

Nikki A. Thiele, PhD

R&D Staff Scientist
Chemical Sciences Division
Oak Ridge National Laboratory
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Professional Experience

Oak Ridge National Laboratory

Staff Scientist, Chemical Sciences Division, Oak Ridge, TN

2023–present

Associate Staff Scientist, Chemical Sciences Division, Oak Ridge, TN

2020–2022

Research focus: Coordination chemistry of underexplored radioactive ions relevant to nuclear medicine; development of new chelation platforms for targeted radionuclide therapy; separation and recovery of critical materials (e.g., rare earth elements); anion recognition

Cornell University

2016–2019

Postdoctoral Associate, Department of Chemistry and Chemical Biology, Ithaca, NY

Advisor: Prof. Justin J. Wilson

Research focus: Ligand development for selective and stable chelation of heavy metal ions (e.g., Ba^{2+} , $^{223}Ra^{2+}$, Ln^{3+} , $^{225}Ac^{3+}$) for diagnostic, therapeutic, and industrial applications

Education

University of Florida

2016

Ph.D. Pharmaceutical Sciences, Department of Medicinal Chemistry, Gainesville, FL

Advisor: Prof. Kenneth Sloan

Dissertation: Prodrug Strategies for Therapeutic Delivery and Neuroprotection in Parkinson's Disease

State University of New York at Potsdam

2009

B.A. Biology, Department of Biology, Potsdam, NY

Teaching and Mentoring

Oak Ridge National Laboratory

Graduate Student Interns:

(3) **D. Mike Todd**, graduate research (GRO) internship, **Fall 2023**

2nd year graduate student, Michigan State University, Department of Chemistry (Advisor: Prof. Alyssa Gaiser)

(2) **Caroline Lara**, GEM student, **Summer 2022**

2nd year graduate student, University of Notre Dame, Department of Biological Sciences (Advisor: Prof. Rebecca Wingert)

(1) **Aohan Hu**, ORISE virtual Graduate Research Summer Internship, **Summer 2021**

4th year graduate student, Cornell University, Department of Chemistry and Chemical Biology (Advisor: Prof. Justin Wilson)

Postdoctoral Associates:

(5) **Dr. Ana Belen Cueva Sola**, **6/2023–present**

Ph.D. Resources Engineering, Korea University of Science and Technology (Dr. Jin-Young Lee, Dr. Rajesh Kumar Jyothi)

(4) **Dr. Md Faizul Islam**, **4/2023–present**

Ph.D. Chemistry, University of South Carolina (Prof. Linda Shimizu)

(3) **Dr. Megan Sibley**, **1/2023–present**

Ph.D. Chemistry, Clemson University (Prof. Modi Wetzler)

(2) **Dr. Briana Schrage**, **7/2022–8/2023**

Ph.D. Inorganic Chemistry, University of Akron (Prof. Christopher Ziegler). Current position: associate staff scientist, Radioisotope Science and Technology Division (ORNL)

(1) **Dr. Janel Dempsey**, **8/2021–7/2022**

Ph.D. Chemistry, Notre Dame (Prof. Bradley Smith). Current position: Applied Photophysics (Beverly, MA).

Technical Staff:

(1) **Megan Simms, 3/2022–8/2022**

B.S. Biochemistry, Metropolitan State University of Denver. Current position: technical staff, Radioisotope Science and Technology Division

Cornell University

Supervised and mentored two undergraduate chemistry majors in synthetic organic chemistry and analytical chemistry techniques

University of Florida

Graded exams for PharmD-level courses including Fundamentals of Medicinal Chemistry, Medicinal Chemistry I, Medicinal Chemistry II, and Structure and Function of Nucleotides

Honors and Awards

Laboratory Space Manager (LSM) Notable, ORNL, 2021

Trainee Scholarly Exchange Program, Weill Cornell/Cornell Ithaca Cross Campus, 2018

First Place Poster, Hunter College Symposium on Radiometals, 2017

Biology Department Scholar, SUNY Potsdam, 2009

Chemistry Department Award, Sullivan County Community College, 2007

Natural & Health Sciences, Mathematics, and Physical Education Division Award, Sullivan County Community College, 2007

Activities

Radiological Laboratory Manager, ORNL, 2020–present

American Chemical Society, Inorganic Chemistry and Nuclear Chemistry & Technology Divisions; Society of Radiopharmaceutical Sciences

Reviewer for: Chemical Science, Inorganic Chemistry, Journal of Nuclear Medicine, Solvent Extraction and Ion Exchange, New Frontiers in Research Fund, JOVE, RSC Advances, ORNL LDRD/SEED

Publications

* denotes corresponding authorship

† denotes co-first authorship

Independent Career

- (26) Simms, M. E.; Sibley, M. M.; Driscoll, D. M.; Kertesz, V.; Damron, J. T.; Ivanov, A. S.;* White, F. D.;* **Thiele, N. A.*** Reining in radium for nuclear medicine: Extra-large chelator development for an extra-large ion. **2023**, *Submitted*.
- (25) White, F. D.;* **Thiele, N. A.***; Simms, M. E.; Cary, S. K. The structure and bonding of a radium coordination compound in the solid state. *Nat. Chem.* **2023**, *Accepted*. *Preprint available on ChemRxiv, [10.26434/chemrxiv-2023-lx8c1](https://doi.org/10.26434/chemrxiv-2023-lx8c1). Highlighted in Chemistry World (First x-ray structure of radium compound gives glimpse of element's coordination chemistry | Research | Chemistry World)*.
- (24) Gilhula, J. C.; Xu, L.; White, F. D.; Adelman, S. L.; Aldrich, K. E.; Batista, E. R.;* Dan, D.; Jones, Z. R.; Kozimor, S. A.;* Lilley, L. M.; Matson, E. M.; Meyer, R. L.; **Thiele, N. A.***; Yang, P.;* Yuan, M. Overcoming challenges facing the complexation of weakly electrophilic metal cations, like Ra^{2+} , Ba^{2+} , and Sr^{2+} . **2023**, *In Review*.
- (23) Cahill, J. F.;* Kertesz, V.; Saint-Vincent, P.; Valentino, H.; Drufva, E.; **Thiele, N. A.**; Michener, J. K. High throughput characterization and optimization of polyamide hydrolase activity using open port sampling interface mass spectrometry. *J. Am. Soc. Mass Spectrom.* **2023**, 34, 1383–1391.
- (22) Premadasa, U. I.; Bocharova, V.; Lin, L.; Genix, A.-C.; Heller, W. T.; Sacci, R. L.; Ma, Y.-Z.; **Thiele, N. A.**; Doughty, B. Tracking molecular transport across oil/aqueous interfaces: Insight into ‘antagonistic’ binding in solvent extraction. *J. Phys. Chem. B*, **2023**, 127, 4886–4895.
- (21) King, A. P.; Gutsche, N. T.; Natarajan, R.; Baidoo, K. E.; Bell, M. M.; Swenson, R.; Lin, F. I.; Sadowski, S. M.; Adler, S.; **Thiele, N. A.**; Wilson, J. J.; Choyke, P. L.; Escorcía, F. E. ^{225}Ac -macropatate: A novel alpha particle peptide receptor radionuclide therapy for neuroendocrine tumors. *J. Nucl. Med.* **2022**, 64, 549–554.
- (20) Gibson, L. D.; Jayanthi, K.; Yang, S.; **Thiele, N. A.**; Anovitz, L. M.; Sacci, R. L.; Navrotsky, A.; Bryantsev, V. S. Characterization of lanthanum monazite surface chemistry and crystal morphology through density functional

- theory and experimental approaches. *J. Phys. Chem. C* **2022**, *126*, 18952–18962.
- (19) Ivanov, A.;* Simms, M. E.; Bryantsev, V. S.; Benny, P. D.; Griswold, J. R.; Delmau, L. H.; **Thiele, N. A.*** Elucidating the coordination chemistry of the radium ion for targeted alpha therapy. *Chem. Commun.* **2022**, 58, 9938–9941. *Highlighted in two segments of the WVLN nightly news (local CBS station, [ORNL scientist working on a more targeted treatment for cancer \(wvlt.tv\)](https://www.chemistryworld.com/news/radium-chelator-researchers-working-to-improve-targeted-cancer-therapies/4016608.article)). Featured in Chemistry World (<https://www.chemistryworld.com/news/radium-chelator-researchers-working-to-improve-targeted-cancer-therapies/4016608.article>). Highlighted by the Department of Energy Isotope Program (ISOTOPE RESEARCH DEVELOPMENT AND... | U.S. DOE Office of Science(SC) ([osti.gov](https://www.osti.gov)))*
- (18) Hu, A.; Simms, M. E.; Kertesz, V.; Wilson, J. J.;* **Thiele, N. A.*** Chelating rare-earth metals (Ln^{3+}) and $^{225}\text{Ac}^{3+}$ with the dual-size-selective macrocyclic ligand py₂-macrodipa. *Inorg. Chem.* **2022**, *61*, 12847–12855.
- (17) Stamberg, D.; **Thiele, N. A.**; Custelcean, R. Synergistic direct air capture of CO₂ with aqueous guanidine/amino acid solvents. *MRS Advances*. **2022**, *7*, 399–403.
- (16) Premadasa, U. I.; Ma, Y.-Z.; Sacci, R. L.; Bocharova, V.; **Thiele, N. A.**; Doughty, B. Understanding self-assembly and the stabilization of liquid/liquid interfaces: The importance of ligand tail branching and oil-phase solvation. *J. Colloid Interface Sci.* **2022**, *609*, 807–814.

Mentored Work

- (15) Fiszbein, D. J.; Brown, V.; **Thiele, N. A.**; Woods, J. J.; Wharton, L.; MacMillan, S. N.; Radchenko, V.; Ramogida, C. F.; Wilson, J. J. Tuning the kinetic inertness of Bi³⁺ complexes: The impact of donor atoms on diaza-18-crown-6 ligands as chelators for ²¹³Bi targeted alpha therapy. *Inorg. Chem.* **2021**, *60*, 9191–9211.
- (14) Abou, D. S.;† **Thiele, N. A.**;† Gutsche, N. T.; Villmer, A.; Zhang, H.; Woods, J. J.; Baidoo, K. E.; Escorcia, F. E.; Wilson, J. J.; Thorek, D. J. Towards the stable chelation of radium for biomedical applications with an 18-membered macrocyclic ligand. *Chem. Sci.* **2021**, *12*, 3733–3742.
- (13) **Thiele, N. A.**; Fiszbein, D. J.; Woods, J. J.; Wilson, J. J. Tuning the separation of light lanthanides using a reverse-size selective aqueous complexant. *Inorg. Chem.* **2020**, *59*, 16522–16530.
- (12) Aluicio-Sarduy, E.;† **Thiele, N. A.**;† Martin, K. E.; Vaughn, B. A.; Devaraj, J.; Olson, A. P.; Barnhart, T. E.; Wilson, J. J.; Boros, E.; Engle, J. W. Establishing radiolanthanum chemistry for targeted nuclear medicine applications. *Chem. Eur. J.* **2020**, *26*, 1238–1242.
- (11) **Thiele, N. A.**; Woods, J. J.; Wilson, J. J. Implementing f-block metal ions in medicine: Tuning the size selectivity of expanded macrocycles. *Inorg. Chem.* **2019**, *58*, 10483–10500. *Invited Forum Article for the issue “Celebrating the Year of the Periodic Table: Emerging Investigators in Inorganic Chemistry”*
- (10) Kelly, J. M.; Amor-Coarasa, A.; Ponnala, S.; Nikolopoulou, A.; Williams Jr., C.; **Thiele, N. A.**; Schlyer, D.; Wilson, J. J.; DiMaggio, S. G.; Babich, J. W. A single dose of ²²⁵Ac-RPS-074 induces a complete tumor response in a LNCaP xenograft model. *J. Nucl. Med.* **2019**, *60*, 649–655.
- (9) **Thiele, N. A.**; MacMillan, S. N.; Wilson, J. J. Rapid dissolution of BaSO₄ by macropa, an eighteen-membered macrocycle with high affinity for Ba²⁺. *J. Am. Chem. Soc.* **2018**, *140*, 17071–17078. *Highlighted in the news: “Macrocyclic Ligand Dissolves Barium Sulfate in Pipelines,” [ChemistryViews.org](https://www.chemistryviews.org)*
- (8) **Thiele, N. A.**; Wilson, J. J. Actinium-225 for targeted α therapy: Coordination chemistry and current chelation approaches. *Cancer Biother. Radiopharm.* **2018**, *33*, 336–348. *Invited review article, 3rd most-read paper from the journal in the last 12 months (6/2018–6/2019)*
- (7) **Thiele, N. A.**; Kärkkäinen, J.; Sloan, K. B.; Rautio, J.; Huttunen, K. M. Secondary carbamate linker can facilitate the sustained release of dopamine from brain-targeted prodrug. *Bioorg. Med. Chem. Lett.* **2018**, *28*, 2856–2860.
- (6) **Thiele, N. A.**; Brown, V.; Kelly, J. M.; Amor-Coarasa, A.; Jermilova, U.; MacMillan, S. N.; Nikolopoulou, A.; Ponnala, S.; Ramogida, C. F.; Robertson, A. K. H.; Rodríguez-Rodríguez, C.; Schaffer, P.; Williams Jr., C.; Babich, J. W.; Wilson, J. J. An eighteen-membered macrocyclic ligand for actinium-225 targeted alpha therapy. *Angew. Chem. Int. Ed.* **2017**, *56*, 14712–14717.
- (5) **Thiele, N. A.**;* Sloan, K. B. A double prodrug with improved membrane permeability over the parent chelator HBED provides superior cytoprotection against hydrogen peroxide. *ChemMedChem.* **2016**, *11*, 1596–1599.
- (4) **Thiele, N. A.**; McGowan, J.; Sloan, K. B. 2-O-Acyl-3-O-(1-acyloxyalkyl) prodrugs of 5,6-isopropylidene- L-ascorbic acid and L-ascorbic acid: antioxidant activity and ability to permeate silicone membranes. *Pharmaceutics* **2016**, *8*, 22.

- (3) **Thiele, N. A.;*** Abboud, K. A.; Sloan, K. B. Novel double prodrugs of the iron chelator *N,N'*-bis(2-hydroxybenzyl)ethylenediamine-*N,N'*-diacetic acid (HBED): Synthesis, characterization, and investigation of activation by chemical hydrolysis and oxidation. *Eur. J. Med. Chem.* **2016**, *118*, 193–207.
- (2) Prybylski, J.; **Thiele, N. A.;** Sloan, K. B. Regioselective synthesis of 2-O-acyl-3-O-(1-acyloxyalkyl) prodrugs of 5,6-isopropylidene-L-ascorbic acid. *Tetrahedron Lett.* **2016**, *57*, 1619–1621.
- (1) McGowan, J.; **Thiele, N.;** Sloan, K. B. Prodrugs of vitamin C: the reaction of 1-acyloxyalkyl-1-iodides with vitamin C 5,6-acetonide. *Tetrahedron Lett.* **2015**, *56*, 5441–5444.

Patents

Granted

- (1) John W. Babich, Justin Wilson, Nikki Thiele, James Kelly, Shashikanth Ponnala. “Macrocyclic complexes of alpha-emitting radionuclides and their use in targeted radiotherapy of cancer.” Patent No US 11,279,698 B2, Granted March 22, 2022. (Cornell)

Under Prosecution

- (1) Nikki Thiele, Justin Wilson. “Metal-Chelating Compositions and their Use in Methods of Removing or Inhibiting Barium Scale.” U.S. Patent Application Publication No. US 2021/0221715 A1, Publication Date July 22, 2021. (Cornell)

Filed

- (2) Justin J. Wilson, Aohan Hu, Nikki Thiele. “Macrocycles and Complexes with Radionuclides useful in Targeted Radiotherapy of Cancer.” International Patent Application No. PCT/US22/31196, Filing Date May 26, 2022. (joint ORNL/Cornell application)
- (1) Daniel Thorek, Diane Abou, Justin Wilson, Nikki Thiele. “Compositions and Methods for Radiotherapy using Chelated Radiotherapeutic Agents and Non-Target Tissue Blockade.” U.S. Patent Application Publication No. US 2022/0152228 A1, Publication Date May 19, 2022. (Cornell)

Provisional

- (1) Nikki Thiele, Janel Dempsey, Bruce Moyer. “Size-Selective Chelators and Their Use as Leaching Agents for the Recovery of Rare Earth Elements.” U. S. Provisional Patent Application No. 63/310,247, Filing Date February 15, 2022. (ORNL)
- (2) Nikki Thiele, Megan Simms. “Macrocyclic Complexes of Radionuclides and Use Thereof.” U. S. Provisional Patent Application No. 63/449,612, Filing Date March 3, 2023. (ORNL)

Presentations

Independent Career

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|--------|---|
| 8/2023 | “Liberating Rare-Earth Elements from Mineral Captivity Using SMART Lixiviants.” American Chemical Society National Meeting. San Francisco, CA, USA (invited talk). |
| 5/2023 | “Actinides in Medicine: Actinium and Beyond.” ORNL Glenn T. Seaborg Initiative Workshop. Oak Ridge, TN, USA (invited talk). |
| 3/2023 | “Chelation Platform Development for Emerging Medical Radionuclides at Oak Ridge National Laboratory.” American Chemical Society National Meeting. Indianapolis, IN, USA (invited talk). |
| 3/2023 | “Advancing Actinium-225 Coordination Chemistry and Chelator Development for Targeted Alpha Therapy.” The Minerals, Metals, and Materials Society Annual Meeting. San Diego, CA, USA (invited talk). |
| 3/2023 | “Taming Exotic Elements for Medicine and Materials: A Coordination Chemistry Approach.” University of Missouri Chemistry Colloquium. Columbia, Missouri, USA (invited talk). |

11/2022	“Establishing the Complexation Thermodynamics of Ra^{2+} and Ac^{3+} : Towards Targeted Separations and Therapeutics.” DOE Isotope Program’s Virtual Seminar Series. On the Horizon: Novel Isotopes and Future Leaders. Virtual (invited talk).
11/2022	“Chelation Platform Development for Emerging Medical Radionuclides at ORNL.” ARIA Workshop, Evolving Targeted Therapies for Cancer. Oak Ridge, TN, USA (invited talk).
10/2022	“Dissolution by Design: Selective Leaching of Rare Earth Elements using SMART Lixiviants.” CMI Diversifying Supply videoconference. Virtual (invited talk).
7/2022	“Chelation Platform Development for Medical Isotopes at Oak Ridge National Lab.” Gordon Research Conference, Radionuclide Theranostics for the Management of Cancer. Newry, ME, USA (poster selected for short talk).
3/2022	“Unconventional Ligand Design Strategies for Precision Recovery of REEs.” American Chemical Society National Meeting. San Diego, CA, USA.
3/2022	“Towards the Development of High-Affinity Chelators for ^{223}Ra Targeted Alpha Therapy: A Stability Constant Roadmap.” American Chemical Society National Meeting. San Diego, CA, USA.
2/2022	“Developing High-Affinity Chelators for Targeted Alpha Therapy Radioisotopes: A Stability Constant Roadmap.” Brigham and Women’s Hospital Joint Program in Nuclear Medicine Seminar Series. Boston, MA, USA (invited talk).
9/2021	“Unveiling the Elusive Coordination Chemistry of Radium and Actinium: Towards Targeted Separations and Therapeutics.” Oak Ridge National Laboratory Radioisotope Portfolio Seminar Series. Oak Ridge, TN, USA.
4/2021	“Unveiling the Elusive Coordination Chemistry of Radium and Actinium: Towards Targeted Separations and Therapeutics.” American Chemical Society National Meeting. Virtual.
10/2020	“Selective Chelation of Metal Ions: Saving Lives, Money, and the Toyota Prius.” State University of New York at Potsdam, Department of Chemistry. Potsdam, NY, USA (invited talk).

Funding

Funding as Lead PI

- (6)** Source of support: DOE AMMTO Critical Materials Innovation Hub
 Proposal/award number: AL-12-350-001
 Title: Advanced Leaching Methods to Recover Critical Materials from Mineral Sources
 Award period: 10/2023–6/2025
 Total amount: \$919,000K/y (with 397K to Dr. Long Qi, Ames Lab)
 Project overview: Development of lixiviant chelators to selectively leach rare earth elements from mineral ores.
- (5)** Source of support: DOE Isotope Program
 Proposal/award number: 0000262370
 Title: Establishing the Chelation Chemistry of Antimony-119 for Targeted Auger Therapy
 Award period: 7/2022–6/2024
 Total amount: \$500,000 (with \$100K to Prof. Jonathan Engle, UW-Madison)
 Project overview: Bifunctional chelator development for Sb-119 to advance its use in targeted Auger therapy applications for the treatment of micrometastases and single-cell disease.
- (4)** Source of support: Laboratory Directed Research and Development Program, ORNL
 Proposal/award number: 10737
 Title: Towards Ultrachelating Ligands for Targeted Radionuclide Therapy
 Award period: 10/2021–9/2024
 Total amount: \$3,495,000
 Project overview: Development of new chelation platforms to expand the use of emerging α -, β -, and Auger electron-emitting radionuclides in targeted radionuclide therapy of cancer. Advancing characterization capabilities for radioactive ions at ORNL.
- (3)** Source of support: DOE AMO Critical Materials Institute
 Proposal/award number: AL-12-350-001
 Title: Dissolution by Design: Selective Leaching of Rare Earth Elements using SMART Lixiviants

Award period: 7/2021–6/2023

Total amount: \$500,000

Project overview: Development of lixiviant chelators to selectively leach rare earth elements from mineral ores.

(2) Source of support: DOE Isotope Program, Core R&D

Proposal/award number: N/A

Title: Unveiling the Elusive Coordination Chemistry of Radium and Actinium for Enhanced Recovery of High-Priority Isotopes

Award period: 10/2020–9/2021

Total amount: \$150,000

Project overview: The objective of this proposal is to advance the understanding of the aqueous coordination chemistry of Ra and Ac with the goal of elucidating the ligand design principles and key molecular interactions that give rise to receptors with high affinity and selectivity for these ions.

(1) Source of support: Laboratory Directed Research and Development Program, ORNL (Strategic Hire)

Proposal/award number: 10067

Title: Liberating Rare Earth Elements from Mineral Captivity: A Molecular Recognition Approach

Award period: 1/2020–9/2021

Total amount: \$327,000

Project overview: Explore selective dissolution of rare earth phosphate using new molecular receptors developed within the project.

Funding as Co-PI

(3) Source of support: DOE Basic Energy Sciences

Proposal/award number: ERKCC08

Title: Principles of Chemical Recognition and Transport in Extractive Separations

Award period: 10/2022–9/2025

Total amount: \$4,350,000

Project overview: Ion binding with amphiphilic receptors organized at liquid-liquid interfaces.

(2) Source of support: AMO Critical Materials Institute

Proposal/award number: N/A

Title: Transformative Rare Earth Recovery with AI-Accelerated Ligand Synthesis and Separation

Award period: 1/2022–6/2023

Total amount: \$1,200,000

Project overview: High throughput synthesis and separations for critical element recovery guided by AI.

(1) Source of support: Laboratory Directed Research and Development Program, ORNL

Proposal/award number: 10259

Title: Dynamic Ligand Libraries from Direct CO₂ Capture

Award period: 10/2020–9/2021

Total amount: \$150,000

Project overview: Use an active data-driven approach that uniquely combines in situ spectroscopies and dynamic covalent chemistry (DCC) to realize the simultaneous capture and conversion of CO₂.