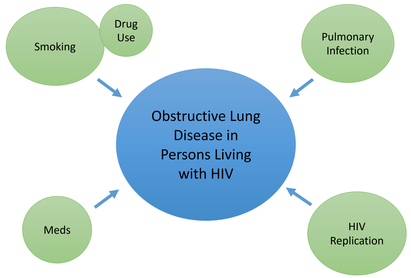
Poster 1375

Protease activity in the lung in HIV-associated obstructive lung disease (OLD)

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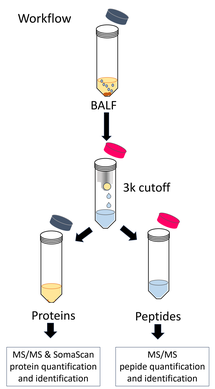
Introduction

Many factors contribute to OLD in the setting of HIV infection



Goal: Identify biomarkers and biological pathways active in HIV-associated HIV

Methods



- Mapped endogenous peptides to their native proteins
- Identified candidate proteases responsible for the peptide cleavages using the MEROPS database.
- Used t-tests to compare average FEV1pp between samples in which each cleaved protein was detected versus absent. We accounted for multiple comparisons using a false discovery rate (FDR) adjustment.

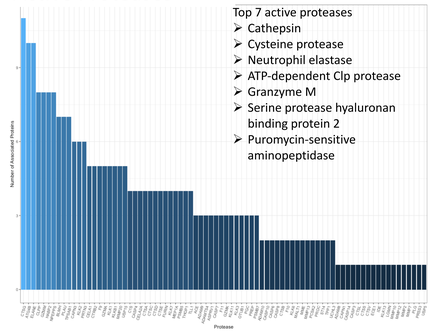
Results

	Case (N=21)	Control (N=24)
Sex Male	15 (71.4%)	17 (70.8%)
Age Mean (SD)	58.6 (7.72)	53.8 (7.62)
Ethnicity		
Black, Non-Hispanic	12 (57.1%)	12 (50.0%)
White, Hispanic/Latino	9 (42.9%)	11 (45.8%)
Asian/Pacific Islander	0 (0%)	1 (4.2%)
Smoking Status		
Former	7 (33.3%)	7 (29.2%)
Never	3 (14.3%)	5 (20.8%)
Current	11 (52.4%)	12 (50.0%)
Receiving ART	20 (95.2%)	22 (91.7%)
FEV1-pp Mean (SD)	68.3 (16.8)	104 (11.2)
FEV1/FVC Mean (SD)	0.560 (0.118)	0.794 (0.0590)
DLCOpp Mean (SD)	73.1 (26.7)	74.6 (22.3)
Viral Load		
<50 Copies	11 (52.4%)	16 (66.7%)
>50 Copies	1 (4.8%)	3 (12.5%)
Missing	9 (42.9%)	5 (20.8%)
Pack-Years Mean (SD)	22.0 (17.3)	14.3 (13.6)

Proteases associated with Lung Function (FEV1pp)

Protease	Mean Correlation with FEV1pp	Combined P-Value	FDR	Name
P14384	0.3634	0.0000	0.0000	Carboxypeptidase M
P00734	0.2704	0.0000	0.0007	Prothrombin
P00749	0.3836	0.0004	0.0054	Urokinase-type plasminogen activator
P20142	0.2758	0.0007	0.0061	Gastricsin
P24158	-0.4621	0.0000	0.0002	Myeloblastin
Q9UKR3	-0.2560	0.0000	0.0002	Kallikrein-13
P07858	-0.3481	0.0001	0.0017	Cathepsin B
P53634	-0.2421	0.0002	0.0028	Dipeptidyl peptidase 1
Q9UNI1	-0.4757	0.0004	0.0053	Chymotrypsin-like elastase family member 1
Q9UBR2	-0.2607	0.0006	0.0059	Cathepsin Z
P14780	-0.2169	0.0005	0.0059	Matrix metalloproteinase-9
P22894	-0.2177	0.0011	0.0091	Neutrophil collagenase MMP8
P08311	-0.1770	0.0014	0.0103	Cathepsin G
P42574	-0.3534	0.0014	0.0103	Caspase-3
P16519	-0.3044	0.0020	0.0136	Neuroendocrine convertase 2
P17655	-0.1851	0.0036	0.0177	Calpain-2 catalytic subunit
P25774	-0.2986	0.0033	0.0177	Cathepsin S
P08246	-0.1994	0.0030	0.0177	Neutrophil elastase
P45974	-0.1581	0.0034	0.0177	Ubiquitin carboxyl-terminal hydrolase 5
P39900	-0.4033	0.0030	0.0177	Macrophage metalloelastase MMP12
P09958	-0.3957	0.0037	0.0177	Furin endoprotease
Q92851	-0.0646	0.0061	0.0280	Caspase-10

Active Proteases



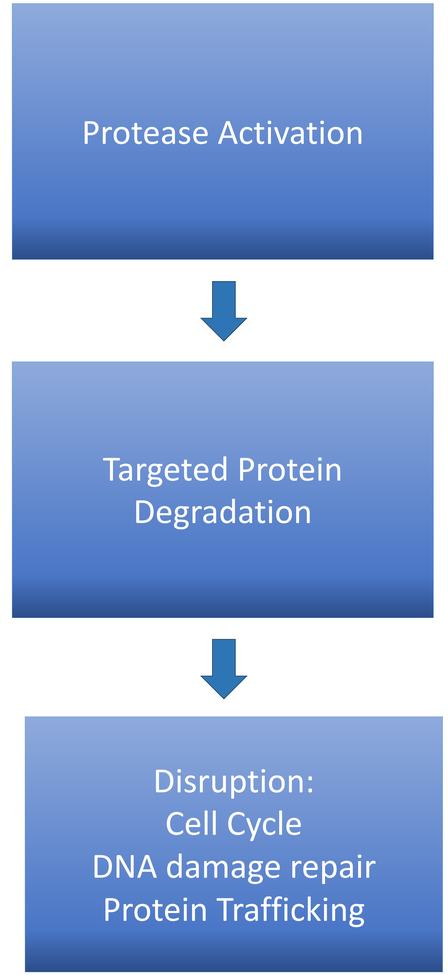
Proteins Targeted by Proteases associated with Lung Function (FEV1pp)

Proteins	UniProt ID	Mean FEV1pp (Present)	Mean FEV1pp (Absent)	P-Value	FDR	Gene
Alpha-enolase	P06733	53.9625	91.8787	0.0004	0.0247	ENO1
Gelsolin	P06396	45.4126	90.3352	0.0008	0.0247	GSN
Histone H4	P62805	61.1725	91.9697	0.0009	0.0247	H4C1
Tubulin beta-4B chain	P68371	55.6507	90.7484	0.0022	0.0414	TUBB4B
Histone H2B type 2-F	Q5QNW6	56.8110	91.3487	0.0036	0.0414	H2BC18
Tubulin alpha-1A chain	Q71U36	64.6865	91.1127	0.0045	0.0414	TUBA1A
Glyceraldehyde-3-phosphate dehydrogenase	P04406	65.3887	91.5802	0.0046	0.0414	GAPDH
Myosin-9	P35579	61.5678	88.5792	0.0046	0.0414	MYH9
Aldehyde dehydrogenase, dimeric NADP-preferring	P30838	61.6220	91.1401	0.0046	0.0414	ALDH3A1
Glutathione S-transferase P	P09211	61.7737	91.1076	0.0054	0.0414	GSTP1
Vimentin	P08670	78.8246	96.0831	0.0054	0.0414	VIM
Isoform A2 of Heterogeneous nuclear ribonucleoproteins A2/B1	P22626-2	66.1016	89.0858	0.0062	0.0425	HNRNPA2B1
Galectin-3	P17931	70.2732	92.4552	0.0066	0.0425	LGALS3
Parkinson disease protein 7	Q99497	62.8499	90.8770	0.0074	0.0442	PARK7
Basic salivary proline-rich protein 1	P04280	66.1060	90.7664	0.0087	0.0486	PRB1

Protease Disrupted Pathways

Pathway	No. Overlapping Genes	No. Pathway Genes	P-Value	Q-Value
SUMO E3 ligases SUMOylate target proteins (cell cycle regulation, DNA damage repair, and protein trafficking)	15	15 (177)	4.94E-06	0.00745
RMTs methylate histone arginines	15	15 (74)	4.94E-06	0.00745
SUMOylation	15	15 (182)	4.94E-06	0.00745
SUMOylation of chromatin organization proteins	14	14 (72)	1.27E-05	0.00745
HDMs demethylate histones	14	14 (50)	1.27E-05	0.00745
PKMTs methylate histone lysines	14	14 (73)	1.27E-05	0.00745
Deposition of new CENPA-containing nucleosomes at the centromere	14	14 (43)	1.27E-05	0.00745
Nucleosome assembly	14	14 (43)	1.27E-05	0.00745
HDACs deacetylate histones	16	17 (94)	2.08E-05	0.00883
HCMV Early Events	16	17 (109)	2.08E-05	0.00883

Conclusions



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