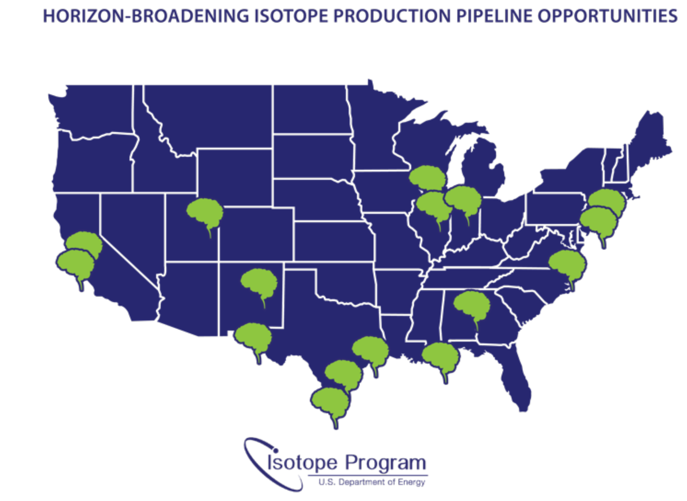
Development and Assessment of New Chelator Resins for Ti and Sc Isotope Separation

Mariae Julia Robis,[2] **Angus J. Koller,**[1] **Lilian Wang,**[1] **Margarita Chernysheva,**[3] **Jonathan Engle,**[3] **and Eszter Boros**[1]

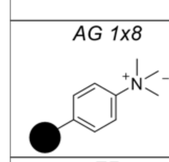
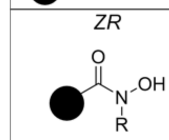
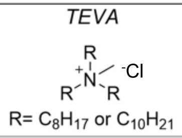
[1]Stony Brook University, [2]Macaulay Honors College – CUNY Lehman College, [3]University of Wisconsin - Madison

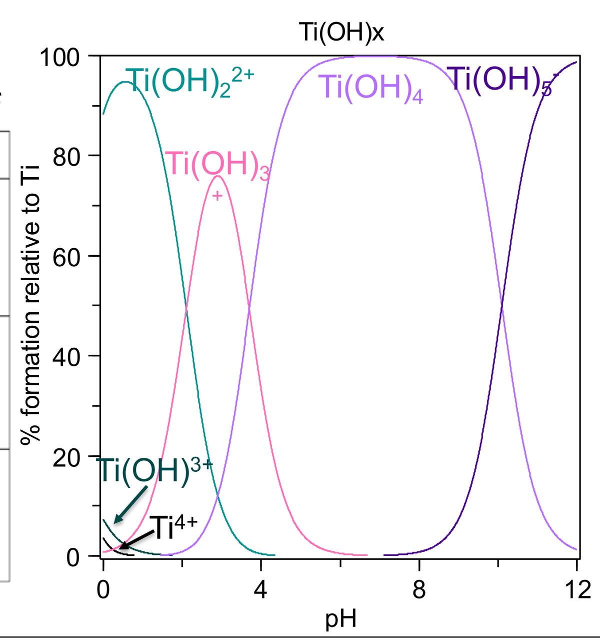


1 - Introduction

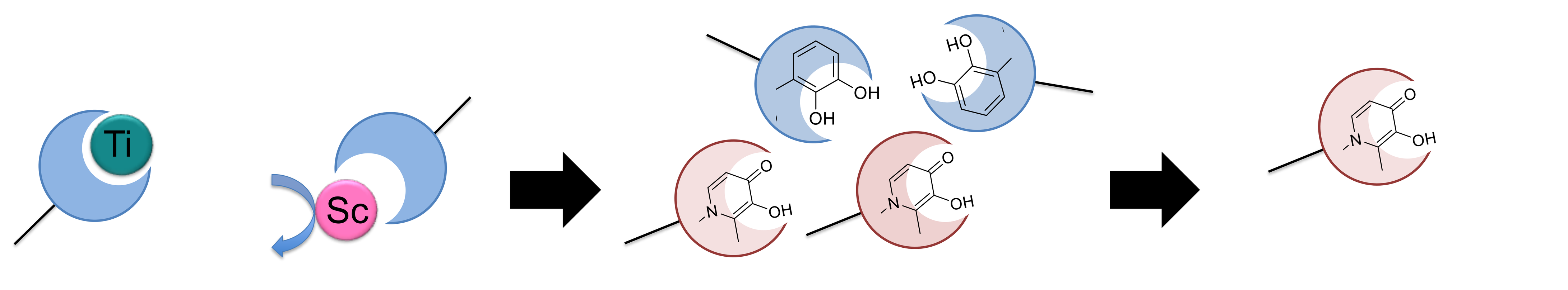
- The $^{44}Ti/^{44}Sc$ generator has potential for clinical use for production of ^{44}Sc ($t_{1/2}$= 3.97h, β^+= 94.27%, $E\beta^+_{avg}$= 632.0 keV, $E\beta^+_{max}$= 1474 keV)
- *Use is hampered by poor separation of ^{44}Sc from the long-lived mother isotope ^{44}Ti ($t_{1/2}$= 60 y), and common elution methods requiring toxic oxalic acid*
- The isotope ^{45}Ti ($t_{1/2}$= 3.08 h, β^+= 85%, $E\beta^+_{avg}$= 0.439 MeV, $E\beta^+_{max}$= 1.04 MeV) is an ideal candidate for PET imaging, produced by proton bombardment of naturally monoisotopic Sc foil via the $^{45}Sc(p,n)^{45}Ti$ reaction between 7-13.5 MeV. The ^{45}Ti is typically eluted in 0.1-1.0 M citric or oxalic acid
- *A lack of efficient separation methods due to the complex speciation and chelation behavior of Ti(IV) has prevented use of ^{45}Ti in nuclear medicine to date.*

Summary of modern $^{44}Ti/^{44}Sc$ Generators

Resin	Eluent	Yield	Additional
AG 1x8 	0.005 M oxalic acid with 0.07 M HCl	97% in 20 mL	Elution reversing and post-processing
ZR 	0.05M HCl	Not clearly stated	Elution reversing
TEVA  R= C_8H_{17} or $C_{10}H_{21}$	0.1 M oxalic acid with 0.2 M HCl	91% in 1 mL	Post-processing



At A Glance



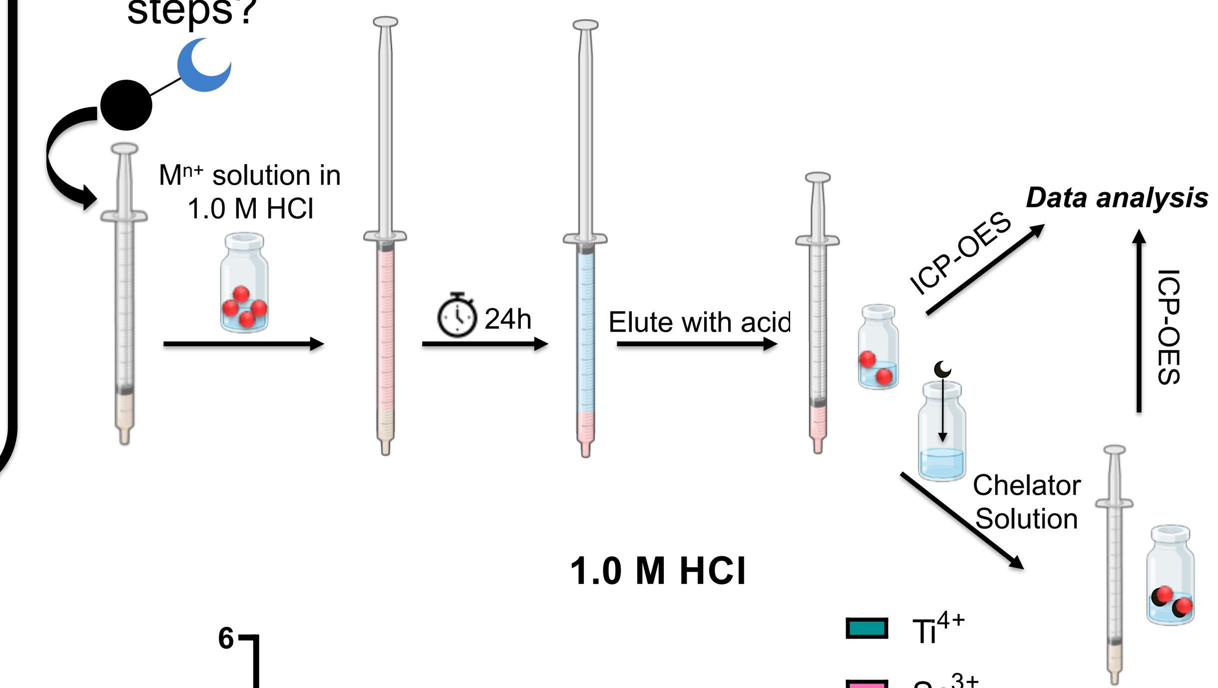
Can we develop new approaches to Sc/Ti separation?

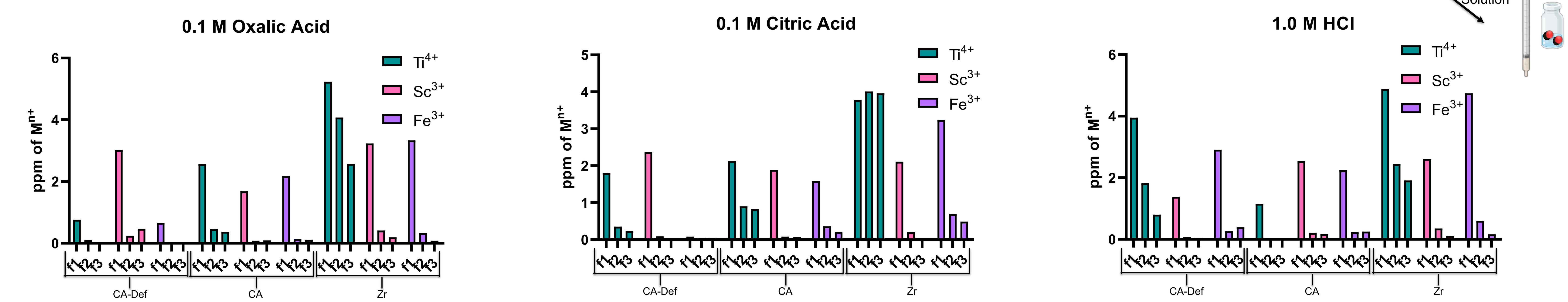
Four chelating resins were tested using ICP-OES and radiochemistry

CA-Def resin demonstrated best Ti/Sc separation at 1 M HCl

3 – $^{nat}Ti/^{nat}Sc$ Separation Analysis

- Can the CA-Def resin separate trace Ti^{4+} from bulk Sc^{3+}?
- Can additional impurities such as Fe^{3+} be removed in the loading step, or with additional washing steps?

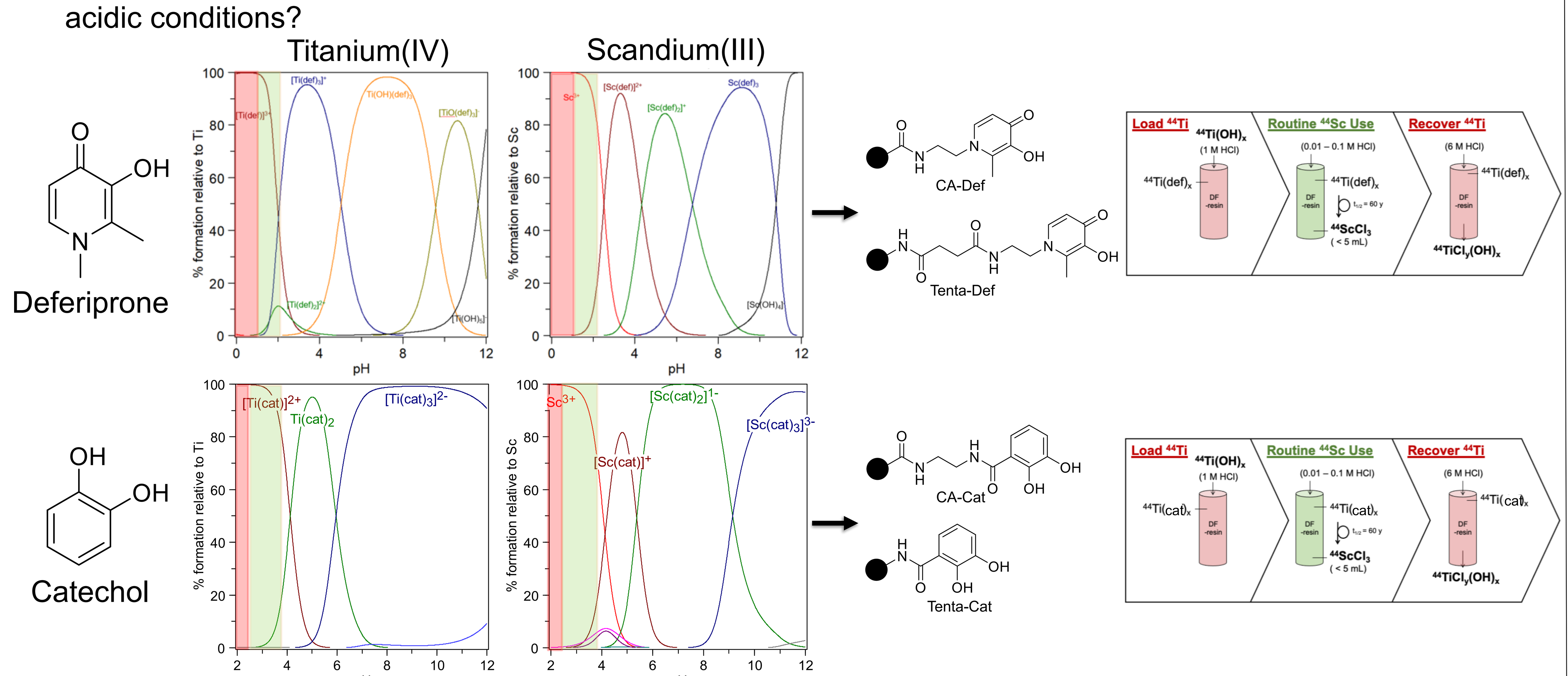




CA-Def resin shows affinity for macroscopic amounts of Ti^{4+} in 1 M HCl. Sc^{3+} and Fe^{3+} impurities can be removed at loading by washing with 0.1 M oxalic acid

2 - Chelator-Based Resins for Separation of Ti^{4+} and Sc^{3+}

- The highly basic deferiprone (def) and catechol (cat) chelators have been previously shown by our group to effectively stabilize titanium in aqueous solution
- Can def and cat chelators be immobilized on solid phase and effectively separate Ti^{4+} and Sc^{3+} under mild acidic conditions?



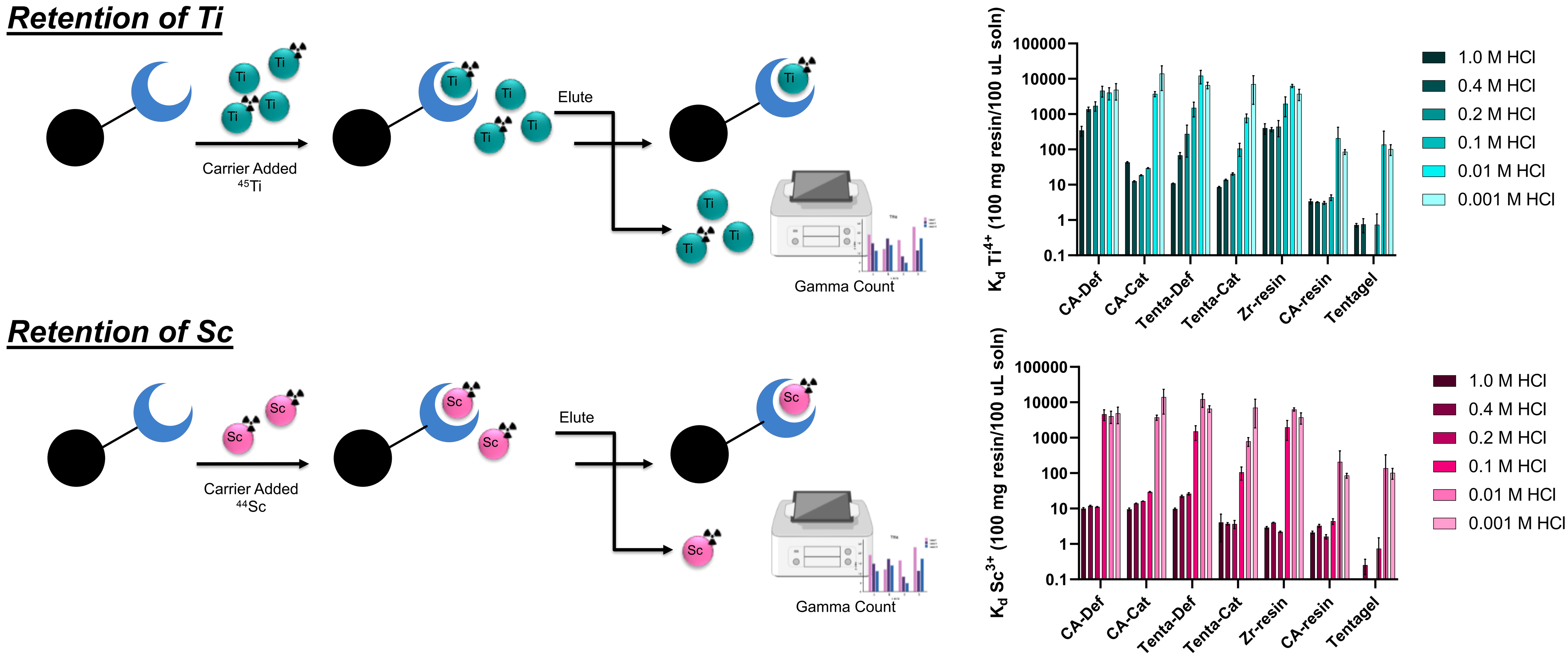
Def and Cat functionalized resins can be effectively synthesized.

4 – $^{44}Ti/^{44}Sc$ Separation Analysis

- Can chelator-based resins separate bulk Ti^{4+} from trace Sc^{3+} under mild conditions?
- Is breakthrough of ^{44}Ti reduced?
- Do the separation properties of immobilized chelators closely resemble that of the solution speciation?

Retention of Ti

Retention of Sc



CA-Def shows effective Ti/Sc separation between 1.0-0.2 M HCl. Ti4+ affinity follows trends predicted by macroscopic solution chemistry experiments, but Sc^{3+} affinity is likely overestimated.

5 - Conclusions:

- Chelating resins were rationally designed based on solution speciation of Ti^{4+} and Sc^{3+}
- CA-Def resin showed the highest potential for the separations of Ti^{4+} and Sc^{3+}
- A model $^{44}Ti/^{44}Sc$ generator using CA-Def showed promise, but improved Ti^{4+} retention is necessary
- Purification of $^{45}Ti^{4+}$ from $^{nat}Sc^{3+}$ and Fe^{3+} shows promise in 1.0 M HCl, limiting the dilution necessary after target dissolution

Acknowledgements:

- This work was supported in part by Department of Energy Isotope Program's Grant DE-SC0022550, the Horizon-broadening Isotope Production Pipeline Opportunities (HIPPO) program.
- The Gordon and Betty Moore Foundation (E. B.) are thanked for generous financial support of this work.

References:

Koller, A. et al. *Angew. Chem. Int. Ed.* **2022,** *in-press*
Chaple, I. et al. *Appl. Radiat. Isot.* **2020**, *166*, 109398
Vavere, A. L. et al. *J. Nucl. Med.* **2005**, *46*, 683-690
Borgias, B. et al. *Inorg. Chem.* **1984**, *23*, 1009–1016