

ETD is Better, Period.

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Background

Electron-Transfer Dissociation (ETD) is widely known as a better fragmentation technology than Collision Induced Dissociation (CID) for identifying post-translationally modified peptides and peptides with higher charge states. However, for general proteomics study that intends to identify all peptides, regardless of the modifications and charge states, ETD has not been demonstrated as a superior method than CID. In this abstract we show that with the recent advancement of peptide identification software using ETD MS/MS data, ETD is indeed better even for general peptide identification.

Method

A Yeast lysate was reduced and alkylated, then digested with LysC, and analyzed with a Thermo LTQ Orbitrap instrument in two 120-minute LC runs. The only difference between the two runs is that one fragments the precursors with CID and the other with ETD. These produced 8467 ETD MS/MS and 12366 CID MS/MS spectra, respectively. The data is presented in Figures 1 and 2.

Figure 1. Screenshot of the Score Histograms from PEAKS Studio 5.3

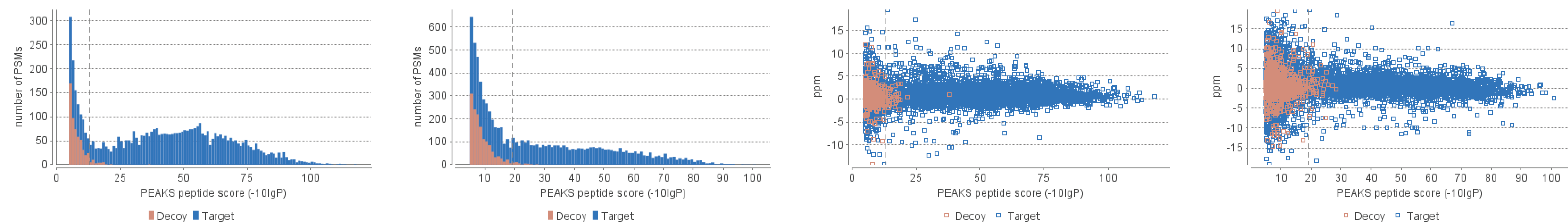
Figure 2. Screenshot of the Precursor Mass Error vs Score Plot from PEAKS Studio 5.3

ETD

CID

ETD

CID

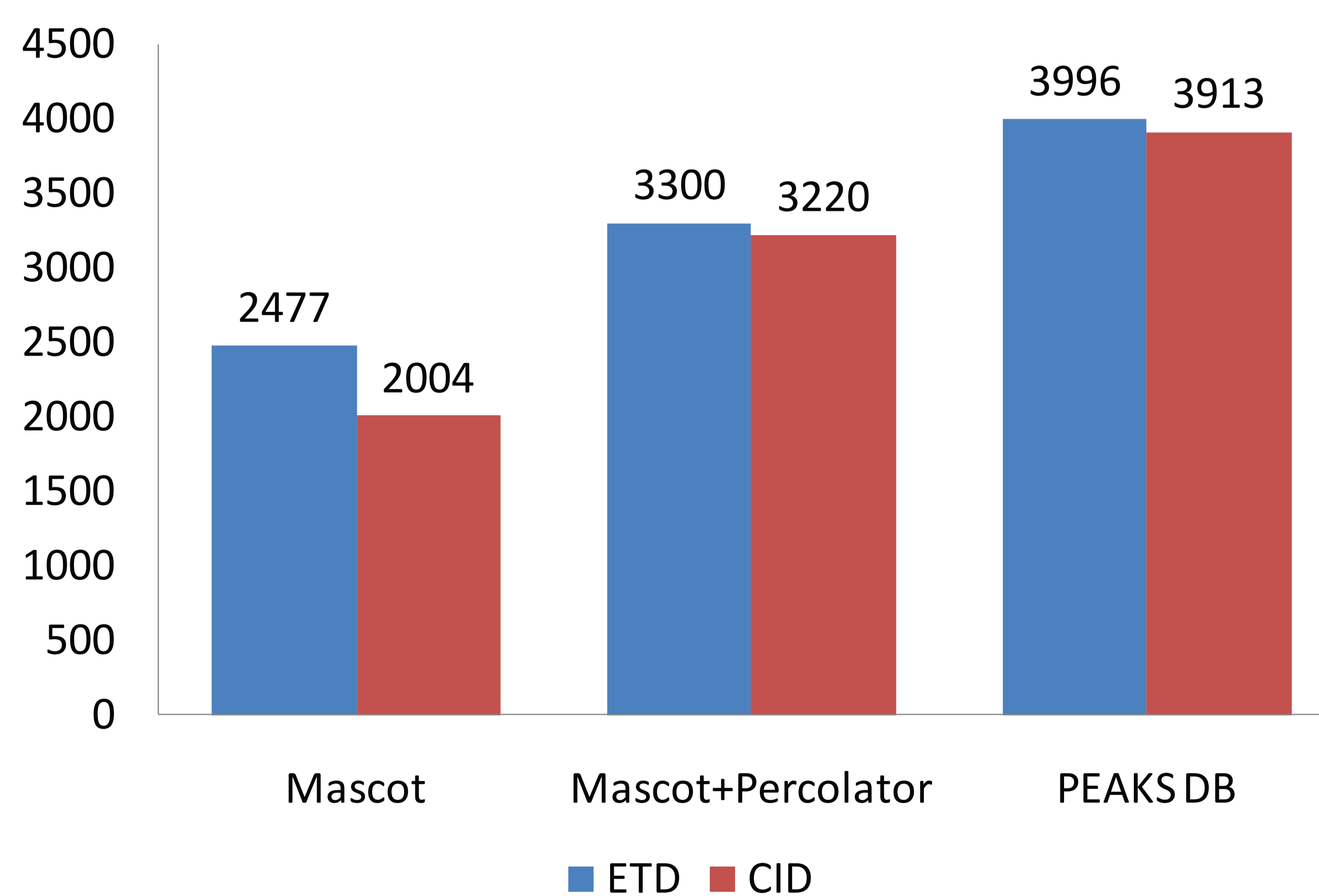


The data was used to identify peptides by searching the Yeast protein sequence database using three different methods: (a) Mascot, (b) Mascot + Percolator, and (c) PEAKS DB. The results on CID and ETD data were compared with each other.

Results

At 1% false discovery rate (FDR), the numbers of peptide-spectrum matches (PSMs) identified by the three methods are shown in Figure 3.

Figure 3. The number of peptide-spectrum matches identified by different approaches at 1% false discovery rate. ETD is better.



Despite that the ETD dataset has fewer MS/MS scans than CID due to the longer ETD scan cycle, ETD was able to provide a higher number of peptide identifications than CID using each of the data analysis methods. The champion was ETD with PEAKS DB, which identified almost twice as many PSMs than CID with Mascot.

Conclusion

With today's peptide identification software, ETD is a better fragmentation technology for general peptide identification with MS/MS.