

CHEMISTRY & BIOCHEMISTRY COLLOQUIUM: Harnessing Chemoselective and Biocompatible Reactivity for Developing New Functional Materials and Biological Probes

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## About the Speaker:

Marco S. Messina is an NIH MOSAIC K99 and UC President's Postdoctoral Fellow at the University of California, Berkeley. He completed his PhD at the University of California, Los Angeles in the laboratories of Profs. Heather D. Maynard and Alexander M. Spokoyny. Research in the two laboratories merged synthetic polymer chemistry, main-group chemistry, and organometallic chemistry with an emphasis on biological applications.



Some research highlights include the discovery that icosahedral boron-rich cluster compounds (B12OR12) could act as strong photooxidants for use in polymer synthesis, the development of glycopolymer materials for the stabilization of protein therapeutics, and the use of organometallic reagents for biomolecule modification. Marco's ongoing research in the laboratory of Prof. Christopher J. Chang involves developing molecular probes for the activity-based sensing of reactive oxygen species (ROS) involved in biological signaling and oxidative stress.

## Abstract:

The development of novel chemical reactions that achieve both high chemoselectivity and biocompatibility provide a foundation for the synthesis and application of new functional materials and biological probes. This presentation will provide two representative examples of this generalizable approach applied to systems spanning the biomolecule to cellular level. First, well-defined and isolable gold(III) organometallic complexes provide reagents for cysteine arylation of biomolecules, mediating the selective and rapid conjugation of small molecule and oligomer substrates to cysteine sites on proteins with high efficiency across a broad pH range. These gold(III) reagents provide access to protein-polymer conjugates through grafting-to and grafting-from approaches. In a second example, selective chemical reactivity principles are applied to developing a tandem activity-based sensing/labeling platform for imaging transcellular hydrogen peroxide (H2O2) signaling. H2O2 is one of many reactive oxygen species that plays vital roles in intracellular signaling and stress processes, but its transient nature has made deciphering its roles in transcellular signaling a significant challenge. We have designed boronate caged small-molecule probes bearing a pendant fluoromethylene that serves as a latent quinone methide source that can undergo a tandem activity-based sensing and biomolecule labeling reaction cascade to produce a spatially localized fluorescence signal upon exposure to H2O2. This strategy enables us to capture and record spatial information on reactive oxygen species fluxes and has enabled us to move beyond studying intracellular H2O2 signaling to identifying and mapping cell-to-cell H2O2 communication.

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