**Introduction**

- Chronic obstructive pulmonary disease (COPD) and HIV can both significantly affect an individual’s quality of life. Additionally, there is increased risk of COPD for people living with HIV (PWH) with 1 in 10 diagnosed.

- COPD is known to have increased inflammation and proteolytic activity within the lungs, which can result in tissue destruction and health decline.

- To uncover mechanisms behind COPD progression in PWH, we have quantified endogenous peptides using MS-based peptidomic analysis of bronchoalveolar lavage fluid (BALF) samples from PWH with or without COPD, and correlating findings to lung function test results (FEV1 percent predicted).

- Based on detected peptide sequences, we used customized software tools to assess potential protease activity enriched in these clinical samples.

- Our analysis has revealed promising new results on endogenous peptides within BALF samples and enriched protease activities that indicate possible COPD pathogenesis in PWH.

**Methods**

1. Acquire intact and degraded protein information and quantitation with Fragpipe.

2. Detected intact proteins were filtered to functionally active proteases/peptidases according to the MEROPS database, a literature-based information and quantitation with Fragpipe.

3. Added MEROPS information for each protease to Excel file.

4. Used z-scores and custom Excel functions to assign peptides to cleavage sites surrounding detected cleaved proteins’ peptides.

5. Performed statistical analyses to determine correlation to FEV1pp.

**Results**

- Table 1. Examples of detected peptides with assigned protease-substrate prediction scores calculated in Excel using custom functions and published substrate sequences found in the MEROPS online database.

**Discussion and Conclusion**

- The PWH with COPD had a higher average amount of peptide and 8,334 significant z-scores calculated compared to PWH without COPD. These results are consistent with increased protease activity in COPD.

- 11,063 unique peptide sequences were detected, and 2,799 had a significant z-score calculated and protease associations assigned. 31 proteins were found significantly correlated to FEV1pp.

- Matrix metalloproteinases, cathespin, kallikreins, caspases, and exopeptidase activities were considered for play major roles in specific cleaving of immune-related proteins and structural tissues.

**Future Directions**

- Complete analysis of protease-substrate correlation.
- Investigate other protease - substrate interaction predictor algorithms and compare.
- Determine candidate quantifiable peptides for activity of proteases.

**Acknowledgements**

We would like to thank the National Institute of Health (NIH) for funding for the study. We also thank the Minnesotans for Medical Research and the Minnesota Partnership for Bioresearch and Biotechnology for supporting our proteomic analysis. We would like to thank the following companies for providing financial support: The National Biomedical Research Foundation, K2 Scientific’s Proteome Discoverer software for PSM matching and prediction algorithms and compare. We would like to thank the following organizations for their support: The Global Council for Biotechnology for Reactions.org.}

**Table 1.** Examples of detected peptides with assigned protease-substrate prediction scores calculated in Excel using custom functions and published substrate sequences found in the MEROPS online database.