Targeted Annotation of Peptides by Selective Infrared Multiphoton Dissociation Mass Spectrometry

Borotto, N.B.[1], McClory, P.J.[1], Martin, B.R.[1], Hakansson, K.[1],

1. Department of Chemistry, University of Michigan

Funding Grants: G.S. Boebinger (NSF DMR-1157490); Hakansson (NIH R01 GM107148); Martin (NIH DP2 GM114848)

Reactive oxygen species, such as hydrogen peroxide, are important second messengers in cellular signaling. In proteins, cysteine is particularly susceptible to redox chemistry and can be oxidized from a thiol (RSH) to sulfenic (RSOH), sulfinic (RSO_2H), or sulfonic acid (RSO_3H) as post-translational modifications (PTMs) that are low in concentration. Here, we demonstrate the preferential activation of S-sulfonated peptides by leveraging the strong S−O bond infrared (IR) absorbance at 10.6 μm.

Tryptic digests of oxidized/non-oxidized proteins or mixtures of oxidized/non-oxidized peptides were either directly infused or introduced to the ion cyclotron resonance mass spectrometer via online HPLC.

For two redox associated-proteins, DJ-1 and AhpC, our infrared multiphoton dissociation (IRMPD) method was able to identify all sulfonic acid-containing peptides following protein oxidation and, in many cases, enabled sequencing and site-specific localization of the modification. In total, we examined selective IRMPD of 75 peptides.

IRMPD allows differentiation of *S*-sulfonated peptides from unmodified peptides, enabling the facile discovery of these modifications. The ability to rapidly identify and sequence modified peptides in a single liquid chromatography mass spectrometry (LC/MS) run is a potentially powerful approach for the analysis of oxidative PTMs in cellular systems.

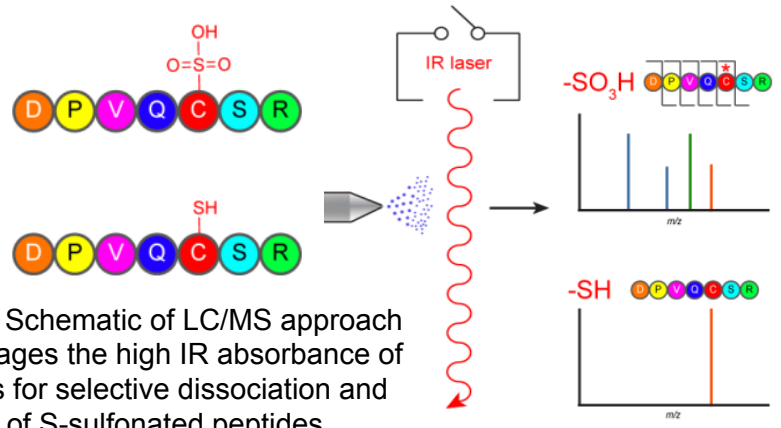

Figure 1. Schematic of LC/MS approach that leverages the high IR absorbance of sulfoxides for selective dissociation and discovery of S-sulfonated peptides.

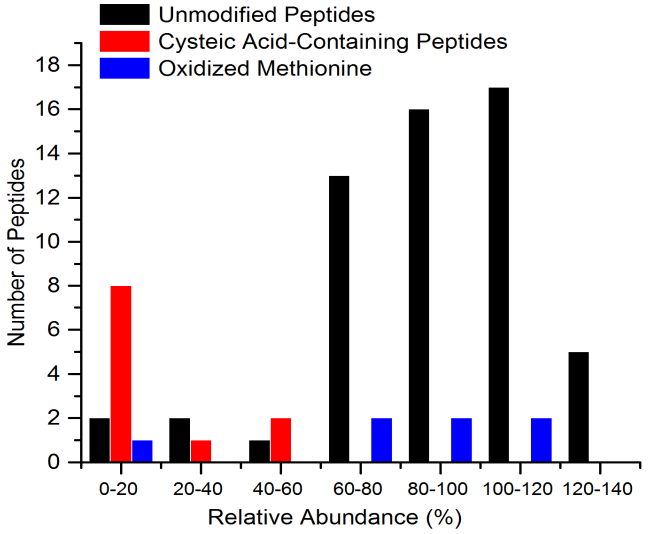

Figure 2. Peptides divided into bins by percent abundance remaining after IR irradiation.

Facilities and instrumentation used: 9.4 tesla FT-ICR mass spectrometer, Ion Cyclotron Resonance Facility

Citation: Nicholas B. Borotto; Phillip J. McClory; Brent R. Martin; Kristina Håkansson; Targeted annotation of S-sulfonylated peptides by selectrive infrared multiphoton dissociation mass spectrometry **Analytical Chemistry 2017,** 89, 8304-8310.