

Supplementary Material

1 Supplementary Tables

Table S1. Demographic and clinical features and pharmacological treatment of the patients included in the study.

Patients	Sex and age	Diagnosis	Pharmacological treatment
#1	M, 82	AD (moderate)	Rivastigmine + Memantine
#2	F, 80	AD (moderate)	Rivastigmine + Memantine
#3	M, 85	AD (mild)	Rivastigmine
#5	F, 63	AD (moderate)	Rivastigmine + Memantine
#6	M, 78	AD (mild)	Donepezil
#7	M, 85	AD (moderate)	Rivastigmine + Memantine
#8	F, 81	AD (mild)	Rivastigmine
#9	F, 78	AD (mild)	Memantine
#10	M, 85	AD (mild)	Rivastigmine + Memantine
#11	F, 80	AD (mild)	Rivastigmine + Memantine
#13	F, 79	AD (mild)	Rivastigmine
#14	F, 82	AD (mild)	Donepezil
#16	F, 83	AD (moderate)	Donepezil + Memantine
#17	F, 63	AD (mild)	Donepezil
#18	F, 80	AD (mild)	Rivastigmine
#19	F, 80	AD (mild)	Rivastigmine
#20	M, 87	AD (mild)	Memantine
#21	M, 81	AD (mild)	Rivastigmine
#22	M, 87	AD (mild)	Donepezil
#23	F, 75	AD (mild)	Rivastigmine
#24	F, 75	AD (mild)	Rivastigmine
#25	F, 83	AD (mild)	Rivastigmine
#26	F, 84	AD (moderate)	Rivastigmine
#27	F, 81	AD (mild)	Rivastigmine
#28	F, 84	AD (moderate)	Memantine
#29	F, 92	AD (moderate)	Memantine
#30	M, 86	AD (moderate)	Memantine
#31	M, 77	AD (moderate)	Donepezil
#32	F, 88	AD (moderate)	Memantine
#33	F, 81	AD (moderate)	Rivastigmine
#34	F, 77	AD (moderate)	Rivastigmine + Memantine
#35	M, 87	AD (mild)	Memantine
#36	M, 84	AD (mild)	Memantine
#37	F, 77	AD (mild)	Rivastigmine
#38	F, 78	AD (mild)	Rivastigmine

Table S2. UniProt-KB code, experimental and theoretical average mass values $\pm$ standard deviations (SD), average (Mav) and monoisotopic ([M+H]⁺), and elution times of proteins and peptides analyzed. Table reported also the m/z values and charge of the multiply-charged ions selected for XIC search in HPLC-low resolution MS, and those ones used for high-resolution MS/MS characterization.

Proteins/peptides	El. time (min $\pm$ 0.5)	Exper. (theor) Mav $\pm$ SD	m/z (charge) for XIC search	Exper. (theor) [M+H] ⁺ $\pm$ SD	m/z (charge) for MS/MS	PTMs
Acid Proline-Rich Proteins						
PRP-1 2P (P02810)	22.2	15515 $\pm$ 2 (15514-15515)	1293.9(+12), 1194.4(+13), 1035.3(+15), 970.7(+16), 913.6(+17)	15506.1 $\pm$ 0.1 (15506.24-15507.22)	1293.19(+12); 1034.75(+15); 970.14(+16); 862.46(+18)	N-Term(Gln->pyro-Glu), S ₈ (Phospho), S ₂₂ (Phospho)
PRP-1 1P	22.9	15435 $\pm$ 2 (15434-15435)	1287.2(+12), 1188.3(+13), 1030.0(+15), 965.7(+16), 908.9(+17)	15426.3 $\pm$ 0.1 (15426.27-15427.26)	1286.52(+12); 1187.64 (+13); 1029.42(+15)	N-Term(Gln->pyro-Glu), S ₈ or S ₂₂ (Phospho)
PRP-1 0P	23.2	15355 $\pm$ 2 (15354-15355)	1280.5(+12), 1182.1(+13), 1024.6(+15), 960.7(+16), 904.2(+17)	15346.3 $\pm$ 0.1 (15346.31-15347.29)	903.72(+17); 853.57(+18)	N-Term(Gln->pyro-Glu)
PRP-1 3P	21.6	15595 $\pm$ 2 (15594-15595)	1418.7(+11), 1300.5(+12), 1200.6(+13), 1040.6(+15), 975.7(+16)	15586.3 $\pm$ 0.1 (15586.21-15587.19)	1732.80(+9); 1114.30(+14); 1040.08(+25); 866.90 (+18)	N-Term(Gln->pyro-Glu) S ₈ , S ₁₇ , S ₂₂ (Phospho)
PRP-3 2P (P02810)	22.8	11161 $\pm$ 1 (11161-11162)	1595.5(+7), 1396.2(+8), 1015.7(+11), 931.1(+12), 859.6(+13)	11155.10 $\pm$ 0.07 (11156.08-11157.06)	1015.19(+11); 930.67(+12); 797.86(+14); 744.74(+15)	N-Term(Gln->pyro-Glu) S ₈ , S ₂₂ (Phospho) Fragment 1-106 of PRP-1
PRP-3 1P	23.4	11081 $\pm$ 1 (11081-11082)	1584.1(+7), 1386.2(+8), 1008.4(+11), 924.5(+12), 853.4(+13)	11076.00 $\pm$ 0.07 (11076.11-11077.09)	1385.51(+8); 1008.61(+11); 924.01(+12); 853.01(+13)	N-Term(Gln->pyro-Glu) S ₈ or S ₂₂ (Phospho)
PRP-3 0P	23.8	11001 $\pm$ 1 (11001-11002)	1376.2(+8), 1101.2(+10), 917.8(+12) 786.8(+14)	10996.01 $\pm$ 0.07 (10996.14-10997.13)	1000.56 (+11); 786.37 (+14)	N-Term(Gln->pyro-Glu)
PRP-3 2P desR₁₀₆	22.8	11004 $\pm$ 1 (11005-11006)	1573.2(+7), 1223.8(+9), 1001.5(+11), 847.6(+13)	10999.85 $\pm$ 0.07 (10999.97-11000.96)	1001.00 (+11); 917.66 (+12)	N-Term(Gln->pyro-Glu) S ₈ , S ₂₂ (Phospho), R ₁₀₆ removal
P-C peptide (P02810)	15.0	4370.9 $\pm$ 0.4 (4370.8)	1457.9(+3), 1093.7(+4)	4369.19 $\pm$ 0.02 (4369.18)	1093.05(+4)	Fragment 107-150 of PRP-1
Statherin						
Statherin (P02808)	29.2	5380.0 $\pm$ 0.5 (5379.7)	1794.2(+3), 1345.9(+4), 1076.9(+5)	5377.46 $\pm$ 0.03 (5377.45)	1345.12(+4)	S ₂ (Phospho); S ₃ (Phospho)
Statherin 1P	28.9	5299.9 $\pm$ 0.5 (5299.7)	1767.6(+3), 1325.9(+4), 1060.9(+5)	5297.50 $\pm$ 0.03 (5297.48)	1325.13(+4)	S ₃ (Phospho)
Fr. des-F₄₃	27.8	5232.4 $\pm$ 0.5 (5232.5)	1745.1(+3), 1309.1(+4), 1047.5(+5)	5230.38 $\pm$ 0.03 (5230.38)	1308.35(+4)	C-Term. F ₄₃ removal
Fr. desT₄₂-F₄₃	27.9	5131.2 $\pm$ 0.5 (5131.4)	1711.4(+3), 1283.8(+4), 1027.2(+5)	5129.33 $\pm$ 0.03 (5129.33)	1283.09(+4)	C-Term. T ₄₂ -F ₄₃ removal
Fr. desD₁	28.7	5264.7 $\pm$ 0.5 (5264.6)	1755.9(+3), 1317.2(+4), 1053.9(+5)	5262.41 $\pm$ 0.03 (5262.42)	1316.36(+4)	N-Term. D ₁ removal

Proteins/peptides	El. time (min ± 0.5)	Exper. (theor) Mav ± SD	m/z (charge) for XIC search	Exper. (theor) [M+H] ⁺ ± SD	m/z (charge) for MS/MS	PTMs
Fr. des1-9	28.5	4127.9 ± 0.4 (4127.6)	1376.9(+3), 1032.9(+4)	4125.99 ± 0.02 (4125.99)	1376.00(+3)	N-Term. 1-9 residue removal
Fr. des1-10	28.0	3971.3 ± 0.4 (3971.4)	1986.7(+2), 1324.8(+3)	3969.90 ± 0.01 (3969.89)	1323.97(+3)	N-Term. 1-10 residue removal
Fr. des1-13	27.5	3645.2 ± 0.4 (3645.0)	1823.6(+2), 1216.1(+3)	3643.68 ± 0.01 (3643.68)	1215.56(+3); 911.92(+4)	N-Term. 1-12 residue removal
P-B peptide						
P-B peptide (P02814)	30.0	5792.9 ± 0.5 (5792.7)	1932.0(+3), 1449.2(+4), 1159.6(+5)	5790.06 ± 0.03 (5790.04)	965.85(+6)	N-Term(Gln->pyro-Glu)
Fr. des1-4	30.0	5371.0 ± 0.5 (5371.3)	1791.4(+3), 1343.8(+4), 1075.3(+5)	5368.84 ± 0.03 (5368.82)	1343.21(+4); 1074.77(+5)	N-Term. 1-4 residue removal
Fr. des1-5	30.3	5215.0 ± 0.5 (5215.1)	1739.4(+3), 1304.8(+4), 1044.0(+5)	5212.75 ± 0.03 (5212.73)	1303.94(+4)	N-Term. 1-5 residue removal
Fr. des1-7	30.1	5060.1 ± 0.5 (5060.9)	1688.0(+3), 1266.2(+4), 1013.2(+5)	5058.67 ± 0.03 (5058.65)	1265.42(+4)	N-Term. 1-7 residue removal
Fr. des1-12	27.5	4549.0 ± 0.5 (4549.3)	1517.5(+3), 1138.3(+4)	4547.10 ± 0.02 (4547.41)	1137.85(+4); 910.48(+5)	N-Term. 1-12 residue removal
Histatins						
Hst-1 (P15515)	21.9	4928.2 ± 0.5 (4928.2)	1644.1(+3), 1233.5(+4)	4926.21 ± 0.02 (4926.20)	704.61(+7)	S2(Phospho)
Hst-1 0P	22.0	4848.2 ± 0.5 (4848.2)	1617.4(+3), 1213.5(+4)	4846.24 ± 0.02 (4846.23)	693.18(+7)	
Hst-3 (P15516)	17.7	4062.2 ± 0.4 (4062.4)	1355.1(+3), 1016.6(+4)	4060.98 ± 0.02 (4060.98)	813.00(+5); 677.67(+6)	
Hst-3 1/25	14.3	3192.4 ± 0.3 (3192.5)	1065.1(+3), 799.1(+4)	3191.62 ± 0.01 (3191.62)	532.78(+6); 456.81(+7)	Fragment 1-25 of Hst-3
Hst-3 1/24	14.6	3036.5 ± 0.3 (3036.3)	1013.2(+3), 760.1(+4)	3035.53 ± 0.01 (3035.52)	607.91(+5); 506.76(+6)	Fragment 1-24 of Hst-3
Cystatins						
A (P01040)	31.8	11005.354 ± 2 (11006.5)	1001.59(+11), 1101.59(+10), 1223.94(+9), 1376.81(+8), 1573.36(+7), 1835.42(+6)	11000.65 ± 0.07 (11000.67)	1375.96 (+8); 847.13 (+13); 786.69 (+14)	
A Nα-Ac.	33	11047.43 ± 2 (11048.5)	1005.41(+11), 1105.85(+10), 1228.61(+9), 1382.06(+8), 1579.36(+7), 1842.42(+6)	11042.55 ± 0.07 (11042.68)	1381.21 (+8); 1227.85 (+9); 789.69 (+14)	N-Term.-α-Acetylation
B-SSG(P04080)	32.8	11485.8 ± 2 (11486.9)	1915.5(+6), 1642.0(+7), 1436.9(+8), 1277.3(+9), 1149.7(+10), 1045.3(+11)	11480.69 ± 0.07 (11480.68)	1149.58 (+10); 1045.25 (+11)	C ₃ Glutathionylation

Proteins/peptides	El. time (min ± 0.5)	Exper. (theor) Mav ± SD	m/z (charge) for XIC search	Exper. (theor) [M+H] ⁺ ± SD	m/z (charge) for MS/MS	PTMs
B-SSC	32.9	11299.8 ± 2 (11300.7)	1884.5(+6), 1615.4(+7), 1413.6(+8), 1256.7(+9), 1131.1(+10), 1028.6(+11)	11294.54 ± 0.07 (11294.61)	-	C ₃ Cysteinylation
B S-S dimer	34.3	22358 ± 2 (22361.3)	1862.4(+12), 1721.1(+13), 1598.2(+14), 1491.8(+15), 1398.6(+16), 1316.4(+17), 1243.3(+18), 1177.9(+19), 1119.1(+20), 1065.8(+21), 1017.4(+22), 973.2(+23)	nd		1 interchaindisulfide bridge
C (P01034)	35.1	13342 ± 2 (13343.1)	1483.57(+9), 1335.32(+10), 1214.02(+11), 1112.93(+12), 1027.40(+13)	13335.32 ± 0.08 (13335.58)	1112.21 (+12); 834.41 (+16)	2 intrachaindisulfidebridges
D-R₂₆ des1-5 (P28325)	37.7	13517 ± 2 (13517.3)	1690.70(+8), 1502.90(+9), 1352.70 (+10), 1229.80 (+11), 1127.4 (+12), 1040.40 (+13)	13509.43± 0.08 (13509.65)	1501.96 (+9); 1351.86 (+10); 965.90 (+14)	N-Term(Gln->pyro-Glu) after 1-5 residue removal, 2 intrachain disulfide bridges
Cystatins S-type						
S1 (P01036)	35.3	14266 ± 2 (14265)	1784.3(+8), 1586.1(+9), 1427.6(+10), 1297.9(+11), 1189.8(+12), 1098.4(+13), 1020.0(+14)	14256.66± 0.09 (14256.77)	1296.98 (+11);1097.60 (+13);1019.27(+14)	S ₃ (Phospo) on cystatin S, 2 intrachain disulfide bridges
S1ox	35.3	14281 ± 2 (14280.7)	1786.40(+8), 1589.70 (+9), 1429.30 (+10), 1299.50 (+11), 1191.30 (+12), 1099.70 (+13)	14272.66 ± 0.09(14272.77)	1428.18 (+10); 1298.43 (+11);1190.31 (+12);892.99 (+16)	S ₃ (Phospo), W ₂₃ oxidation, 2 intrachaindisulfide bridges
S2	35.3	14346 ± 2 (14345)	1794.3(+8), 1595.0(+9), 1435.6(+10), 1305.2(+11), 1196.5(+12), 1104.5(+13), 1025.7(+14)	14336.58 ± 0.09 (14336.74)	1434.57 (+10); 1195.65 (+12); 896.98 (+16)	S ₁ , S ₃ (di-Phospo) on cystatin S, 2 intrachain disulfide bridges
SN (P01037)	34.6	14312 ± 2 (14313)	1790.0(+8), 1591.2(+9), 1432.2(+10), 1302.1(+11), 1193.7(+12), 1101.9(+13), 1023.3(+14)	13304.03 ± 0.09 (13304.09)	951.22 (+14); 740.06 (+18)	2 intrachaindisulfide bridges
SNox	34.6	14328 ± 2 (14328)	1792.30(+8), 1593.20 (+9), 1434.00 (+10), 1303.30 (+11), 1195.20 (+12), 1103.30 (+13)	14320.10± 0.09 (14320.09)	1302.74 (+11);1194.26 (+12);1102.47 (+13); 955.61 (+15); 1103.85 (+13); 1025.07 (+14); 956.80 (+15); 897.06 (+16); 844.35 (+17); 797.50 (+18)	W ₂₃ oxidation
SA (P09228)	36.8	14347 ± 2 (14346)	1794.4(+8), 1595.1(+9), 1435.7(+10), 1305.3(+11), 1196.6(+12), 1104.6(+13), 1025.8(+14)	14338.02± 0.09 (14338.01)		1 intrachaindisulfide bridge
Antileukoproteinase						
SLPI (P03973)	26.2	11702.2 ± 1 (11706)	1952.64(+6), 1673.84(+7), 1464.73(+8), 1302.10(+9)	11703.29 ± 0.07 (11702.36)	1301.26(+9); 1171.24(+10)	8 intrachain disulfide bridges
α-Defensins						
α-defensin 1 (P59665)	23.5	3442.5 ± 2 (3442.1)	1772.03(+2), 1148.36(+3), 861.52(+4)	3440.45 ± 0.01 (3440.52)	861.13(+4); 689.10(+5)	2 intrachain disulfide bridges
α-defensin 2 (P59665/6)	23.5	3370.4 ± 1 (3370.9)	1686.49(+2), 1124.66(+3), 843.75(+4)	3370.41 ± 0.01 (3370.44)	1124.48(+3); 843.61(+4); 675.09(+5)	2 intrachain disulfide bridges
α-defensin 3 (P59666)	23.5	3485 ± 2 (3486.1)	1744.03(+2), 1163.03(+3), 872.52(+4)	3484.53 ± 0.01 (3484.51)	872.13(+4)	2 intrachain disulfide bridges

Proteins/peptides	El. time (min ± 0.5)	Exper. (theor) Mav ± SD	m/z (charge) for XIC search	Exper. (theor) [M+H] ⁺ ± SD	m/z (charge) for MS/MS	PTMs
α-defensin 4 (P12838)	27.2	33708 ± 1 (3709.4)	1855.71(+2), 1237.48(+3), 928.36(+4)	3707.68 ± 0.01 (3707.77)	927.94(+4)	2 intrachain disulfide bridges
Thymosins β4						
Tβ4 (P62328)	18.5	4964.0 ± 1 (4963.5)	1655.51(+3), 1241.88(+4), 993.71(+5)	4961.50 ± 0.02 (4961.48)	877.76(+6)	N-Term.-α-Acetylation
S100A proteins						
S100A12 (P80511)	40.0	10444 ± 2 (10443.9)	1306.5(+8), 1161.4(+9), 1045.4(+10), 950.4(+11)	10438.74 ± 0.07 (10438.49)	1044.75 (+10); 803.88 (+13); 696.83 (+15)	M ₁ removal
S100A7 (P31151)	37.0	11367 ± 2 (11367.8)	1422.0(+8), 1264.1(+9), 1137.8(+10), 1034.4(+11)	11360.43 ± 0.07(11361.52)	1263.28 (+9); 1033.77 (+11); 947.71 (+12); 874.89 (+13)	M ₁ removal, N-Term.-α-Acetylation, D ₂₇ variant
S100A8(P05109)	40.4	10833 ± 2 (10834.5)	1355.3(+8), 1204.8(+9), 1084.5(+10), 985.9(+11)	10826.60 ± 0.07 (10828.657)	985.42(+11); 903.39(+12); 833.97(+13)	
S100A8 hyperoxidized	39.3	10915 ± 2 (10914.6)	1365.3(+8), 1213.7(+9), 1092.5(+10), 993.2(+11)	10908.40 ± 0.07 (10908.631)	840.05 (+13)	C ₄₂ -SO ₃ H and W ₅₄ dioxidation or C ₄₂ -SO ₃ H and W ₅₄ oxidation and M _{1/78} oxidation
S100A8 SNO	40.8	10863 ± 2 (10863.5)	1358.9(+8), 1208.1(+9), 1087.3(+10), 988.6(+11)	10858.67 ± 0.07(10857.647)	836.13 (+13); 776.47 (+14); 724.78 (+15)	C ₄₂ nitrosylation
S100A9(S) (P06702)	42.2	12690 ± 2 (12689.2)	1410.9(+9), 1269.9(+10), 1154.6(+11), 1058.4(+12), 977.1(+13)	12682.21 ± 0.08 (12682.293)	1410.03 (+9); 1269.13 (+10); 1057.77 (+12); 976.48 (+13); 846.42 (+15); 705.52 (+18)	N-Term.-α-Acetylation after 1-5 residue removal
S100A9(S) 1P	42.2	12770 ± 2 (12769.2)	1419.8(+9), 1277.9(+10), 1161.8(+11), 1065.1(+12), 983.3(+13)	12762.05 ± 0.08 (12762.26)	912.96 (+14); 852.29 (+15); 798.96 (+16)	N-Term.-α-Acetylation after 1-5 residue removal, T ₁₀₈ (Phospho)
S100A9(S) M-ox	41.3	12706 ± 2 (12705.2)	1412.7(+9), 1271.5(+10), 1156.0(+11), 1059.8(+12), 978.3(+13)	12698.39 ± 0.08 (12698.288)	907.95 (+14); 847.49 (+15)	N-Term.-α-Acetylation after 1-5 residue removal, M _{89 or 78 or 76 or 58} oxidation
S100A9(S) M-ox 1P	41.3	12786 ± 2 (12785.2)	1421.9(+9), 1279.5(+10), 1163.3(+11), 1066.4(+12), 984.5(+13)	12778.21 ± 0.08 (12778.255)	1420.70 (+9); 983.87 (+13); 913.66 (+14)	N-Term.-α-Acetylation after 1-5 residue removal, T ₁₀₈ (Phospho), M _{89 or 78 or 76 or 58} oxidation
S100A9(L) SSG	41.5	13459 ± 2 (13458.1)	1346.8(+10), 1224.5(+11), 1122.5(+12), 1036.3(+13), 962.3(+14)	13450.51 ± 0.08 (13450.55)	1035.58 (+13); 961.68 (+14); 841.60 (+16); 792.15 (+17); 748.20 (+18)	M ₁ removal, N-Term.-α-Acetylation, C ₂ glutathionylation

Table S3: XIC peak areas values (mean $\pm$ SD) normalized on TPC and frequencies of proteins/peptides resulted with similar levels between AD group and HC group. (•), not statistically significant p-values. (NA), absence of a protein.

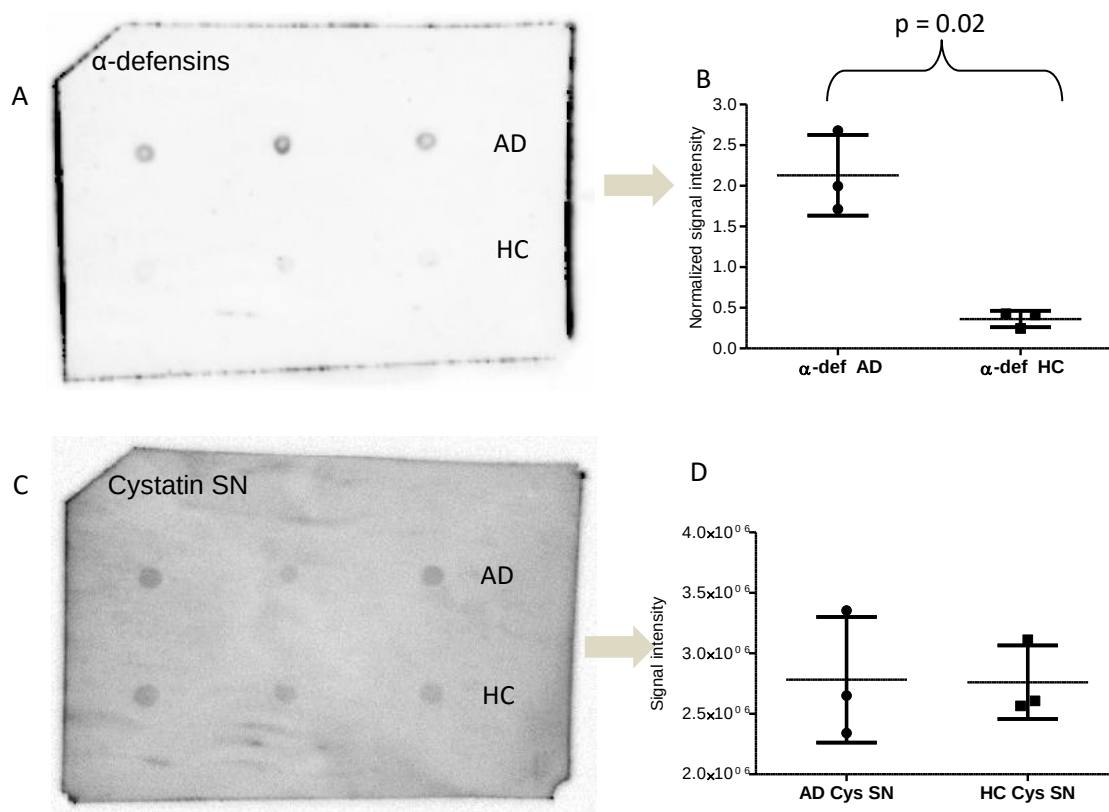
Protein/peptide	XIC Peak Areas $\times 10^5$ (mean $\pm$ SD) and Frequency		p-values AD vs HC
	AD	HC	
PRP-1 2P	37.6 $\pm$ 27.2 (34/35)	28.8 $\pm$ 18.7 (34/34)	•
PRP-1 1P	5.0 $\pm$ 4.3 (34/35)	3.8 $\pm$ 3.5 (31/34)	•
PRP-1 0P	0.2 $\pm$ 0.6 (8/35)	0.3 $\pm$ 0.3 (19/34)	•
PRP-1 3P	0.09 $\pm$ 0.2 (8/35)	0.3 $\pm$ 0.4 (16/34)	•
PRP-3 2P	13.0 $\pm$ 10.4 (35/35)	9.4 $\pm$ 6.7 (34/34)	•
PRP-3 1P	2.1 $\pm$ 1.9 (35/35)	1.5 $\pm$ 1.1 (32/34)	•
PRP-3 0P	0.06 $\pm$ 0.1 (10/35)	0.04 $\pm$ 0.07 (9/34)	•
PRP-3 2P, desR ₁₀₆	1.8 $\pm$ 1.8 (31/35)	2.4 $\pm$ 2.2 (28/34)	•
Stath. 1P	0.3 $\pm$ 0.4 (29/35)	0.3 $\pm$ 0.2 (24/34)	•
Stath. desT ₄₂ -F ₄₃	0.4 $\pm$ 0.4 (26/35)	0.2 $\pm$ 0.2 (30/34)	•
Stath. desD ₁	0.4 $\pm$ 0.5 (32/35)	0.3 $\pm$ 0.3 (30/34)	•
Stath. des1-10	0.3 $\pm$ 0.3 (26/35)	0.2 $\pm$ 0.2 (27/34)	•
P-B peptide	7.8 $\pm$ 6.6 (35/35)	6.4 $\pm$ 4.4 (34/34)	•
P-B des1-4	0.6 $\pm$ 0.8 (2/35)	0.7 $\pm$ 0.6 (32/34)	•
P-B des1-5	0.8 $\pm$ 0.8 (34/35)	1.0 $\pm$ 1.1 (34/34)	•
P-B des1-7	1.3 $\pm$ 2.3 (34/35)	0.8 $\pm$ 0.5 (34/34)	•
P-B des1-12	0.7 $\pm$ 0.7 (34/35)	0.8 $\pm$ 1.3 (31/34)	•
SLPI	0.1 $\pm$ 0.2 (13/35)	0.06 $\pm$ 0.09 (13/34)	•
Hst-3	0.6 $\pm$ 1.0 (18/35)	0.4 $\pm$ 0.7 (18/34)	•
Hst-3 1/25	0.2 $\pm$ 0.3(9/35)	0.2 $\pm$ 0.3 (17/34)	•
Hst-3 1/24	1.1 $\pm$ 1.5 (20/35)	0.6 $\pm$ 0.9 (10/34)	•
Cyst A N α -Ac	0.2 $\pm$ 0.2 (24/35)	0.2 $\pm$ 0.5 (23/34)	•
Cyst. C	0.1 $\pm$ 0.4 (6/35)	0.08 $\pm$ 0.2 (5/34)	•
Cyst. D-R ₂₆ des1-5	0.3 $\pm$ 0.4 (13/35)	0.3 $\pm$ 0.4 (16/34)	•
Cyst S1 tot	6.4 $\pm$ 8.8 (31/35)	4.1 $\pm$ 3.7 (30/34)	•
Cyst. S2	1.6 $\pm$ 2.6 (20/35)	1.2 $\pm$ 1.2 (26/34)	•
Cyst. SN tot	12.3 $\pm$ 21.3 (32/35)	6.7 $\pm$ 6.6 (29/34)	•
Cyst. SA	1.4 $\pm$ 3.4 (8/35)	0.5 $\pm$ 1.2 (7/34)	•
S100A7	0.3 $\pm$ 0.7 (13/35)	0.2 $\pm$ 0.3 (11/34)	•

Table S4: XIC peak areas values (mean $\pm$ SD) normalized on TPC, frequencies and p-values obtained by statistical analysis by comparing the three patients' groups treated with different therapies by non-parametric ANOVA with the Krustal-Wallis test and Dunn's post test. p-values > 0.05 are not statistically significant (•).

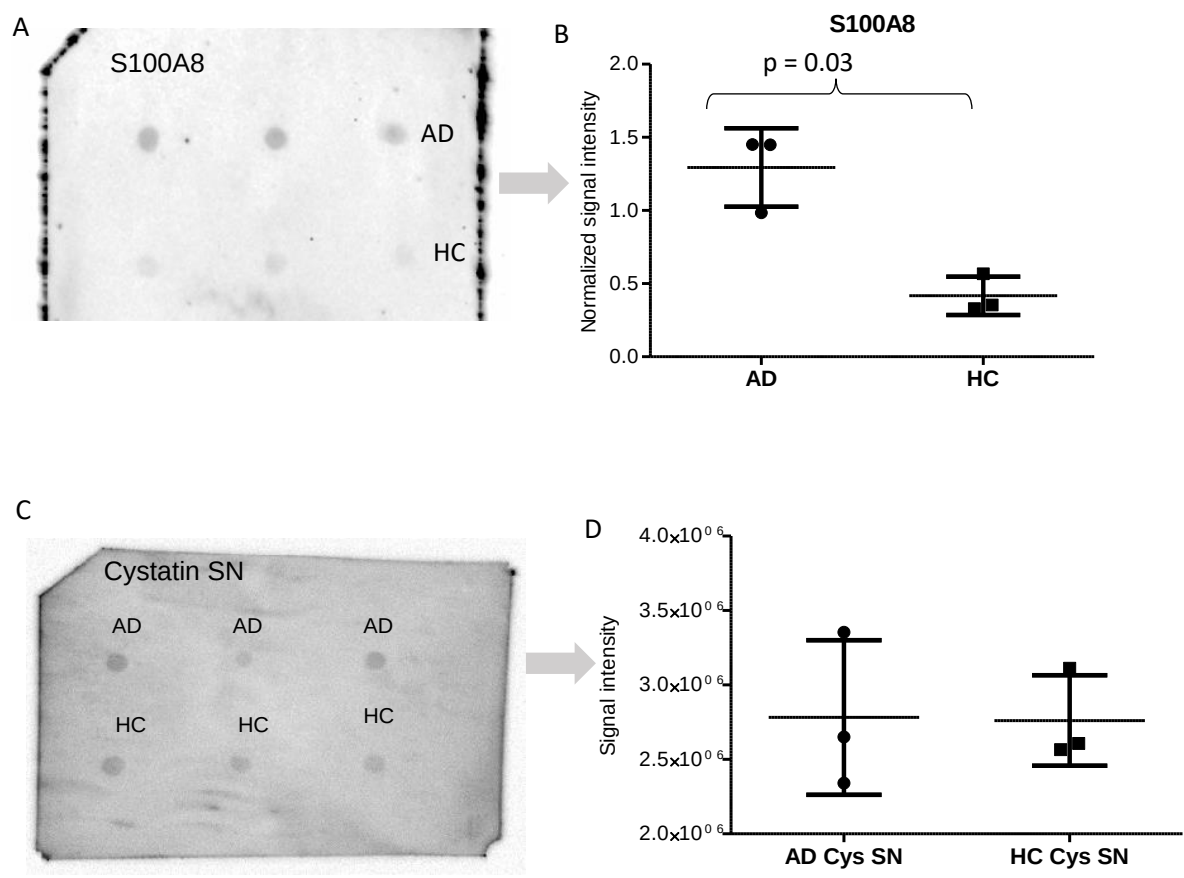
Peptide	XIC Peak Areas $\times 10^5$ (mean $\pm$ SD) and Frequency				ANOVA p value
	G1 (nr 19)	G2 (nr 8)	G3 (nr 8)	HC (nr 34)	
α -defensin 1	2.2 $\pm$ 2.3 (19)	2.3 $\pm$ 1.8 (8)	0.6 $\pm$ 0.8 (5)	0.5 $\pm$ 0.6 (24)	p < 0.0001 (G1vs G3*, G2 vs G3*, G1 vs HC***, G2 vs HC**)
α -defensin 2	1.5 $\pm$ 1.5 (19)	1.5 $\pm$ 1.2 (7)	0.4 $\pm$ 0.6 (5)	0.4 $\pm$ 0.4 (27)	p = 0.0003 (G1vs G3*, G1 vs HC**, G2 vs HC*)
α -defensin 3	0.7 $\pm$ 0.5 (16)	0.8 $\pm$ 0.5 (8)	0.2 $\pm$ 0.4 (2)	0.2 $\pm$ 0.3 (17)	p < 0.0001 (G1vs G3*, G2 vs G3*, G1 vs HC***, G2 vs HC**)
α -defensin 4	0.2 $\pm$ 0.3 (8)	0.4 $\pm$ 0.2 (8)	0.04 $\pm$ 0.08 (2)	0.05 $\pm$ 0.1 (11)	p = 0.0004 (G1vs G2*, G2 vs G3**, G2 vs HC***)
T β 4	0.5 $\pm$ 0.6 (14)	1.1 $\pm$ 0.9 (8)	0.2 $\pm$ 0.4 (3)	0.2 $\pm$ 0.4 (16)	p = 0.002 (G2vs G3**, G2 vs HC**)
Stath. 2P	8.8 $\pm$ 7.7 (19)	5.9 $\pm$ 4.4 (6)	11.0 $\pm$ 7.1 (8)	1.1 $\pm$ 0.9 (33)	p < 0.0001 (G1 vs HC***, G2vs HC*, G3 vs HC***)
Stath. Des1-9	0.5 $\pm$ 0.6 (16)	0.6 $\pm$ 0.9 (6)	0.8 $\pm$ 0.6 (7)	0.08 $\pm$ 0.1 (24)	p = 0.0002 (G1 vs HC**, G3 vs HC**)
P-C peptide	9.3 $\pm$ 5.1 (19)	8.6 $\pm$ 12.6 (6)	12.3 $\pm$ 6.9 (8)	5.6 $\pm$ 4.4 (34)	p = 0.01 (G3 vs HC*)
Cyst. B tot	2.0 $\pm$ 2.2 (18)	1.9 $\pm$ 1.6 (8)	0.9 $\pm$ 1.2 (7)	9.3 $\pm$ 5.1 (27)	p = 0.006 (G1vs HC*, G2 vs HC*)
Cyst A	1.8 $\pm$ 1.6 (17)	2.9 $\pm$ 1.9 (8)	1.2 $\pm$ 0.9 (7)	1.0 $\pm$ 0.9 (29)	p = 0.02 (G2 vs HC*)
S100A8 tot	1.1 $\pm$ 1.5 (12)	0.9 $\pm$ 1.1 (6)	0.4 $\pm$ 0.5 (4)	0.08 $\pm$ 0.2(5)	p < 0.0001 (G1 vs HC***, G2 vs HC**)
S100A8-SNO	1.1 $\pm$ 2.3 (9)	0.7 $\pm$ 1.0 (3)	Not detected	Not detected	p < 0.0001 (G1 vs G3*, G1 vs HC***)
S100A9(S) tot	1.1 $\pm$ 1.5 (18)	0.9 $\pm$ 1.1 (7)	0.4 $\pm$ 0.5 (7)	0. .5 $\pm$ 0.8 (16)	p < 0.0001 (G1 vs HC***, G2 vs HC*)

2 Supplementary Figures

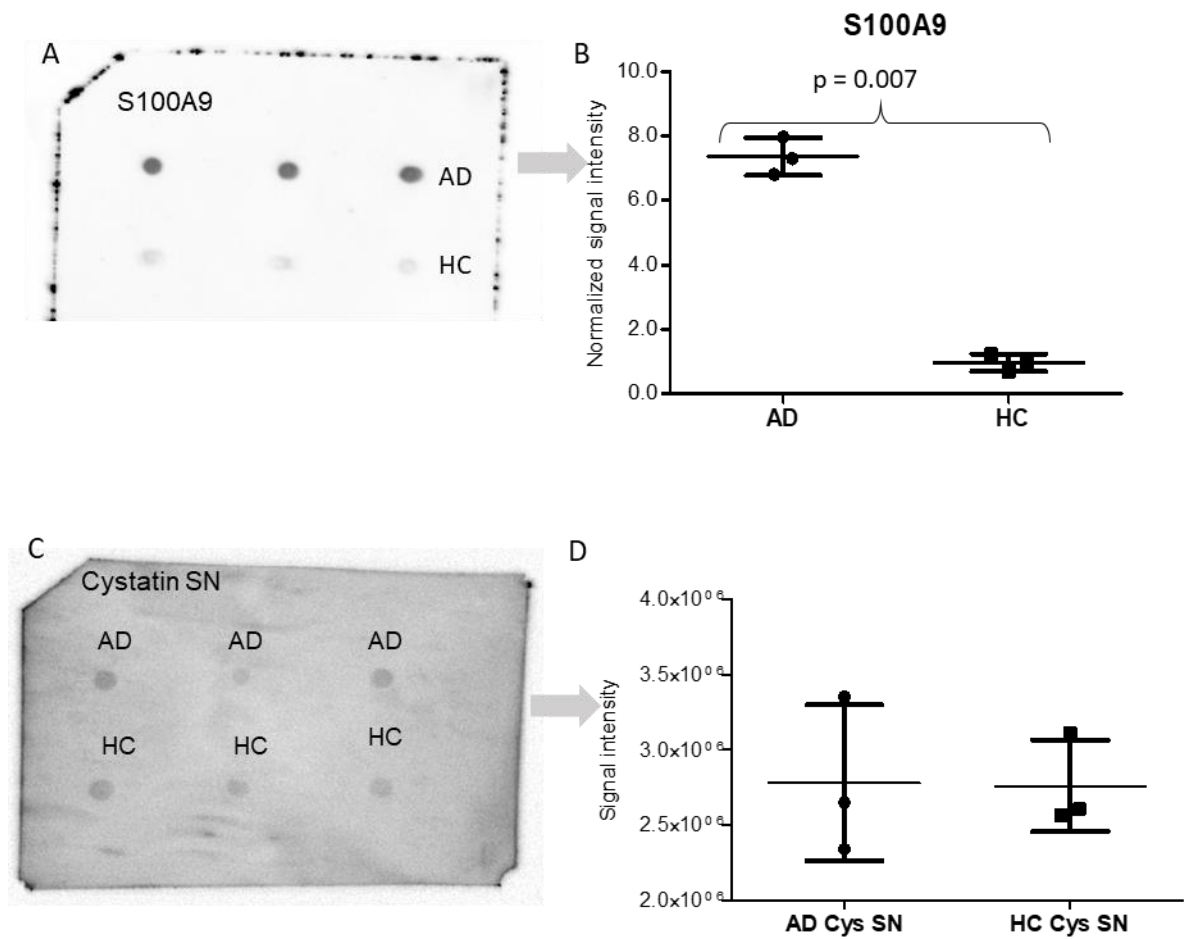
Supplementary Figure S1. Immune-detection analysis of the total α -defensins by dot-blotting of a triplicate of a salivary pools of AD samples and HC samples (panel A), statistical analysis of the normalized signal intensity of the AD and HC spots (panel B). Normalization performed on cystatin SN signal (panel C). Statistical comparison between SN signals in AD and HC (panel D).



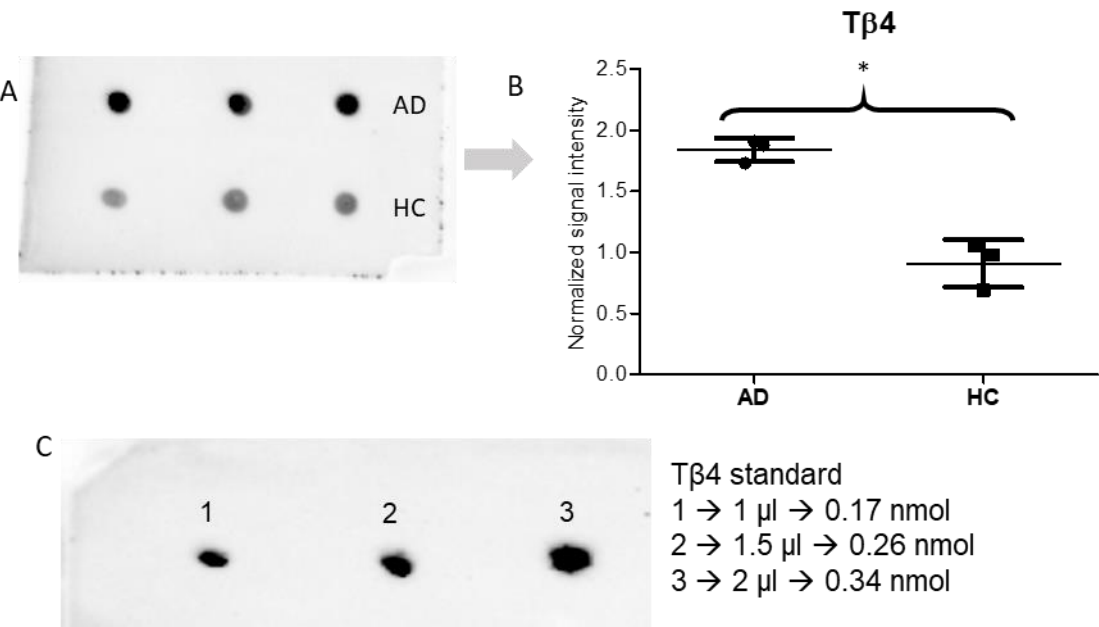
Supplementary Figure S2. Immune-detection analysis of the total S100A8 by dot-blotting of a triplicate of a salivary pools of AD samples and HC samples (panel A), statistical analysis of the normalized signal intensity of the AD and HC spots (panel B). Normalization performed on cystatin SN signal (panel C). Statistical comparison between SN signals in AD and HC(panel D).



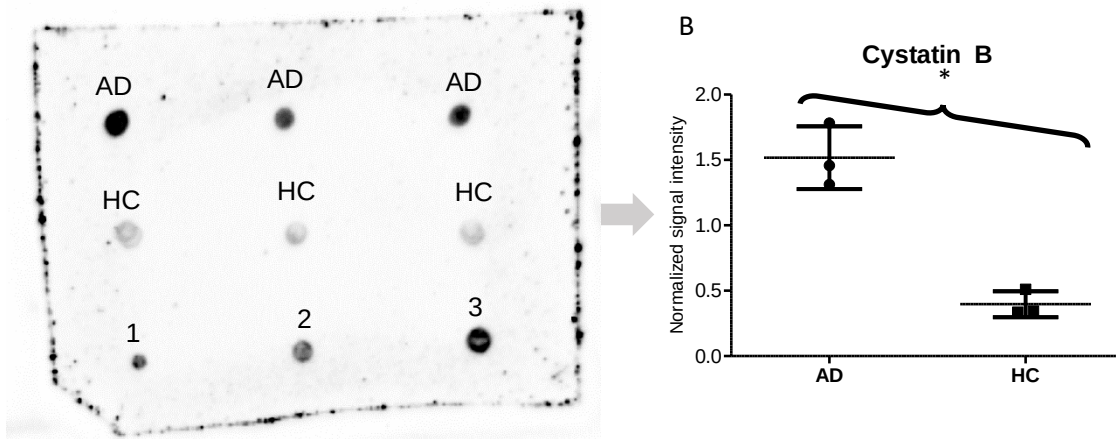
Supplementary Figure S3. Immune-detection analysis of the total S100A9 by dot-blotting of a triplicate of a salivary pools of AD samples and HC samples (panel A), statistical analysis of the normalized signal intensity of the AD and HC spots (panel B). Normalization performed on cystatin SN signal (panel C). Statistical comparison between SN signals in AD and HC(panel D).



Supplementary Figure S4. Immune-detection analysis of T β 4 by dot-blotting of a triplicate of a salivary pools of AD samples and HC samples (panel A), statistical analysis of the normalized signal intensity of the AD and HC spots (panel B). Normalization performed on the signal of the standard T β 4 0.26 nmol (panel C).



Supplementary Figure S5. Immune-detection analysis of cystatin B by dot-blotting of a triplicate of a salivary pools of HC samples and AD samples, and of the HPLC-enriched fraction of cystatin B prepared from human saliva, blotted at different amounts indicated as 1, 2, and 3, (panel A). Statistical analysis of the normalized signal intensity of the AD and HC spots with respect the standard 2 at 0.2 μg of total proteins (panel B).



Enriched cystatin B fraction from human saliva

1 $\rightarrow$ 0.5 μl $\rightarrow$ 0.1 μg of total proteins

2 $\rightarrow$ 1 μl $\rightarrow$ 0.2 μg of total proteins

3 $\rightarrow$ 2 μl $\rightarrow$ 0.4 μg of total proteins