# Supplement

## Supplementary document for Ludvigsen and Pedersen et al., Proteomic profiling identifies outcome-predictive markers in patients with peripheral T-cell lymphoma, not otherwise specified

This supplementary document includes

**Supplementary Figure S1**. 2D-PAGE analyses

**Supplementary Table S1.** Clinical parameters for the 18 patients with PTCL-NOS selected for proteomics

**Supplementary Table S2**. List of identified differentially expressed proteins between non-neoplastic tonsils (n=8) and PTCL-NOS (n=18) by LC-MS/MS (Analysis A)

**Supplementary Table S3.** List of identified differentially expressed proteins between PTCL-NOS patients belonging to Cluster1, C1 (n=7) and Cluster 2, C2 (n=11) by LC-MS/MS (Analysis B)

**Supplementary Table S4.** List of identified differentially expressed proteins between PTCL-NOS patients with primary refractory disease (*i.e.* PD and survival <100 days, (G1)) and patients who showed initial chemosensitivity (*i.e.* CR and survival > 2 years (G2)) by LC-MS/MS (Analysis C)

**Supplementary Table S5.** List of UniProt identifications as input to pathway enrichment analysis by Reactome Pathway

**Supplementary Table S6.** Analysis A: N vs PTCL-NOS. Pathway enrichment analysis by Reactome Pathway Database

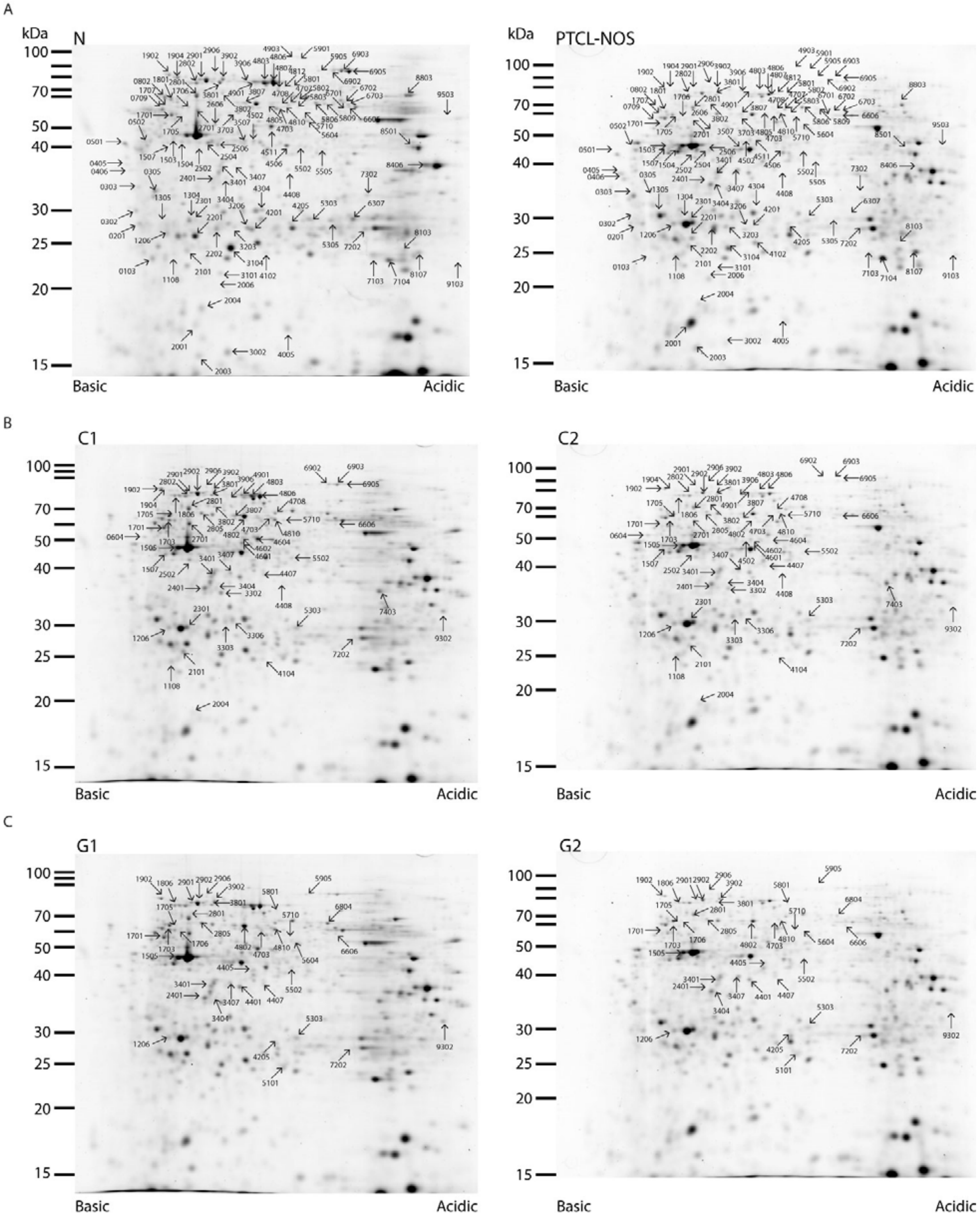
**Supplementary Table S7.** Clinico-pathological and molecular features of the PTCL-NOS cohort selected for proteomics according to PCA- and outcome analysis

**Supplementary Table S8.** Analysis B: C1 vs C2. Pathway enrichment analysis by Reactome Pathway Database

**Supplementary Table S9.** Analysis B: G1 vs G2. Pathway enrichment analysis by Reactome Pathway Database

# Supplementary Tables

## Supplementary Figure S1



Supplementary Figure S1. **2D-PAGE analyses.** Representative gels of A) N and PTCL-NOS; B) C1 *versus* C2; and C) G1 and G2. All ≥2-fold differentially expressed spots were excised and peptides were identified by LC-MS/MS. The 4-digit numbers are the specific numbers of the differentially expressed spots that are presented in supplementary tables S2, S3, and S4.

2D-PAGE: two-dimensional polyacrylamide gel electrophoresis; LC-MS/MS: liquid chromatography tandem mass spectrometry; N: Non-neoplastic tissue; PTCL-NOS: peripheral T-Cell lymphoma, not otherwise specified.

# Supplementary Tables

**Supplementary Table S1.** Clinical parameters for the 18 patients with PTCL-NOS selected for proteomics.

| Patient | Age, years | Sex | IPI | Treatment | Initial treatment response | Status at follow-up | Days to death or follow-up | Cluster |
|---|---|---|---|---|---|---|---|---|
| 1 | 78 | M | high | CHOP | PD | dead | 17 | C1 |
| 2 | 20 | F | high | CHOP | PD | dead | 18 | C1 |
| 3 | 67 | M | high | no treatment | PD | dead | 26 | C1 |
| 4 | 64 | F | high-int | CEOP | PD | dead | 84 | C1 |
| 5 | 58 | F | low | CHOP | PR | dead | 159 | C2 |
| 6 | 56 | M | low-int | CHOP | PR | dead | 181 | C2 |
| 7 | 45 | M | high-int | MACOP-B | N/A | dead | 208 | C1 |
| 8 | 28 | M | low-int | CHOP | PR | dead | 453 | C1 |
| 9 | 54 | M | low-int | CHOP | PR | dead | 553 | C2 |
| 10 | 74 | F | high-int | CHOP | CR | dead | 572 | C2 |
| 11 | 51 | M | low | CHOP+HDT/ASCT | CR | alive | 770 | C2 |
| 12 | 81 | M | low-int | MIME | CR | dead | 778 | C1 |
| 13 | 77 | F | high-int | CHOP | CR | dead | 797 | C2 |
| 14 | 32 | F | low | CHOEP+HDT/ASCT | CR | dead | 805 | C2 |
| 15 | 25 | F | low-int | CHOP+HDT/ASCT | CR | alive | 951 | C2 |
| 16 | 48 | M | high-int | CHOP | CR | dead | 991 | C2 |
| 17 | 48 | M | low-int | CHOEP+HDT/ASCT | CR | alive | 2417 | C2 |
| 18 | 58 | M | low-int | CHOP | CR | alive | 2856 | C2 |

IPI: international prognostic index; PD: progressive disease; PR: partial remission; CR: complete remission; C1: cluster 1; C2: cluster 2; N/A: not available.

CHOP:cyclophosphamide, doxorubicin, vincristine, prednisone; CHOEP: cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone; MACOP-B: methotrexate, cytarabine, cyclophosphamide, vincristine, prednisone, bleomycin; MIME: methyl-GAG, ifosfamide, methotrexate, etoposide; HDT/ASCT: high-dose chemotherapy with autologous stem-cell transplantation.

**Supplementary Table S2.** List of identified differentially expressed proteins between non-neoplastic tonsils (n=8) and PTCL-NOS (n=18) by LC-MS/MS (Analysis A)

| SSP | Identification | Expression | Fold change | Peptides | Mascot Score | Mr (Da) | SwissProt |
|---|---|---|---|---|---|---|---|
| | **N vs PTCL-NOS** | | | | | | |
| 0103 | Translationally-controlled tumor protein | Down PTCL-NOS | 9.09 | 1 | 103 | 19697 | TCTP_HUMAN |
| 0201 | Serum albumin fragment | Down PTCL-NOS | 9.09 | 4 | 295 | 71317 | ALBU_HUMAN |
| | Ig gamma-1 chain C region fragment | | | 1 | 88 | 36596 | IGHG1_HUMAN |
| | Proteasome subunit alpha type-5-A | | | 1 | 64 | 26565 | PSA5_HUMAN |
| | Ig kappa chain C region | | | 1 | 52 | 11773 | IGKC_HUMAN |
| 0302 | 14-3-3 protein sigma | Down PTCL-NOS | 10.00 | 2 | 152 | 27871 | 1433S_HUMAN |
| 0303 | Vimentin fragment | Up PTCL-NOS | 4.28 | 4 | 203 | 53676 | VIME_HUMAN |
| | 40S ribosomal protein SA | | | 1 | 83 | 32947 | RSSA_HUMAN |
| 0305 | Actin fragment | Down PTCL-NOS | 11.11 | 5 | 238 | 42052 | ACTB_HUMAN |
| 0405 | Actin | Up PTCL-NOS | 7.71 | 2 | 174 | 42052 | ACTB_HUMAN |
| | Serum albumin fragment | | | 3 | 160 | 71317 | ALBU_HUMAN |
| | Desmoplakin fragment | | | 2 | 129 | 334021 | DESP_HUMAN |
| | Alpha-1-antitrypsin fragment | | | 2 | 89 | 46878 | A1AT_HUMAN |
| | Histone H2A type 1C | | | 1 | 85 | 14127 | H2A1B_HUMAN |
| | Fibrinogen beta chain fragment | | | 1 | 72 | 49900 | FIBB_HUMAN |
| | Haemoglobin subunit beta | | | 1 | 69 | 16102 | HBB_HUMAN |
| | Ig kappa chain C region | | | 1 | 69 | 11773 | IGKC_HUMAN |
| | Galectin-7 | | | 1 | 64 | 15123 | LEG7_HUMAN |
| | Fibrinogen gamma chain fragment | | | 1 | 46 | 52106 | FIBG_HUMAN |
| | Tubulin fragment | | | 1 | 46 | 59788 | TBA1A_HUMAN |
| 0406 | Alpha-1-antitrypsin fragment | Up PTCL-NOS | 5.63 | 3 | 112 | 46878 | A1AT_HUMAN |
| | Calreticulin fragment | | | 1 | 60 | 48283 | CALR_HUMAN |
| 0501 | Calreticulin | Down PTCL-NOS | 2.63 | 4 | 250 | 48283 | CALR_HUMAN |
| 0502 | Vimentin | Up PTCL-NOS | 3.07 | 10 | 565 | 53676 | VIME_HUMAN |
| 0709 | Tubulin | Down PTCL-NOS | 3.35 | 7 | 480 | 50095 | TBB5_HUMAN |
| | Vimentin | | | 2 | 113 | 53676 | VIME_HUMAN |
| 1108[2] | Actin fragment | Up PTCL-NOS | 53.64 | 4 | 237 | 42052 | ACTB_HUMAN |
| | Histon H4 | | | 1 | 40 | 11360 | H4_HUMAN |
| 1206 | Actin fragment | Up PTCL-NOS | 23.82 | 4 | 236 | 42052 | ACTB_HUMAN |
| 1304 | Actin fragment | Up PTCL-NOS | 8.30 | 8 | 508 | 42052 | ACTB_HUMAN |
| | GMP synthase [glutamine-hydrolyzing] fragment | | | 1 | 41 | 59791 | GUAA_DECAR |
| 1305[2] | Pyruvate dehydrogenase E1 component subunit alpha | Up PTCL-NOS | 11.09 | 1 | 39 | 38995 | ODPA_ACHLA |

|  |  |  |  |  |  |  |  |
|---|---|---|---|---|---|---|---|
|  | fragment |  |  | 9 | 528 | 42094 | ACTG_RANLE[3] |
|  | Actin fragment |  |  |  |  |  |  |
| 1503 | Haptoglobin | Down PTCL-NOS | 2.13 | 3 | 162 | 45861 | HPT_HUMAN |
| 1504 | Actin | Up PTCL-NOS | 3.41 | 8 | 527 | 42052 | ACTB_HUMAN |
|  | Haptoglobin |  |  | 2 | 104 | 45861 | HPT_HUMAN |
| 1507 | NI | Up PTCL-NOS | 44.99 |  |  |  |  |
| 1701 | ATP synthase subunit beta, mitochondrial | Down PTCL-NOS | 3.23 | 15 | 990 | 56525 | ATPB_HUMAN |
|  | Vimentin |  |  | 4 | 221 | 53676 | VIME_HUMAN |
| 1706 | NI | Down PTCL-NOS | 2.00 |  |  |  |  |
| 1707 | Vimentin | Up PTCL-NOS | 10.26 | 9 | 538 | 53676 | VIME_HUMAN |
|  | Lysozyme C |  |  | 1 | 82 | 16982 | LYSC_HUMAN |
|  | BPI fold-containing family B member 1 |  |  | 2 | 78 | 52580 | BPIB1_HUMAN |
| 1902 | 78 kDa glucose-regulated protein | Down PTCL-NOS | 3.45 | 20 | 1234 | 72402 | GRP78_HUMAN |
| 1904 | 78 kDa glucose-regulated protein | Down PTCL-NOS | 4.55 | 9 | 572 | 72402 | GRP78_HUMAN |
|  | Ig alpha-1 chain C region |  |  | 2 | 108 | 38587 | IGHA1_HUMAN |
|  | Lysozyme C |  |  | 2 | 79 | 16982 | LYSC_HUMAN |
|  | Lactotransferrin |  |  | 2 | 64 | 80014 | TRFL_HUMAN |
|  | Mammaglobin-B |  |  | 1 | 56 | 11104 | SG2A1_HUMAN |
|  | Ig kappa chain C region |  |  | 1 | 53 | 11773 | IGKC_HUMAN |
|  | Immunoglobulin J chain |  |  | 1 | 49 | 18543 | IGJ_HUMAN |
| 2001[2] | Actin fragment | Up PTCL-NOS | 16.03 | 4 | 381 | 42052 | ACTB_HUMAN |
| 2003 | Actin fragment | Up PTCL-NOS | 2.22 | 2 | 114 | 42381 | ACTA_HUMAN |
|  | Tubulin fragment |  |  | 1 | 66 | 50820 | TBA1A_HUMAN |
| 2004[2] | HLA class I histocompatibility antigen, B7 alpha chain fragment | Down PTCL-NOS | 2.56 | 1 | 106 | 40777 | 1B07_HUMAN |
| 2006 | Actin fragment | Up PTCL-NOS | 87.18 | 3 | 171 | 42052 | ACTB_HUMAN |
| 2101 | NI | Up PTCL-NOS | 5.27 |  |  |  |  |
| 2202 | Actin fragment | Up PTCL-NOS | 4.11 | 6 | 440 | 42052 | ACTB_HUMAN |
| 2301 | Actin fragment | Up PTCL-NOS | 11.93 | 6 | 335 | 42052 | ACTB_HUMAN |
| 2401 | Tubulin fragment | Up PTCL-NOS | 3.14 | 6 | 346 | 50095 | TBB5_HUMAN |
| 2502 | Albumin fragment | Up PTCL-NOS | 6.39 | 5 | 199 | 71317 | ALBU_HUMAN |
| 2504 | Albumin fragment | Down PTCL-NOS | 2.44 | 2 | 183 | 71317 | ALBU_HUMAN |
| 2506[2] | Leukocyte elastase inhibitor | Down PTCL-NOS | 2.26 | 1 | 66 | 42829 | ILEU_HUMAN |
| 2606 | NI | Down PTCL-NOS | 4.76 |  |  |  |  |
| 2801 | 60 kDa heat shock protein, mitochondrial | Down PTCL-NOS | 2.33 | 10 | 702 | 61187 | CH60_HUMAN |
| 2802 | Plastin-2 | Down PTCL-NOS | 2.33 | 13 | 808 | 70814 | PLSL_HUMAN |
| 2901 | Heat shock cognate 71 kDa protein | Down PTCL-NOS | 4.55 | 11 | 607 | 71082 | HSP7C_HUMAN |
|  | Plastin-2 |  |  | 2 | 90 | 70814 | PLSL_HUMAN |
| 3002 | NI | Down PTCL-NOS | 3.57 |  |  |  |  |
| 3101 | Adenine phosphoribosyltransferase | Down PTCL-NOS | 2.86 | 2 | 125 | 19766 | APT_HUMAN |
| 3104 | Glutathione S-transferase P | Down PTCL-NOS | 2.00 | 3 | 297 | 23569 | GSTP1_HUMAN |
|  | Suprabasin fragment |  |  | 1 | 106 | 60562 | SBSN_HUMAN |
| 3203 | Heat shock protein beta-1 | Up PTCL-NOS | 2.15 | 3 | 233 | 22826 | HSPB1_HUMAN |
| 3206 | Peroxiredoxin-4 | Down PTCL-NOS | 2.22 | 3 | 170 | 30749 | PRDX4_HUMAN |
| 3407 | Alpha-enolase fragment | Up PTCL-NOS | 8.23 | 6 | 519 | 47481 | ENOA_HUMAN |

|  |  |  |  |  |  |  |  |
|---|---|---|---|---|---|---|---|
| 3507 | Moesin fragment | Up PTCL-NOS | 2.48 | 2 | 68 | 67892 | MOES_HUMAN |
| 3801 | Heat shock 70 kDa protein 1A/1B<br>Plastin-2 | Down PTCL-NOS | 3.35 | 13<br>2 | 671<br>64 | 70294<br>70814 | HSP71_HUMAN4<br>PLSL_HUMAN |
| 3802 | T-complex protein 1 subunit epsilon | Down PTCL-NOS | 3.13 | 2 | 91 | 60089 | TCPE_HUMAN |
| 3807 | Protein disulfide-isomerase A3 | Down PTCL-NOS | 2.33 | 2 | 180 | 57143 | PDIA3_HUMAN |
| 3902 | Stress-70 protein, mitochondrial | Down PTCL-NOS | 2.70 | 17 | 1251 | 73920 | GRP75_HUMAN |
| 3906 | Alpha-synuclein<br>Serum albumin | Down PTCL-NOS | 2.44 | 4<br>4 | 542<br>191 | 14451<br>71317 | SYUA_HUMAN<br>ALBU_HUMAN |
| 4005 | Alpha-synuclein | Down PTCL-NOS | 2.56 | 1 | 58 | 14451 | SYUA_HUMAN |
| 4102 | Heat shock cognate 71 kDa protein fragment<br>Heat shock 70 kDa protein 1A/1B fragment<br>Chaperone protein DnaK fragment<br>Protein DJ-1 | Up PTCL-NOS | 3.32 | 7<br>2<br>2<br>1 | 552<br>291<br>100<br>71 | 71082<br>70294<br>68430<br>20050 | HSP7C_HUMAN<br>HSP71_HUMAN<br>DNAK_EHRSE<br>PARK7_HUMAN |
| 4201 | Peroxiredoxin 4<br>Heat shock protein beta-1 | Down PTCL-NOS | 3.57 | 4<br>1 | 189<br>47 | 30749<br>22826 | PRDX4_HUMAN<br>HSPB1_HUMAN |
| 4304[2] | NI | Down PTCL-NOS | 2.78 |  |  |  |  |
| 4408 | 60S acidic ribosomal protein P0 | Down PTCL-NOS | 10.00 | 4 | 205 | 34423 | RLA0_HUMAN |
| 4502 | Actin | Up PTCL-NOS | 8.60 | 5 | 246 | 42052 | ACTB_HUMAN |
| 4511 | NI | Down PTCL-NOS | 3.31 |  |  |  |  |
| 4703 | Aldehyde dehydrogenase, mitochondrial | Down PTCL-NOS | 6.25 | 6 | 440 | 56859 | ALDH2_HUMAN |
| 4707 | Serum albumin fragment | Up PTCL-NOS | 6.14 | 5 | 358 | 71317 | ALBU_HUMAN |
| 4708 | NI | Up PTCL-NOS | 2.21 |  |  |  |  |
| 4803 | Serum albumin | Down PTCL-NOS | 2.78 | 22 | 1543 | 71317 | ALBU_HUMAN |
| 4805 | Protein disulfide-isomerase | Down PTCL-NOS | 2.23 | 2 | 94 | 57146 | PDIA3_HUMAN |
| 4806 | Serum albumin | Down PTCL-NOS | 3.45 | 26 | 1639 | 71317 | ALBU_HUMAN |
| 4807[2] | Serum albumin fragment | Up PTCL-NOS | 2.31 | 4 | 215 | 71317 | ALBU_HUMAN |
| 4812 | Serum albumin | Up PTCL-NOS | 2.19 | 5 | 266 | 71317 | ALBU_HUMAN |
| 4901 | Serum albumin | Down PTCL-NOS | 3.13 | 17 | 641 | 71317 | ALBU_HUMAN |
| 4903 | NI | Down PTCL-NOS | 5.26 |  |  |  |  |
| 5305 | Phosphomanno mutase 1<br>Phosphoglycerate mutase 2<br>Ig lambda-2 chain C region | Down PTCL-NOS | 4.17 | 4<br>3<br>1 | 176<br>105<br>61 | 28406<br>28948<br>11458 | PMM2_HUMAN<br>PGAM1_HUMAN<br>LAC2_HUMAN |
| 5505 | Protein disulfide-isomerase A6 | Up PTCL-NOS | 2.53 | 1 | 104 | 48490 | PDIA6_HUMAN |
| 5604 | Rab GDP dissociation inhibitor beta | Down PTCL-NOS | 2.38 | 3 | 133 | 51087 | GDIB_HUMAN |
| 5710 | Serum albumin fragment | Up PTCL-NOS | 21.52 | 2 | 113 | 71317 | ALBU_HUMAN |
| 5801 | Leukotriene A-4 hydrolase | Down PTCL-NOS | 2.70 | 2 | 94 | 69868 | LKHA_HUMAN[5] |
| 5803 | NI | Down PTCL-NOS | 100.00 |  |  |  |  |
| 5806 | NI | Down PTCL-NOS | 14.29 |  |  |  |  |
| 5809 | Succinyl-CoA:3-ketoacid coenzyme A transferase 1, mitochondrial | Down PTCL-NOS | 3.45 | 6 | 270 | 56578 | SCOT1_HUMAN |
| 5901 | Gelsolin<br>Hemoglobin subunit beta | Down PTCL-NOS | 5.00 | 2<br>2 | 113<br>45 | 80966<br>16160 | GELS_HUMAN<br>HBB_CALTO |
| 5905 | NI | Down PTCL-NOS | 3.57 |  |  |  |  |
| 6606 | Protein disoulfide-isomerase A3<br>Serum albumin fragment | Up PTCL-NOS | 5.23 | 3<br>3 | 420<br>128 | 57146<br>71317 | PDIA3_HUMAN<br>ALBU_HUMAN |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 6701 | Protein disoulfide-isomerase A3 | Up PTCL-NOS | 4.30 | 3 | 153 | 57293 | PDIA3_HUMAN |
| 6702 | Cytosol aminopeptidase | Up PTCL-NOS | 2.62 | 5 | 268 | 56530 | AMPL_HUMAN |
| 6703 | Cytosol aminopeptidase<br>Serum albumin fragment | Up PTCL-NOS | 2.27 | 5<br>5 | 400<br>265 | 56530<br>71317 | AMPL_HUMAN<br>ALBU_HUMAN |
| 6902 | Serotransferrin | Down PTCL-NOS | 2.70 | 8 | 493 | 79294 | TRFE_HUMAN |
| 6903 | Serotransferrin<br>Serum albumin | Down PTCL-NOS | 2.78 | 12<br>1 | 808<br>50 | 79294<br>71244 | TRFE_HUMAN<br>ALBU_HUMAN |
| 6905 | Serotransferrin<br>Peroxiredoxin-1 | Down PTCL-NOS | 3.13 | 13<br>2 | 840<br>94 | 79294<br>22324 | TRFE_HUMAN<br>PRDX1_HUMAN |
| 7103 | Peroxiredoxin-1<br>Serotransferrin fragment | Down PTCL-NOS | 4.55 | 6<br>4 | 334<br>231 | 22324<br>79294 | PRDX1_HUMAN<br>TRFE_HUMAN |
| 7104 | Superoxid dismutase<br>Ras-related C3 botulinum toxin substrate 2 | Up PTCL-NOS | 2.04 | 2<br>1 | 127<br>43 | 24878<br>21814 | SODM_HUMAN<br>RAC2_HUMAN |
| 7202 | Triosephasphate isomerase[1] | Down PTCL-NOS | 2.17 | 7 | 428 | 31057 | TPIS_HUMAN |
| 7302 | NI | Down PTCL-NOS | 3.23 | | | | |
| 8103 | Glyceraldehyde-3-phosphate dehydrogenase fragment<br>Flavin reductase (NADPH) | Up PTCL-NOS | 4.29 | 5<br>2 | 305<br>125 | 36201<br>22219 | G3P_HUMAN<br>BLVRB_HUMAN |
| 8107 | Peroxiredoxin-1[1]<br>Serum albumin fragment<br>Glyceraldehyde-3-phosphate dehydrogenase[1] fragment<br>Stress-70 protein, mitochondrial fragment | Up PTCL-NOS | 2.63 | 9<br>3<br>2<br>2 | 483<br>170<br>113<br>67 | 22324<br>71317<br>36201<br>73981 | PRDX1_HUMAN<br>ALBU_HUMAN<br>G3P_HUMAN<br>GRP75_BOVIN |
| 8406 | Glyceraldehyde-3-phosphate dehydrogenase<br>Malate dehydrogenase, mitochondrial | Down PTCL-NOS | 2.44 | 5<br>5 | 455<br>308 | 36201<br>35937 | G3P_HUMAN<br>MDHM_HUMAN |
| 9103 | Transgelin | Up PTCL-NOS | 19.55 | 3 | 166 | 22653 | TAGL_HUMAN |
| 9503 | Aspartate aminotransferase, mitochondrial | Down PTCL-NOS | 2.50 | 5 | 360 | 47886 | AATM_HUMAN |

[1] Additional peptides identified from other species.

[2] Contaminant with dermicidin, filaggrin , or cingulin.

[3] For bioinformatic analysis ACTB_HUMAN where all identified peptides occurr.

[4] HSP71_HUMAN has been changed to HS71A_HUMAN.

[5] LKHA_HUMAN has been changed to LKHA4_HUMAN.

N: non-neoplastic lymphoid tissue, NI: not identified, PTCL-NOS: peripheral T-cell lymphoma, not otherwise specified, SSP: spot number on the 2D-PAGE gels

**Supplementary Table S3.** List of identified differentially expressed proteins between PTCL-NOS patients belonging to Cluster1, C1 (n=7) and Cluster 2, C2 (n=11) by LC-MS/MS (Analysis B)

| SSP | Identification | Expression | Fold change | Peptides | Mascot Score | Mr (Da) | SwissProt |
|---|---|---|---|---|---|---|---|
| | **C1 vs. C2** | | | | | | |
| 0604 | NI | Up C1 | 2.13 | | | | |
| 1108[2] | Actin fragment<br>Histon H4 | Up C2 | 2.36 | 4<br>1 | 237<br>40 | 42052<br>11360 | ACTB_HUMAN<br>H4_HUMAN |
| 1206 | Actin fragment | Up C2 | 2.43 | 4 | 236 | 42052 | ACTB_HUMAN |
| 1505 | Actin<br>Vimentin fragment | Up C1 | 2.33 | 6<br>3 | 396<br>96 | 42052<br>53676 | ACTB_HUMAN<br>VIME_HUMAN |
| 1507 | NI | Up C2 | 2.36 | | | | |
| 1701 | ATP synthase subunit beta, mitochondrial<br>Vimentin | Up C1 | 2.94 | 15<br>4 | 990<br>221 | 56525<br>53676 | ATPB_HUMAN<br>VIME_HUMAN |
| 1703 | Vimentin<br>Tubulin | Up C1 | 3.85 | 4<br>2 | 172<br>59 | 53676<br>50804 | VIME_HUMAN<br>TBA1B_HUMAN |
| 1705 | NI | Up C1 | 3.03 | | | | |
| 1806 | Lamin-B1<br>Plastin-2 | Up C1 | 3.03 | 11<br>6 | 667<br>332 | 66653<br>70814 | LMNB1_HUMAN<br>PLSL_HUMAN |
| 1902 | 78 kDa glucose-regulated protein | Up C1 | 2.26 | 20 | 1234 | 72402 | GRP78_HUMAN |
| 1904 | 78 kDa glucose-regulated protein<br>Ig alpha-1 chain C region<br>Lysozyme C<br>Lactotransferrin<br>Mammaglobin-B<br>Ig kappa chain C region<br>Immunoglobulin J chain | Up C1 | 2.78 | 9<br>2<br>2<br>2<br>1<br>1<br>1 | 572<br>108<br>79<br>64<br>56<br>53<br>49 | 72402<br>38587<br>16982<br>80014<br>11104<br>11773<br>18543 | GRP78_HUMAN<br>IGHA1_HUMAN<br>LYSC_HUMAN<br>TRFL_HUMAN<br>SG2A1_HUMAN<br>IGKC_HUMAN<br>IGJ_HUMAN |
| 2004[2] | HLA class I histocompatibility antigen, B7 alpha chain fragment | Up C2 | 2.44 | 1 | 106 | 40777 | 1B07_HUMAN |
| 2101 | NI | Up C2 | 2.46 | | | | |
| 2301 | Actin fragment | Up C2 | 2.20 | 6 | 335 | 42052 | ACTB_HUMAN |
| 2401 | Tubulin fragment | Up C1 | 2.13 | 6 | 346 | 50095 | TBB5_HUMAN |
| 2502 | Albumin fragment | Up C2 | 2.12 | 5 | 199 | 71317 | ALBU_HUMAN |
| 2701 | Thymidin phosphorylase<br>Actin | Up C1 | 4.55 | 10<br>3 | 703<br>163 | 50323<br>42052 | TYPH_HUMAN<br>ACTB_HUMAN |
| 2801 | 60 kDa heat shock protein, mitochondrial | Up C1 | 3.45 | 10 | 702 | 61187 | CH60_HUMAN |
| 2802 | Plastin-2 | Up C1 | 3.13 | 13 | 808 | 70814 | PLSL_HUMAN |
| 2805 | Plastin-2 | Up C1 | 2.94 | 4 | 248 | 70814 | PLSL_HUMAN |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | 60 kDa heat shock protein, mitochondrial | | | 1 | 57 | 61187 | CH60_HUMAN |
| 2901 | Heat shock cognate 71 kDa protein | Up C1 | 7.14 | 11 | 607 | 71082 | HSP7C_HUMAN |
| | Plastin-2 | | | 2 | 90 | 70814 | PLSL_HUMAN |
| 2902 | Heat shock cognate 71 kDa protein | Up C1 | 4.55 | 16 | 1013 | 71082 | HSP7C_HUMAN |
| 2906 | NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial | Up C1 | 2.70 | 2 | 129 | 80443 | NDUS1_HUMAN |
| 3302 | NI | Up C1 | 2.56 | | | | |
| 3303 | NI | Up C2 | 4.15 | | | | |
| 3306 | NI | Up C1 | 2.13 | | | | |
| 3401 | Tubulin fragment | Up C1 | 2.78 | 3 | 284 | 50788 | TBA1A_HUMA |
| 3404 | NI | Up C1 | 3.57 | | | | |
| 3407 | Alpha-enolase fragment | Up C2 | 2.08 | 6 | 519 | 47481 | ENOA_HUMAN |
| 3801 | Heat shock 70 kDa protein 1A/1B | Up C1 | 3.85 | 13 | 671 | 70294 | HSP71_HUMAN |
| | Plastin-2 | | | 2 | 64 | 70814 | PLSL_HUMAN |
| 3802 | T-complex protein 1 subunit epsilon | Up C1 | 7.69 | 2 | 91 | 60089 | TCPE_HUMAN |
| 3807 | Protein disulfide-isomerase A3 | Up C1 | 2.44 | 2 | 180 | 57143 | PDIA3_HUMAN |
| 3902 | Stress-70 protein, mitochondrial | Up C1 | 3.70 | 17 | 1251 | 73920 | GRP75_HUMAN |
| 3906 | Alpha-synuclein | Up C1 | 3.57 | 4 | 542 | 14451 | SYUA_HUMAN |
| | Serum albumin | | | 4 | 191 | 71317 | ALBU_HUMAN |
| 4104 | NI | Up C1 | 2.86 | | | | |
| 4407 | NI | Up C1 | 3.23 | | | | |
| 4408 | 60S acidic ribosomal protein P0 | Up C1 | 6.25 | 4 | 205 | 34423 | RLA0_HUMAN |
| 4601 | NI | Up C1 | 2.17 | | | | |
| 4602 | NI | Up C1 | 3.13 | | | | |
| 4604 | NI | Up C1 | 2.50 | | | | |
| 4703 | Aldehyde dehydrogenase, mitochondrial | Up C1 | 9.09 | 6 | 440 | 56859 | ALDH2_HUMAN |
| 4708 | NI | Up C2 | 2.87 | | | | |
| 4802 | Protein disulfide-isomerase A3 | Up C1 | 2.22 | 12 | 602 | 56747 | PDIA3_HUMAN |
| | Protein disulfide-isomerase A3 | | | 1 | 79 | 4084 | PDIA3_PAPHA |
| 4803 | Serum albumin | Up C1 | 3.03 | 22 | 1543 | 71317 | ALBU_HUMAN |
| 4806 | Serum albumin | Up C1 | 2.70 | 26 | 1639 | 71317 | ALBU_HUMAN |
| 4810[2] | Protein disulfide-isomerase A3 | Up C1 | 4.35 | 1 | 103 | 57146 | PDIA3_HUMAN |
| 4901 | Serum albumin | Up C1 | 2.13 | 17 | 641 | 71317 | ALBU_HUMAN |
| 5303 | Endoplasmic reticulum resident protein 29 | Up C1 | 2.04 | 3 | 78 | 29032 | ERP29_HUMAN |
| | Proteasome subunit alpha type-6 | | | 2 | 69 | 27838 | PSA6_HUMAN |
| 5502 | Galactokinase | Up C1 | 2.50 | 2 | 61 | 42702 | GALK1_HUMAN |
| 5710 | Serum albumin fragment | Up C2 | 7.47 | 2 | 113 | 71317 | ALBU_HUMAN |
| 6606 | Protein disoulfide-isomerase A3 | Up C2 | 2.50 | 3 | 420 | 57146 | PDIA3_HUMAN |
| | Serum albumin fragment | | | 3 | 128 | 71317 | ALBU_HUMAN |
| 6902 | Serotransferrin | Up C1 | 2.63 | 8 | 493 | 79294 | TRFE_HUMAN |
| 6903 | Serotransferrin | Up C1 | 2.70 | 12 | 808 | 79294 | TRFE_HUMAN |
| | Serum albumin | | | 1 | 50 | 71244 | ALBU_HUMAN |
| 6905 | Serotransferrin | Up C1 | 2.04 | 13 | 840 | 79294 | TRFE_HUMAN |
| | Peroxiredoxin-1 | | | 2 | 94 | 22324 | PRDX1_HUMAN |
| 7202 | Triosephosphate isomerase[1] | Up C2 | 2.99 | 7 | 428 | 31057 | TPIS_HUMAN |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 7403 | NI | Up C1 | 2.27 | | | | |
| 9302 | Ezrin fragment | Up C1 | 2.38 | 2 | 140 | 69484 | EZRI_HUMAN |

[1] Additional peptides identified from other species.

[2] Contaminant with dermicidin, filaggrin, or cingulin.

N: non-neoplastic lymphoid tissue, NI: not identified, PTCL-NOS: peripheral T-cell lymphoma, not otherwise specified, SSP: spot number on the 2D-PAGE gels

**Supplementary Table S4.** List of identified differentially expressed proteins between PTCL-NOS patients with primary refractory disease (*i.e.* PD and survival <100 days, (G1)) and patients who showed initial chemosensitivity (*i.e.* CR and survival > 2 years (G2)) by LC-MS/MS (Analysis C)

| SSP | Identification | Expression | Fold change | Peptides | Mascot Score | Mr (Da) | SwissProt |
|---|---|---|---|---|---|---|---|
| | **G1 vs. G2** | | | | | | |
| 1206 | Actin fragment | Up G2 | 2.63 | 4 | 236 | 42052 | ACTB_HUMAN |
| 1505 | Actin fragment<br>Vimentin fragment | Up G1 | 2.28 | 6<br>3 | 396<br>96 | 42052<br>53676 | ACTB_HUMAN<br>VIME_HUMAN |
| 1701 | ATP synthase subunit beta, mitochondrial<br>Vimentin | Up G1 | 3.74 | 15<br>4 | 990<br>221 | 56525<br>53676 | ATPB_HUMAN<br>VIME_HUMAN |
| 1703 | Vimentin<br>Tubulin | Up G1 | 5.02 | 4<br>2 | 172<br>59 | 53676<br>50804 | VIME_HUMAN<br>TBA1B_HUMAN |
| 1705 | NI | Up G1 | 3.58 | | | | |
| 1706 | NI | Up G1 | 2.64 | | | | |
| 1806 | Lamin-B1<br>Plastin-2 | Up G1 | 3.39 | 11<br>6 | 667<br>332 | 66653<br>70814 | LMNB1_HUMAN<br>PLSL_HUMAN |
| 1902 | 78 kDa glucose-regulated protein | Up G1 | 6.25 | 20 | 1234 | 72402 | GRP78_HUMAN |
| 2401 | Tubulin fragment | Up G1 | 2.43 | 6 | 346 | 50095 | TBB5_HUMAN |
| 2801 | 60 kDa heat shock protein, mitochondrial | Up G1 | 3.71 | 10 | 702 | 61187 | CH60_HUMAN |
| 2805 | Plastin-2<br>60 kDa heat shock protein, mitochondrial | Up G1 | 4.61 | 4<br>1 | 248<br>57 | 70814<br>61187 | PLSL_HUMAN<br>CH60_HUMAN |
| 2901 | Heat shock cognate 71 kDa protein<br>Plastin-2 | Up G1 | 6.03 | 11<br>2 | 607<br>90 | 71082<br>70814 | HSP7C_HUMAN<br>PLSL_HUMAN |
| 2902 | Heat shock cognate 71 kDa protein | Up G1 | 4.90 | 16 | 1013 | 71082 | HSP7C_HUMAN |
| 2906 | NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial | Up G1 | 2.80 | 2 | 129 | 80443 | NDUS1_HUMAN |
| 3401 | Tubulin fragment | UP G1 | 3.03 | 3 | 284 | 50788 | TBA1A_HUMA |
| 3404 | NI | Up G1 | 4.21 | | | | |
| 3407 | Alpha-enolase fragment | Up G2 | 2.22 | 6 | 519 | 47481 | ENOA_HUMAN |
| 3801 | Heat shock 70 kDa protein 1A/1B<br>Plastin-2 | Up G1 | 3.74 | 13<br>2 | 671<br>64 | 70294<br>70814 | HSP71_HUMAN<br>PLSL_HUMAN |
| 3902 | Stress-70 protein, mitochondrial | Up G1 | 3.67 | 17 | 1251 | 73920 | GRP75_HUMAN |
| 4205 | Enoyl-CoA hydratase, mitochondrial<br>Enoyl-CoA hydratase, mitochondrial | Up G1 | 2.71 | 2<br>1 | 162<br>85 | 31864<br>31823 | ECHM_PONAB<br>ECHM_HUMAN |
| 4401 | NI | Up G1 | | | | | |
| 4405 | Alpha-enolase | Up G2 | 3.85 | 2 | 83 | 47481 | ENOA_HUMAN |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 4407 | NI | Up G1 | | | | | |
| 4703 | Aldehyde dehydrogenase, mitochondrial | Up G1 | 6.97 | 6 | 440 | 56859 | ALDH2_HUMAN |
| 4802 | Protein disulfide-isomerase A3<br>Protein disulfide-isomerase A3 | Up G1 | 2.02 | 12<br>1 | 602<br>79 | 56747<br>4084 | PDIA3_HUMAN<br>PDIA3_PAPHA |
| 4810[2] | Protein disulfide-isomerase A3 | Up G1 | 5.48 | 1 | 103 | 57146 | PDIA3_HUMAN |
| 5101 | Protein DJ-1<br>Thioredoxin-dependent peroxide reductase, mitochondrial | Up G1 | 2.16 | 3<br>1 | 144<br>59 | 20064<br>28406 | PARK7_HUMAN<br>PRDX3HUMAN |
| 5303 | Endoplasmic reticulum resident protein 29<br>Proteasome subunit alpha type-6 | Up G1 | 2.47 | 3<br>2 | 78<br>69 | 29032<br>27838 | ERP29_HUMAN<br>PSA6_HUMAN |
| 5502 | Galactokinase | Up G1 | 3.46 | 2 | 61 | 42702 | GALK1_HUMAN |
| 5604 | Rab GDP dissociation inhibitor beta | Up G1 | 2.58 | 3 | 133 | 51087 | GDIB_HUMAN |
| 5710 | Serum albumin fragment | Up G2 | 7.14 | 2 | 113 | 71317 | ALBU_HUMAN |
| 5801 | Leukotriene A-4 hydrolase | Up G1 | 1.79 | 2 | 94 | 69868 | LKHA4_HUMAN |
| 5905 | NI | Up G1 | 5.88 | | | | |
| 6606 | Protein disoulfide-isomerase A3<br>Serum albumin fragment | Up G2 | 2.94 | 3<br>3 | 420<br>128 | 57146<br>71317 | PDIA3_HUMAN<br>ALBU_HUMAN |
| 6804 | Coronin-1A | Up G1 | 2.62 | 4 | 260 | 51678 | COR1A_HUMAN |
| 7202 | Triosephasphate isomerase[1] | Up G2 | 2.94 | 7 | 428 | 31057 | TPIS_HUMAN |
| 9302 | Ezrin fragment | Up G1 | 2.35 | 2 | 140 | 69484 | EZRI_HUMAN |

[1] Additional peptides identified from other species.

[2] Contaminant with dermicidin, filaggrin , or cingulin.

N: non-neoplastic lymphoid tissue, NI: not identified, PTCL-NOS: peripheral T-cell lymphoma, not otherwise specified, SSP: spot number on the 2D-PAGE gels

**Supplementary Table S5.** List of UniProt identifications as input to pathway enrichment analysis by Reactome Pathway

| **N vs PTCL-NOS** | | **C1 vs C2** | | **G1 vs G2** | |
|---|---|---|---|---|---|
| **Submitted identifier** | **Found identifier** | **Submitted identifier** | **Found identifier** | **Submitted identifier** | **Found identifier** |
| SCOT1_HUMAN | P55809 | ALDH2_HUMAN | P05091 | ALDH2_HUMAN | P05091 |
| AATM_HUMAN | P00505 | TPIS_HUMAN | P60174 | TPIS_HUMAN | P60174 |
| SODM_HUMAN | P04179 | EZRI_HUMAN | P15311 | EZRI_HUMAN | P15311 |
| GSTP1_HUMAN | P09211 | VIME_HUMAN | P08670 | VIME_HUMAN | P08670 |
| PDIA6_HUMAN | Q15084 | GRP75_HUMAN | P38646 | GRP75_HUMAN | P38646 |
| SYUA_HUMAN | P37840 | GALK1_HUMAN | P51570 | GALK1_HUMAN | P51570 |
| GDIB_HUMAN | P50395 | CH60_HUMAN | P10809 | CH60_HUMAN | P10809 |
| TRFE_HUMAN | P02787 | TBA1A_HUMAN | Q71U36 | TBA1A_HUMAN | Q71U36 |
| HS71A_HUMAN | P0DMV8 | TRFE_HUMAN | P02787 | ECHM_HUMAN | P30084 |
| G3P_HUMAN | P04406 | HS71A_HUMAN | P0DMV8 | GDIB_HUMAN | P50395 |
| APT_HUMAN | P07741 | TYPH_HUMAN | P19971 | HS71A_HUMAN | P0DMV8 |
| MOES_HUMAN | P26038 | PDIA3_HUMAN | P30101 | PDIA3_HUMAN | P30101 |
| LKHA4_HUMAN | P09960 | ACTB_HUMAN | P60709 | ACTB_HUMAN | P60709 |
| ACTB_HUMAN | P60709 | PLSL_HUMAN | P13796 | LKHA4_HUMAN | P09960 |
| CALR_HUMAN | P27797 | GRP78_HUMAN | P11021 | PLSL_HUMAN | P13796 |
| TCPE_HUMAN | P48643 | TCPE_HUMAN | P48643 | GRP78_HUMAN | P11021 |
| ENOA_HUMAN | P06733 | ENOA_HUMAN | P06733 | ENOA_HUMAN | P06733 |
| 1B07_HUMAN | P01889 | 1B07_HUMAN | P01889 | ALBU_HUMAN | P02768 |
| TBB5_HUMAN | P07437 | ALBU_HUMAN | P02768 | NDUS1_HUMAN | P28331 |
| A1AT_HUMAN | P01009 | NDUS1_HUMAN | P28331 | ATPB_HUMAN | P06576 |
| ALDH2_HUMAN | P05091 | ATPB_HUMAN | P06576 | HSP7C_HUMAN | P11142 |
| TPIS_HUMAN | P60174 | HSP7C_HUMAN | P11142 | TBB5_HUMAN | P07437 |
| VIME_HUMAN | P08670 | RLA0_HUMAN | P05388 | PARK7_HUMAN | Not found |
| GRP75_HUMAN | P38646 | TBB5_HUMAN | P07437 | COR1A_HUMAN | Not found |
| CH60_HUMAN | P10809 | | | | |
| 1433S_HUMAN | P31947 | | | | |
| PRDX1_HUMAN | Q06830 | | | | |
| PDIA3_HUMAN | P30101 | | | | |
| PLSL_HUMAN | P13796 | | | | |
| HPT_HUMAN | P00738 | | | | |
| GRP78_HUMAN | P11021 | | | | |
| ALBU_HUMAN | P02768 | | | | |
| HSPB1_HUMAN | P04792 | | | | |
| ACTA_HUMAN | P62736 | | | | |
| ATPB_HUMAN | P06576 | | | | |
| PRDX4_HUMAN | Q13162 | | | | |
| HSP7C_HUMAN | P11142 | | | | |
| RLA0_HUMAN | P05388 | | | | |
| ILEU_HUMAN | P30740 | | | | |
| TAGL_HUMAN | Not found | | | | |
| TCTP_HUMAN | Not found | | | | |
| AMPL_HUMAN | Not found | | | | |

**Supplementary Table S6.** Analysis A: N vs PTCL-NOS. Pathway enrichment analysis by Reactome Pathway Database

| Pathway identifier | Pathway name | #Entities found | #Entities total | Entities pValue | Entities FDR |
|---|---|---|---|---|---|
| **N vs PTCL-NOS** | | | | | |
| R-HSA-6798695 | Neutrophil degranulation | 12 | 480 | 1.58E-07 | 5.41E-05 |
| R-HSA-8950505 | Gene and protein expression by JAK-STAT signaling after Interleukin-12 stimulation | 5 | 38 | 3.80E-07 | 6.51E-05 |
| R-HSA-447115 | Interleukin-12 family signaling | 5 | 57 | 2.74E-06 | 3.12E-04 |
| R-HSA-70263 | Gluconeogenesis | 4 | 34 | 9.38E-06 | 7.98E-04 |
| R-HSA-168256 | Immune System | 22 | 2444 | 1.96E-05 | 0.001333733 |
| R-HSA-3371453 | Regulation of HSF1-mediated heat shock response | 4 | 73 | 1.79E-04 | 0.010204995 |
| R-HSA-983170 | Antigen Presentation: Folding, assembly and peptide loading of class I MHC | 4 | 93 | 4.46E-04 | 0.017086172 |
| R-HSA-3371556 | Cellular response to heat stress | 4 | 93 | 4.46E-04 | 0.017086172 |
| R-HSA-3299685 | Detoxification of Reactive Oxygen Species | 3 | 39 | 4.64E-04 | 0.017086172 |
| R-HSA-70326 | Glucose metabolism | 4 | 96 | 5.03E-04 | 0.017086172 |
| R-HSA-390450 | Folding of actin by CCT/TriC | 2 | 10 | 6.98E-04 | 0.019343666 |
| R-HSA-381183 | ATF6 (ATF6-alpha) activates chaperone genes | 2 | 10 | 6.98E-04 | 0.019343666 |
| R-HSA-8957275 | Post-translational protein phosphorylation | 4 | 107 | 7.52E-04 | 0.019343666 |
| R-HSA-2262752 | Cellular responses to stress | 7 | 405 | 8.06E-04 | 0.019343666 |
| R-HSA-381033 | ATF6 (ATF6-alpha) activates chaperones | 2 | 12 | 1.00E-03 | 0.02199553 |
| R-HSA-381426 | Regulation of Insulin-like Growth Factor (IGF) transport and uptake by Insulin-like Growth Factor Binding Proteins (IGFBPs) | 4 | 124 | 0.001294948 | 0.025730899 |
| R-HSA-450408 | AUF1 (hnRNP D0) binds and destabilizes mRNA | 3 | 56 | 0.001314227 | 0.025730899 |
| R-HSA-3371568 | Attenuation phase | 2 | 14 | 0.001354258 | 0.025730899 |
| R-HSA-114608 | Platelet degranulation | 4 | 128 | 0.001454192 | 0.026175449 |
| R-HSA-76005 | Response to elevated platelet cytosolic Ca2+ | 4 | 133 | 0.001671898 | 0.028422273 |
| R-HSA-1268020 | Mitochondrial protein import | 3 | 64 | 0.001920646 | 0.030694974 |
| R-HSA-5653656 | Vesicle-mediated transport | 9 | 764 | 0.002078018 | 0.030694974 |
| R-HSA-8953897 | Cellular responses to external stimuli | 7 | 482 | 0.002192498 | 0.030694974 |
| R-HSA-168249 | Innate Immune System | 13 | 1489 | 0.002852866 | 0.039940117 |
| R-HSA-70171 | Glycolysis | 3 | 76 | 0.003115775 | 0.040505071 |
| R-HSA-8862803 | Deregulated CDK5 triggers multiple neurodegenerative pathways in Alzheimer's disease models | 2 | 23 | 0.003576396 | 0.042916752 |
| R-HSA-8863678 | Neurodegenerative Diseases | 2 | 23 | 0.003576396 | 0.042916752 |
| R-HSA-3371571 | HSF1-dependent transactivation | 2 | 24 | 0.00388475 | 0.046617001 |
| R-HSA-901042 | Calnexin/calreticulin cycle | 2 | 26 | 0.004537216 | 0.048811446 |
| R-HSA-450531 | Regulation of mRNA stability by proteins that bind AU-rich elements | 3 | 88 | 0.00468609 | 0.048811446 |
| R-HSA-449147 | Signaling by Interleukins | 8 | 706 | 0.004810609 | 0.048811446 |
| R-HSA-389957 | Prefoldin mediated transfer of substrate to CCT/TriC | 2 | 27 | 0.004881145 | 0.048811446 |

UniProt identifications were used from spots where a single protein was identified together with spots with more protein identifications but where one single protein dominated as judged by the number of peptide, identifications being more than 2-fold above that for other proteins.
FDR: false discovery rate; N: non-neoplastic lymphoid tissue.

**Supplementary Table S7.** Clinico-pathological and molecular features of the PTCL-NOS cohort selected for proteomics according to PCA- and outcome analysis.

| | **PCA-analysis(n=18)** | | | **Outcome-analysis (n=12)** | | |
|---|---|---|---|---|---|---|
| **Feature** | **C1 (n=7)** | **C2 (n=11)** | **P** | **[G1] Primary refractory disease and OS < 100 days (n=4)** | **[G2] Chemosensitive disease and OS > 2 years (n=8)** | **P** |
| Age, years | | | | | | |
| median | 64 | 54 | | 50 | 65 | |
| range | 20-81 | 25-76 | 0.14 | 25-81 | 20-77 | 0.22 |
| ≤60 | 3 | 9 | | 6 | 1 | |
| >60 | 4 | 2 | | 2 | 3 | |
| Sex | | | | | | |
| female | 2 | 5 | 0.64 | 3 | 2 | 1.00 |
| male | 5 | 6 | | 5 | 2 | |
| Ann Arbor Stage | | | | | | |
| I-II | 2 | 4 | 0.58 | 3 | 1 | 0.46 |
| III-IV | 5 | 7 | | 5 | 3 | |
| PS (WHO) | | | | | | |
| 0-1 | 2 | 9 | 0.11 | 5 | 1 | 0.54 |
| ≥2 | 5 | 2 | | 3 | 3 | |
| LDH> UNL | | | | | | |
| yes | 6 | 7 | 0.60 | 4 | 4 | 0.21 |
| no | 1 | 4 | | 4 | 0 | |
| B symptoms | | | | | | |
| yes | 5 | 10 | 0.53 | 7 | 3 | 1.00 |
| no | 2 | 1 | | 1 | 1 | |
| BM-involvement* | | | | | | |
| no | 3 | 7 | 0.58 | 6 | 1 | 0.41 |
| yes | 2 | 3 | | 2 | 1 | |
| IPI | | | | | | |
| ≤2 | 2 | 8 | 0.079 | 0 | 6 | - |
| >2 | 5 | 3 | | 4 | 2 | |
| Plateles | | | | | | |
| <150 · $10^9$/l | 3 | 2 | 0.33 | 1 | 2 | 0.24 |
| ≥150 · $10^9$/l | 4 | 9 | | 7 | 2 | |
| Anemia | | | | | | |
| (Hb<12 g/dl) | 3 | 8 | 0.33 | 6 | 1 | 0.22 |
| yes | 4 | 3 | | 2 | 3 | |
| no | | | | | | |
| TCR-RA | | | | | | |
| polyclonal | 2 | 4 | 1.00 | 4 | 1 | 0.70 |
| monoclonal | 5 | 6 | | 3 | 3 | |
| inconclusive | 0 | 1 | | 1 | 0 | |

TCR-RA: T-cell receptor gene rearrangement using BIOMED-2 protocol; BM: bone marrow; P: P-values (using Fischer's exact test).
*missing information in 1 case,

**Supplementary Table S8.** Analysis B: C1 vs C2. Pathway enrichment analysis by Reactome Pathway Database

| **Pathway identifier** | **Pathway name** | **#Entities found** | **#Entities total** | **Entities pValue** | **Entities FDR** |
|---|---|---|---|---|---|
| | **C1 vs C2** | | | | |
| R-HSA-3371453 | Regulation of HSF1-mediated heat shock response | 4 | 73 | 1.87E-05 | 0.003977301 |
| R-HSA-389957 | Prefoldin mediated transfer of substrate to CCT/TriC | 3 | 27 | 2.90E-05 | 0.003977301 |
| R-HSA-3371556 | Cellular response to heat stress | 4 | 93 | 4.78E-05 | 0.003977301 |
| R-HSA-389958 | Cooperation of Prefoldin and TriC/CCT in actin and tubulin folding | 3 | 32 | 4.79E-05 | 0.003977301 |
| R-HSA-8950505 | Gene and protein expression by JAK-STAT signaling after Interleukin-12 stimulation | 3 | 38 | 7.96E-05 | 0.005250719 |
| R-HSA-373760 | L1CAM interactions | 4 | 120 | 1.27E-04 | 0.007011309 |
| R-HSA-437239 | Recycling pathway of L1 | 3 | 48 | 1.58E-04 | 0.007428816 |
| R-HSA-390450 | Folding of actin by CCT/TriC | 2 | 10 | 2.26E-04 | 0.008622525 |
| R-HSA-3371497 | HSP90 chaperone cycle for steroid hormone receptors (SHR) | 3 | 56 | 2.48E-04 | 0.008622525 |
| R-HSA-447115 | Interleukin-12 family signaling | 3 | 57 | 2.61E-04 | 0.008622525 |
| R-HSA-1268020 | Mitochondrial protein import | 3 | 64 | 3.66E-04 | 0.01013828 |
| R-HSA-1852241 | Organelle biogenesis and maintenance | 5 | 297 | 4.01E-04 | 0.01013828 |
| R-HSA-392499 | Metabolism of proteins | 12 | 2009 | 4.23E-04 | 0.01013828 |
| R-HSA-3371568 | Attenuation phase | 2 | 14 | 4.41E-04 | 0.01013828 |
| R-HSA-983170 | Antigen Presentation: Folding, assembly and peptide loading of class I MHC | 3 | 93 | 0.001077829 | 0.022911747 |
| R-HSA-390466 | Chaperonin-mediated protein folding | 3 | 95 | 0.001145587 | 0.022911747 |
| R-HSA-3371571 | HSF1-dependent transactivation | 2 | 24 | 0.001278233 | 0.023547106 |
| R-HSA-391251 | Protein folding | 3 | 101 | 0.00136487 | 0.023547106 |
| R-HSA-389960 | Formation of tubulin folding intermediates by CCT/TriC | 2 | 25 | 0.001385124 | 0.023547106 |
| R-HSA-2262752 | Cellular responses to stress | 5 | 405 | 0.001614958 | 0.025839331 |
| R-HSA-8949613 | Cristae formation | 2 | 31 | 0.002112805 | 0.030582976 |
| R-HSA-5626467 | RHO GTPases activate IQGAPs | 2 | 31 | 0.002112805 | 0.030582976 |
| R-HSA-5609976 | Defective GALK1 can cause Galactosemia II (GALCT2) | 1 | 1 | 0.002184498 | 0.030582976 |
| R-HSA-70263 | Gluconeogenesis | 2 | 34 | 0.002531386 | 0.032074565 |
| R-HSA-168256 | Immune System | 12 | 2444 | 0.002617066 | 0.032074565 |
| R-HSA-114608 | Platelet degranulation | 3 | 128 | 0.00267288 | 0.032074565 |
| R-HSA-76005 | Response to elevated platelet cytosolic Ca2+ | 3 | 133 | 0.002977139 | 0.035725662 |
| R-HSA-8856828 | Clathrin-mediated endocytosis | 3 | 138 | 0.003301995 | 0.03632194 |
| R-HSA-8953897 | Cellular responses to external stimuli | 5 | 482 | 0.003444908 | 0.037893993 |
| R-HSA-449147 | Signaling by Interleukins | 6 | 706 | 0.003475777 | 0.038233543 |
| R-HSA-5619110 | Defective SLCO1B1 causes hyperbilirubinemia, Rotor type (HBLRR) | 1 | 2 | 0.004364423 | 0.043246051 |
| R-HSA-5619058 | Defective SLCO1B3 causes hyperbilirubinemia, Rotor type (HBLRR) | 1 | 2 | 0.004364423 | 0.043246051 |
| R-HSA-380612 | Metabolism of serotonin | 1 | 2 | 0.004364423 | 0.043246051 |

| | | | | | |
|---|---|---|---|---|---|
| R-HSA-1280215 | Cytokine Signaling in Immune system | 7 | 1013 | 0.004805117 | 0.043246051 |
| R-HSA-190828 | Gap junction trafficking | 2 | 48 | 0.004952122 | 0.044569094 |
| R-HSA-157858 | Gap junction trafficking and regulation | 2 | 50 | 0.005359124 | 0.048232116 |

UniProt identifications were used from spots where a single protein was identified together with spots with more protein identifications but where one single protein dominated as judged by the number of peptide identifications being more than 2-fold above that for other proteins.

FDR: false discovery rate.

**Supplementary Table S9.** Analysis B: G1 vs G2. Pathway enrichment analysis by Reactome Pathway Database

| Pathway identifier | Pathway name | #Entities found | #Entities total | Entities pValue | Entities FDR |
|---|---|---|---|---|---|
| | **G1 vs G2** | | | | |
| R-HSA-3371453 | Regulation of HSF1-mediated heat shock response | 4 | 73 | 1.87E-05 | 0.005759043 |
| R-HSA-3371556 | Cellular response to heat stress | 4 | 93 | 4.78E-05 | 0.007366875 |
| R-HSA-373760 | L1CAM interactions | 4 | 120 | 1.27E-04 | 0.012170614 |
| R-HSA-437239 | Recycling pathway of L1 | 3 | 48 | 1.58E-04 | 0.012170614 |
| R-HSA-3371497 | HSP90 chaperone cycle for steroid hormone receptors (SHR) | 3 | 56 | 2.48E-04 | 0.01513604 |
| R-HSA-1268020 | Mitochondrial protein import | 3 | 64 | 3.66E-04 | 0.018674534 |
| R-HSA-3371568 | Attenuation phase | 2 | 14 | 4.41E-04 | 0.01939497 |
| R-HSA-3371571 | HSF1-dependent transactivation | 2 | 24 | 0.001278233 | 0.048448745 |
| R-HSA-389957 | Prefoldin mediated transfer of substrate to CCT/TriC | 2 | 27 | 0.001611307 | 0.048448745 |
| R-HSA-2262752 | Cellular responses to stress | 5 | 405 | 0.001614958 | 0.048448745 |
| R-HSA-8949613 | Cristae formation | 2 | 31 | 0.002112805 | 0.049462968 |
| R-HSA-5626467 | RHO GTPases activate IQGAPs | 2 | 31 | 0.002112805 | 0.049462968 |
| R-HSA-5609976 | Defective GALK1 can cause Galactosemia II (GALCT2) | 1 | 1 | 0.002184498 | 0.049462968 |
| R-HSA-389958 | Cooperation of Prefoldin and TriC/CCT in actin and tubulin folding | 2 | 32 | 0.002248317 | 0.049462968 |
| R-HSA-70263 | Gluconeogenesis | 2 | 34 | 0.002531386 | 0.049724256 |
| R-HSA-168256 | Immune System | 12 | 2444 | 0.002617066 | 0.049724256 |

UniProt identifications were used from spots where a single protein was identified together with spots with more protein identifications but where one single protein dominated as judged by the number of peptide identifications being more than 2-fold above that for other proteins.
FDR: false discovery rate.