

Abstract

Title: IsoLAIT: A Framework for Identification of Enzyme-Substrate Pairs from the Cellular Milieu using Native Mass Spectrometry

Abstract: In the complex cellular milieu, understanding which enzymes catalyze which reactions is paramount for deciphering biology and disease. There are still many enzymes of which their exact functions or substrates are not known. Conversely, we know the nature of some biotransformations, but not precisely which enzymes are responsible. Identifying enzyme-substrate pairs is impeded by the fact that enzyme-substrate interactions are inherently transient. We have developed a framework, IsoLAIT, which readily identifies both substrate and enzyme from whole cells without purification. First, a probe is used to create a tightly bound enzyme-substrate complex. Then, this persistent complex is identified via native mass spectrometry. Additionally, the unique isotope pattern imparted by the probe makes facile the detection of even unknown substrates and enzymes. The utility of IsoLAIT is demonstrated with thiopurine methyltransferase and S-adenosylvinthionine, an analogue of common substrate, S-adenosylmethionine.

KALLI C. CATCOTT

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Education

Ph.D., Chemistry & Chemical Biology, Northeastern University **2016**
B.S., Biochemistry/Chemistry, University of California, San Diego **2007**

Experience

Mersana Therapeutics, Cambridge, Massachusetts

Scientist **2017 - Present**

Bioconjugation Chemist working on antibody-drug conjugate production and analysis. Responsible for delivering material for internal projects as well as collaborations. Charged with investigating and improving current and potential conjugation platforms.

- Developed and maintained a tracking system for materials and conjugation requests.
- Founding member of the Mersana Green Committee and helped spearhead internal environmental projects.
- Wrote and implemented several SOPs for various conjugation technologies.

Northeastern University, Boston, Massachusetts

PhD Candidate – Advisor: Z. Sunny Zhou **2012 - 2016**

Research Assistant in the Zhou lab in the Department of Chemistry and Chemical Biology, worked on methyltransferases and methylation. Research activities included enzyme substrate engineering, protein labeling, and enzyme expression and purification.

- Developed a probe and platform for identifying substrate-enzyme pairs utilizing native MS.
- Awarded “Excellence in Graduate Research” for the Chemistry Department in 2015-2016.

ImmunoGen, Waltham, Massachusetts

Research Associate III **2012 - 2013**

Research Associate in biochemistry department, worked on antibody-drug conjugations for internal projects as well as collaborations. Charged with producing and characterizing conjugates for R&D purposes as well as for toxicity studies.

- Developed and implemented a high-throughput method for preparing conjugates on the microscale, which uses 1/5th of the material and increases conjugation efficiency 10-fold.
- Implemented a department-wide project tracking system that increased accountability and reduced redundancy.

CV Partners (Amgen Contractor), Thousand Oaks, California

Associate Scientist II **2011**

Lead researcher in a new department charged with developing methods for antibody-fluorophore conjugation, antibody and protein lyophilization, preparation of antibody cocktails and assay development. Led experimental design and process implementation.

- Designed and tested sample preparation methods and immunological assays for detecting phosphorylation with a new assay platform.
- Developed a protocol that saw a ten-fold increase in yield over outsourced conjugates at one-tenth the cost.

Life Technologies (Previously Invitrogen), Camarillo, California

Senior Associate Manufacturing Specialist (Laboratory Lead) **2010**

Designed and executed purification methods and subsequently characterized various monoclonal and polyclonal antibodies. Technical resource for antibody purification team.

Production Associate II, Antibodies **2008 – 2010**

Purified and validated polyclonal antibodies using affinity chromatography and western blotting. Responsible for process and material troubleshooting.

Production Associate I, Assay **2007 – 2008**

Produced and optimized components for use in plate and flow cytometry based immunological assays.

Awards and Presentations

Csaba Horvath Memorial Symposium, Orange, CT **October 2016**

Connecticut Separation Science Council

Oral Presentation: *Isotope-Labeled, Activity-based Identification and Tracking: A Framework for Identifying Enzyme-Substrate Pairs*

Boston Symposium on Organic and Bioorganic Chemistry **October 2016**

Oral Presentation: *Identifying Enzyme-Substrate Pairs from Cells with Native Mass Spectrometry: The IsoLAIT Framework*

Excellence in Graduate Research Award **2016**

Department of Chemistry and Chemical Biology, Northeastern University

PacifiChem, Honolulu HI **December 2015**

American Chemical Society

Oral Presentation: *Methyltransferase engineering: Using substrate analogs to turn alkylators into oxidizers*

Women Chemists Committee / Eli Lilly Travel Award **Fall/Winter 2015**

American Chemical Society

Selected Publications

Identifying Unknown Enzyme-Substrate Pairs from the Cellular Milieu with Native Mass Spectrometry. **Kalli C. Catcott**, Jing Yan, Wanlu Qu, Vicky H. Wysocki, Zhaohui Sunny Zhou. *ChemBioChem*. 18(7), 613-617, **2017**. doi:10.1002/cbic.201600634

Capturing Unknown Substrates via in situ Formation of Tightly Bound Bisubstrate Adducts: S-Adenosyl-Vinthonine as a Functional Probe for AdoMet-Dependent Methyltransferases. Wanlu Qu, **Kalli C. Catcott**, Kun Zhang, Shanshan Liu, Jason J. Guo, Jisheng Ma, Michael Pablo, James Glick, Yuan Xiu, Nathaniel Kenton, Xiaoyu Ma, Richard I. Duclos Jr., Zhaohui Sunny Zhou. *Journal of the American Chemical Society*. 138(9), 2877-2880, **2016**. doi:10.1021/jacs.5b05950

Microscale screening of antibody libraries as maytansinoid antibody-drug conjugates. **Kalli C. Catcott**, Molly A. McShea, Carl Uli Bialucha, Kathy L. Miller, Stuart W. Hicks, Parmita Saxena, Thomas G. Gesner, Mikias Woldegiorgis, Megan E. Lewis, Chen Bai, Michael S. Fleming, Seth A. Ettenberg, Hans K. Erickson, Nicholas C. Yoder. *mAbs*. 8(3), 513-523, **2016**. doi:10.1080/19420862.2015.1134408