*UNIVERSITY OF RHODE ISLAND*
*Department of Chemistry*
*SEMINAR*

*3:00 P.M., Monday, Feburary 3, 2025*
*Room 105 – Beaupre Center*

# *Prof. Joshua Kritzer*

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# *Chemical Biology Tools for Measuring Drug Delivery*

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**Chemical Biology Tools for Measuring Drug Delivery**

**Abstract**: Large-molecule therapeutics including peptides, oligonucleotides, and proteins make up a large and growing portion of the drug development pipeline. One of the greatest barriers to developing these drugs is cell penetration. Most enter the cell through a complex pathway involving endocytosis followed by endosomal escape. This process is so poorly understood and difficult to study that it is challenging simply to measure how much compound has actually accessed the cytosol at any given point. The Kritzer Lab has developed new tools for making these and related measurements. The Chloroalkane Penetration Assay (CAPA) is a versatile assay that measures cell penetration using cellularly expressed HaloTag protein and a small chloroalkane tag on the molecule-of-interest. CAPA has been used by the Kritzer group to measure cell penetration for many classes of peptide and oligonucleotide therapeutics, to measure penetration to different subcellular compartments, and to measure relative penetration in different cell types. CAPA has also been adopted by academic and industrial groups all over the world to investigate cell penetration. The Kritzer group has also used molecular evolution to produce new HaloTag variants which work optimally with a fluorogenic benzothiadiazole dye. The resulting "BenzoTag" system allows for turn-on, no-wash cell labeling in seconds. BenzoTag is currently being applied to produce a "turn-on" version of CAPA for continued investigation of drug delivery and mechanisms of endosomal escape.

**Bio**: Joshua Kritzer is a Professor of Chemistry at Tufts University in Medford, MA, with appointments in the Molecular Microbiology Program and the Cell, Molecular and Developmental Biology Program at Tufts University's School of Graduate Biomedical Sciences in Boston, MA. The Kritzer lab combines approaches from chemistry, biology, and biotechnology to solve foundational problems in drug discovery. Current projects include discovering constrained peptides for difficult-to-target proteins in autophagy, and measuring cytosolic penetration of peptide and oligonucleotide therapeutics. Prof. Kritzer has won numerous teaching and mentoring awards, and his academic awards include the Smith Family Award for Excellence in Biomedical Research, an NIH New Innovator Award, and a Sanofi iAward for projects involving cross-disciplinary solutions to pressing problems in chemical biology and drug development.