

PEAKS-DB Substantially Improved Peptide Identification with ETD Mass Spectrometry



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Introduction

Peptide identification is a central task in mass spectrometry based proteomics. Existing approaches include: (1) protein sequence database search with uninterpreted spectra, (2) de novo sequencing, (3) database search of de novo sequence tags, and (4) spectral library search. These approaches are usually performed separately according to the circumstances. In this abstract, we present the PEAKS-DB software that combines the first three approaches to significantly improve the sensitivity and reduce the FDR of peptide identification.

Method

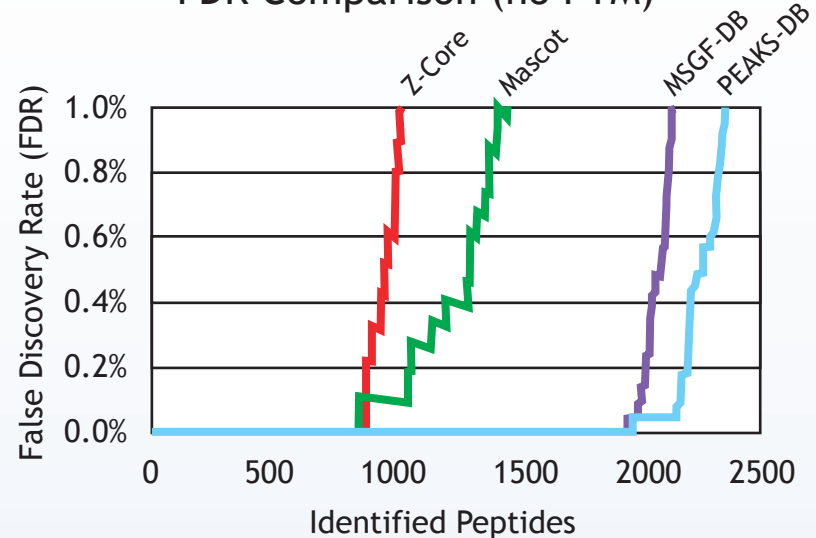
The data analysis includes four major steps:

1. PEAKS algorithm is used to conduct de novo sequencing on each of the MS/MS spectra.
2. A sequence tag approach is carried out to select a short list of (up to 10,000) proteins from a large protein sequence database.
3. A few hundred high quality spectra (as determined by the sequence tag approach) are searched against the protein shortlist. This serves as a “pre-search” to determine the mass error distributions of the precursor ions.
4. All spectra are searched against the protein shortlist. The precursor error distribution estimated in the pre-search step, the similarity between a database peptide and the de novo sequencing result of a spectrum, as well as a few other features of the peptide-spectrum-match are used to provide a better scoring function for this step.

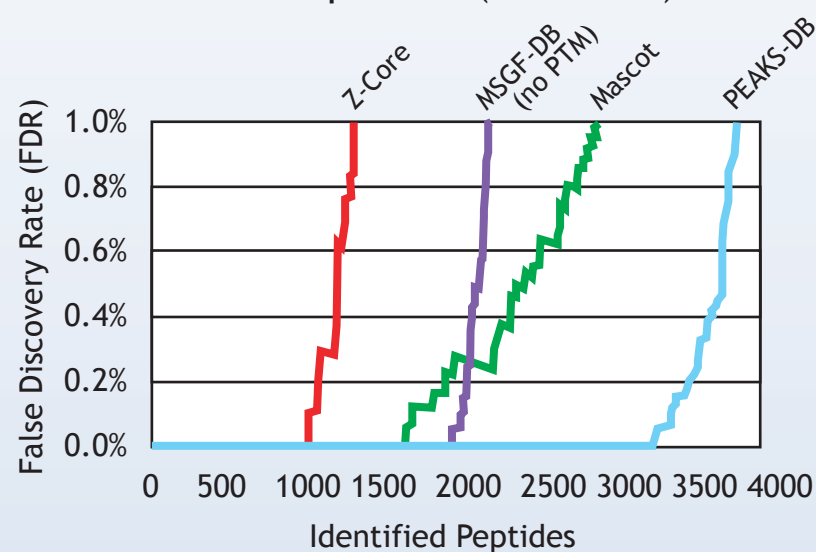
Results

PEAKS-DB was compared with Mascot, MSGF-DB, and ZCore on a dataset produced with a fraction of Yeast lysate on an Orbitrap ETD mass spectrometer. MSGF-DB does not support variable PTM and therefore two comparisons, with and without variable PTMs, were conducted. With a combined target and decoy database, the false discovery rates (FDR) were estimated and plotted in Figure 1. PEAKS-DB demonstrated a remarkably superior performance over other engines.

FDR Comparison (no PTM)



FDR Comparison (with PTM)



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