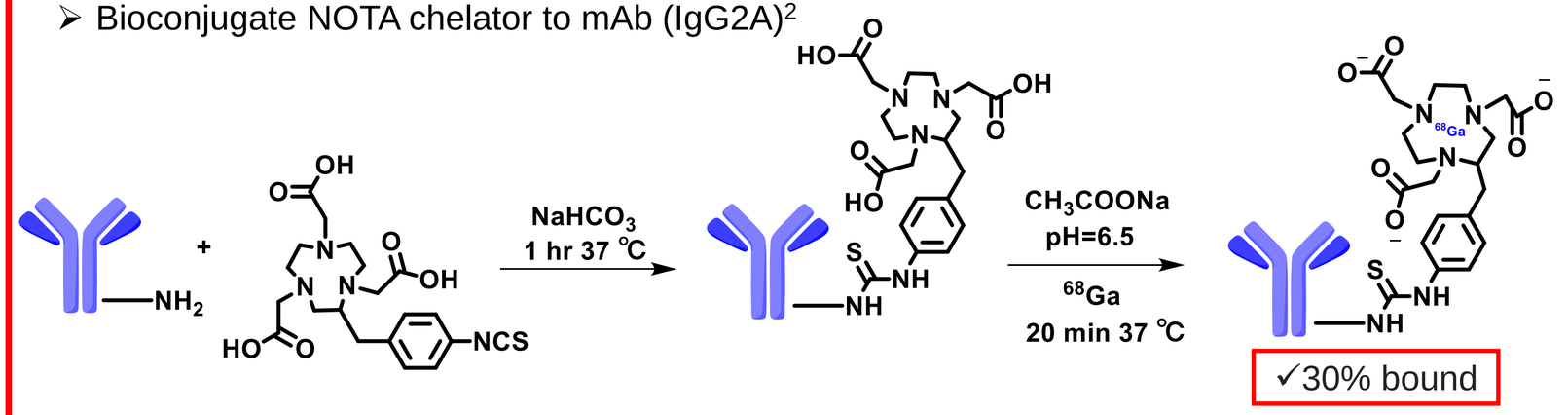
- Synthesize 4-fluoronaphthol (4FN)[1] precursor



Result:
- ✓ 59% yield (n=3)
- ✓ ^{1}H, ^{13}C, 2D NMR
- ✓ Mass Spec

Antibody Labeling

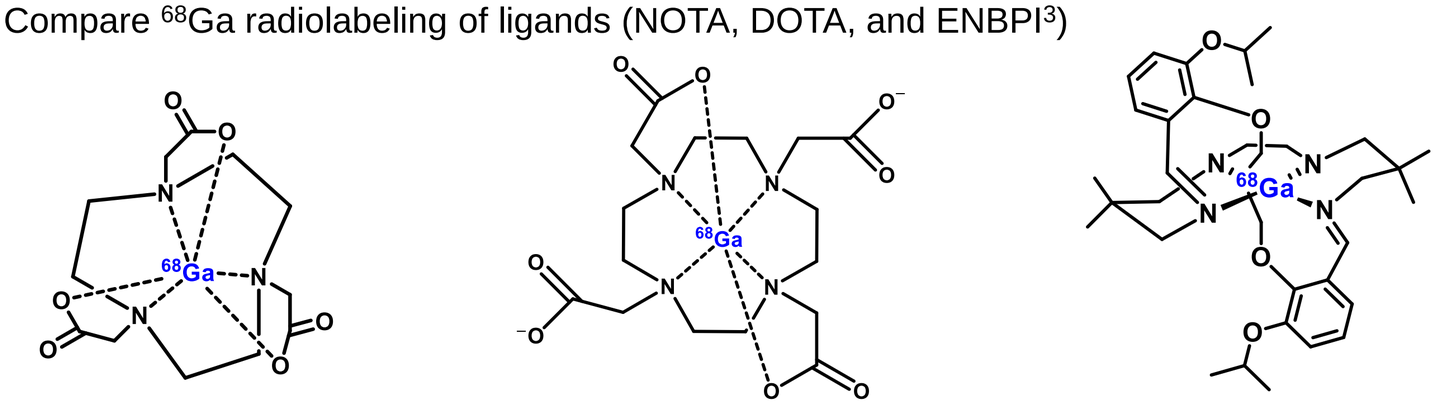
- Bioconjugate NOTA chelator to mAb (IgG2A)[2]



✓30% bound

Comparison of Ligands

- Compare ^{68}Ga radiolabeling of ligands (NOTA, DOTA, and ENBPI[3])



NOTA:
$NaHCO_3$
pH=8
20 min 80℃
✓31% bound

DOTA:
$NaHCO_3$
pH=8
20 min 80℃
✓72% bound

ENBPI:
CH_3COONa
pH=6.5
20 min 80℃
✓91% bound

Conclusion

Overall, small molecules and antibodies were radiolabeled for potential applications of diagnostic imaging in small animals. The 4FN precursor was successfully synthesized and purified, whereas the IgG2A mAb was chelated and radiolabeled. Additionally, we conducted a comparative analysis of 3 ligands and ENBPI demonstrated the highest percentage of bound ^{68}Ga.