Analytical Instrumentation, Methods & Materials

Gas-Phase Purification of Peptides Reaps Accuracy in Mass Spectrometry Quantitation

View U.S. Patent No. 9,698,001 in PDF format.

WARF: P110234US02

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The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing a novel approach for determining the relative and uncontaminated abundance of tagged peptides within complex samples that is less arduous and more biomedically relevant than extant methods.

Overview

Maturing protein analysis technologies continue to elucidate life's chemical architecture with a precision even recently unimaginable. Mass spectrometry (MS), which ionizes and fragments proteins for data to identify their amino acid sequence, has resulted in the cataloguing of many of the thousands of such molecules that can comprise a single cell.

Still, tallying the abundance of proteins and peptides remains a challenge in the field of proteomics. Stable isotope labeling by amino acids (SILAC) is the most sophisticated measuring technique, performed with high-resolution tandem mass spectrometry (MS/MS). Labor and time requirements (up to six months), though, make SILAC impractical for large-scale experiments. Also, the method is incompatible with human tissue and biofluids. Isobaric tagging, another molecule labeling procedure, allows relative quantification of up to eight entire protein sets simultaneously. Isolated at lower resolution, however, minutely different tag signals essentially can overlap, skewing measurements and relegating the method to low-complexity samples.

A new approach to isobaric tagging is needed to combat the pervasive drawback of precursor interference that has hamstrung its potential.

The Invention

UW–Madison researchers have developed a method to eliminate interference by directly segregating ions of interest from similarly massed and charged non-targets or contaminants that were unintentionally co-isolated between stages of MS/MS.

This is accomplished using samples embedded with isobaric tags. Following initial ionization, an established proton transfer reaction (PTR) is commenced, reducing the charges of ions in the gas phase by introducing even-electron anions. The populations thus diverge according to mass-to-charge ratio, with the precursors of interest able to be selected.

During subsequent analysis of the purged ions, their tags are cleaved, fragmenting into charged particles that generate data readouts. Relative abundance of the purified peptides thus can be derived with significantly improved accuracy.

Applications

- Fundamental gene and protein function research
- Biomedical tandem mass spectrometry

Key Benefits

- Precision peptide quantification
- Large-scale, simultaneous comparison of up to eight proteomes
- Compatibility with human tissue and biofluid tagging
- Ready implementation as software update or bundle

Additional Information

For More Information About the Inventors

- Joshua Coon

Related Technologies

- For more information about inexpensive, ionizable labeling reagents, see WARF reference number P06069US.
- For more information about modifying data acquisition methods to prevent interference mass spectra, see WARF reference number P100173US02.

Related Intellectual Property

- View Divisional Patent in PDF format.

Publications

- Swaney D.L., Wenger C.D. and Coon J.J. 2010. Value of Using Multiple Proteases for Large-Scale Mass Spectrometry-Based Proteomics. Journal of Proteome Res. 1323-1329.

Tech Fields

- Analytical Instrumentation, Methods & Materials : Mass spectrometry

For current licensing status, please contact Jennifer Gottwald at jennifer@warf.org or 608-960-9854