

Conferencia:

In Situ Synthesis and Modification of Phospholipid Membranes

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Neal K. Devaraj

University of California – San Diego

24/07/15

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Aula de Seminarios do
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10:00 h

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XUNTA DE GALICIA

CONSELLERÍA DE CULTURA, EDUCACIÓN
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Abstract:

Our group has a strong interest in applying covalent coupling reactions to the formation and modification of phospholipid membranes. We have utilized chemoselective reactions, such as copper-catalyzed triazole formation or the native chemical ligation, to drive the *de novo* synthesis of phospholipid membranes. To interface synthetic membranes proteins, we have recently developed protein reactive membrane anchors utilizing SNAP-tags. Light driven spatiotemporal control over proteoliposome formation is possible using photocaged membrane anchors. Finally, we have developed self-reproducing membranes by embedding lipid synthesizing autocatalysts. Continued development of selective bioconjugation reactions will facilitate the interfacing of synthetic molecules with biological systems for new capabilities.

Curriculum Vitae
Neal K. Devaraj Ph. D.
Assistant Professor of Chemistry and Biochemistry, University of California, San Diego

Positions

2011-Present University of California, San Diego, La Jolla CA — Assistant Professor
2007-2011 Harvard Medical School, Boston, MA — Postdoctoral Fellow
2002-2007 Stanford University, Stanford, CA — Ph.D. Chemistry
1998-2002 Massachusetts Institute of Technology, Cambridge, MA — B. S. Chemistry & B. S. Biology

Awards/Honors

2014 - Royal Society of Chemistry Emerging Investigator
2013 - NSF CAREER Award
2013 - Department of Defense MURI Award
2012 - Thieme Chemistry Journal Award
2010 - NIH Research Scientist Career Development Award
2007 - American Chemical Society Young Investigator Award Division of Inorganic Chemistry
2005 - NSF East Asia and Pacific Summer Institutes Award
2002 - Stanford Graduate Fellowship
2002 - MIT Department of Chemistry Alpha Chi Sigma Undergraduate Research Award

Peer Reviewed Publications

- 30.** A. K. Rudd, J. M. V. Cuevas, N. K. Devaraj "SNAP-tag Reactive Lipid Anchors Enable Targeted and Spatiotemporally Controlled Localization of Proteins to Phospholipid Membranes," *J. Am. Chem. Soc.*, 2015, DOI: 10.1021/jacs.5b00040
- 29.** H. Wu, B. T. Cisneros, C. M. Cole, N. K. Devaraj "Bioorthogonal Tetrazine-Mediated Transfer Reactions Facilitate Reaction Turnover in the Nucleic Acid-Templated Detection of microRNA," *J. Am. Chem. Soc.*, 2014, 136(52), 17942-17945.
- 28.** R. J. Brea, C. M. Cole, N. K. Devaraj "In situ Vesicle Formation by Native Chemical Ligation," *Angew. Chem. Int. Ed.*, 2014, 53(51), 14102-14105.
- 27.** H. Wu, J. Yang, J. Šečkutė, N. K. Devaraj "In-situ Synthesis of Alkenyl Tetrazines for Highly Fluorogenic Bioorthogonal Live Cell Imaging Probes," *Angew. Chem. Int. Ed.*, 2014, 53 (23), 5805-5809.
- 26.** B. Nichols, Z. Qin, J. Yang, D. R. Vera, N. K. Devaraj "68Ga Chelating Bioorthogonal Tetrazine Polymers for the Multistep labeling of Cancer Biomarkers," *Chem. Comm.*, 2014, 50 (40), 5215-5217.

- 25.** J. Yang, Y. Liang, J. Seckute, K. Houk, N. K. Devaraj "Synthesis and Reactivity Comparisons of 1-Methyl-3-Substituted Cyclopropene Minitags for Tetrazine Bioorthogonal Reactions," *Chem. Eur. J.* , 2014, 20 (12), 3365-3375.
- 24.** J. Seckute, N. K. Devaraj "Expanding Room for Tetrazine Ligations in the In Vivo Chemistry Toolbox," *Curr. Opin. Chem. Biol.*, 2013, 17(5), 761-767.
- 23.** J. Seckute, J. Yang, N. K. Devaraj "Rapid Oligonucleotide-Templated Fluorogenic Tetrazine Cycloadditions," *Nucl. Acids Res.*, 2013, 41(15) e148.
- 22.** C.M. Cole, J. Yang, J. Šečutè, N. K. Devaraj, "Fluorescent Live-Cell Imaging of Metabolically Incorporated Unnatural Cyclopropene-Mannosamine Derivatives," *ChemBioChem*, 2013, 14(2), 205-208.
- 21.** N. K. Devaraj, "Advancing Tetrazine Bioorthogonal Reactions through the Development of New Synthetic Tools," *Synlett.*, 2012, 23(15): 2147-2152.
- 20.** J. Yang, J. Seckute, C. M. Cole, N. K. Devaraj "Live-Cell Imaging of Cyclopropene Tags with Fluorogenic Tetrazine Cycloadditions," *Angew. Chem. Int. Ed.*, 2012, 51(30), 7476-7479.
- 19.** J. Yang, M. R. Karver, W. Li, S. Sagu, N. K. Devaraj "Metal-Catalyzed One-Pot Synthesis of Tetrazines Directly from Aliphatic Nitriles and Hydrazine," *Angew. Chem. Int. Ed.*, 2012, 51(21), 5222-5225.
- 18.** I. Budin, N. K. Devaraj "Membrane Assembly Driven by a Biomimetic Coupling Reaction," *J. Am. Chem. Soc.*, 2012, 134(2), 751-753.
- 17.** N. K. Devaraj, G. M. Thurber, E. J. Keliher, B. Marinelli, R. Weissleder, "Reactive Polymer Enables Efficient In Vivo Chemistry," *Proc. Nat. Acad. Sci. USA*, 2012, 109 (13), 4762-4767.
- 16.** N. K. Devaraj, R. Weissleder "Biomedical Applications of Tetrazine Cycloadditions," *Acc. Chem. Res.*, 2011, 44(9), 816-827.
- 15.** J. B. Haun, N. K. Devaraj, B. S. Marinelli, H. Lee, R. Weissleder "Probing Intracellular Biomarkers and Mediators of Cell Activation Using Nanosensors and Bioorthogonal Chemistry" *ACS Nano*, 2011, 5 (4), 3204-3213.
- 14.** J. B. Haun, N. K. Devaraj, S. A. Hilderbrand, H. Lee, R. Weissleder "Bioorthogonal Chemistry Amplifies Nanoparticle Binding and Enhances Signal Detection" *Nature Nanotech*, 2010, 5(9), 660-5.

13. H. S. Han, N. K. Devaraj, J. Lee, S. A. Hilderbrand, R. Weissleder, M. G. Bawendi "Development of a Bioorthogonal and Highly Efficient Conjugation Method for Quantum Dots Using Tetrazine Norbornene Cycloaddition" *J. Am. Chem. Soc.*, 2010, 132(23), 7838-9.
12. N. K. Devaraj, S. A. Hilderbrand, R. Upadhyay, R. Mazitschek, R. Weissleder "Bioorthogonal Turn-On Probes for Imaging Small Molecules Inside Living Cells" *Angew. Chem. Int. Ed.*, 2010, 49(16), 2869-2872.
11. N. K. Devaraj, R. Upadhyay, J. B. Haun, S. A. Hilderbrand, R. Weissleder "Fast and Sensitive Pretargeted Labeling of Cancer Cells via Tetrazine/*Trans*-Cyclooctene Cycloaddition" *Angew. Chem. Int. Ed.*, 2009, 48(38), 7013-7016.
10. N. K. Devaraj, E. J. Keliher, G. M. Thurber, M. Nahrendorf, R. Weissleder "¹⁸F Labeled Nanoparticles for *in-vivo* PET-CT Imaging" *Bioconjugate Chem.*, 2009, 20(2) 397-401.
9. N. K. Devaraj, R. Weissleder, S. A. Hildebrand "Tetrazine-Based Cycloadditions: Application to Pretargeted Live Cell Labeling" *Bioconjugate Chem.*, 2008, 19(12), 2297-2299.
8. N. K. Devaraj, J. P. Collman, "Copper Catalyzed Azide-Alkyne Cycloadditions on Solid Surfaces: Applications and Future Directions" *QSAR and Comb. Sci.*, 2007, 26(11), 1253-1260.
7. J. P. Collman; R. A. Decreau; Y. Yan; Y. Yang; N. K. Devaraj, "Synthesis of Cytochrome c Oxidase Models that can be Covalently Attached onto Electrode Surfaces" *J. Org. Chem.*, 2007, 72(8), 2794-2802.
6. J. P. Collman, N. K. Devaraj, R. A. Decreau, Y. Yang, Y. Yan, W. Ebina, T. A. Eberspacher, C. E. D. Chidsey, "A Cytochrome c Oxidase Model Catalyzes the Four-Electron Reduction of Oxygen under Rate-Limiting Electron Flux" *Science*, 2007, 315, 5818, 1565-1568.
5. N. K. Devaraj, R. A. Decreau, J. P. Collman, C. E. D. Chidsey, "Rate of Interfacial Electron Transfer Through the 1,2,3-Triazole 'Click' Linkage," *J. Phys. Chem. B.*, 2006, 110(32), 15955-15962.
4. J. P. Collman, N.K. Devaraj, T. A. Eberspacher, C. E. D. Chidsey, "Mixed Azide-terminated Monolayers; A Platform for Modifying Electrode Surfaces," *Langmuir*, 2006, 22(6), 2457-2464.
3. N. K. Devaraj, P. H. Dinolfo, C. E. D. Chidsey, J. P. Collman, "Selective Functionalization of Independently Addressable Microelectrodes by Electrochemical Activation and Deactivation of a Coupling Catalyst," *J. Am. Chem. Soc.*, 2006, 128 (6), 1794 -1795.
2. N. K. Devaraj, G. P. Miller, W. Ebina, B. Kakaradov, J. P. Collman, E. T. Kool, C. E. D. Chidsey, "Chemoselective Coupling of Oligonucleotides to Self Assembled Monolayers," *J. Am. Chem. Soc.*, 2005, 127(24), 8600-8601.

1. J. P. Collman, N. K. Devaraj, C. E. D. Chidsey, "Clicking Functionality onto Electrode Surfaces," *Langmuir*, 2004, (20), 1051-1053.

Book Chapters

1. N. K. Devaraj, R. Weissleder, "Click Chemistry": Applications to Molecular Imaging" *Molecular Imaging Principles and Practice*, Eds. R. Weissleder, B. D. Ross, A. Rehemtulla, S. S. Gambhir, 2010, Chapter 29.

Current Research Funding

1. W911NF-13-1-0383, Department of Defense (Army Research Office), Multidisciplinary University Research Initiative (MURI), "Dynamic Artificial Cells Composed of Synthetic Bioorthogonal Membranes," 09/01/2013-08/31/2018, \$6,250,000, Role: PI

2. K01EB010078, National Institutes of Health, Mentored Career Development Award (K01), "Fast In Vivo Click Chemistries for PET Imaging," 05/10/2010-04/30/2015, \$880,903, Role: PI

3. CHE-1254611, National Science Foundation, CAREER Award, "Vesicle Growth Driven by Catalytic Lipid Synthesis," 09/01/2013-08/31/2018, \$650,000, Role: PI

4. W9132T-14-2-0002, Department of Defense (Army Corps of Engineers), Cooperative Agreement, "Controlling Functional Group Architecture in Artificial Cells," 03/01/2014-02/28/2017, \$180,000, Role: PI