**Supplementary Figure 1:** Recombinant VgrG4CTD.

A) Schematic representation of the plasmid used for the recombinant protein expression. B) Recombinant VgrG4-CTD primary sequence. The histidine tag and the thrombin recognition site are shadowed in gray.
Supplementary Figure 2: VgrG4-CTD purification on a nickel affinity column.

A) Polyacrylamide electrophoresis showing: (1) protein profile of *E. coli* expressing VgrG4-CTD; (2) non-bound fraction; (3 and 4) column washings; and (5 and 6) VgrG4-CTD eluted in 500 mM imidazole buffer. B) Chromatographic profile of VgrG4-CTD in a nickel affinity column. The red arrows point to VgrG4-CTD band and peak.
Supplementary Figure 3: Protein profile of the cell lysates used in pulldown experiments. M: membrane-enriched fractions, C: soluble fractions. The molecular weights of the Kaleidoscope prestained protein standard (Biorad) are shown in kDa.
| Accession     | Score  | Mass   | N° of matches | N° of significant matches | N° of sequences | N° of significant sequences | emPAI | Description                                                                 |
|--------------|--------|--------|---------------|---------------------------|----------------|-----------------------------|-------|-----------------------------------------------------------------------------|
| MYH9_HUMAN   | 1005   | 227646 | 32            | 28                        | 28             | 25                          | 0.52  | Myosin-9 OS=Homo sapiens GN=MYH9 PE=1 SV=4                                 |
| TBB5_HUMAN   | 846    | 50095  | 17            | 17                        | 11             | 11                          | 1.55  | Tubulin beta chain OS=Homo sapiens GN=TUBB PE=1 SV=2                      |
| TBA1C_HUMAN  | 502    | 50548  | 16            | 16                        | 13             | 13                          | 1.53  | Tubulin alpha-1C chain OS=Homo sapiens GN=TUBA1C PE=1 SV=1                |
| ANXA2_HUMAN  | 413    | 38808  | 11            | 11                        | 9              | 9                           | 1.52  | Annexin A2 OS=Homo sapiens GN=ANXA2 PE=1 SV=2                            |
| ACTB_HUMAN   | 372    | 42052  | 14            | 14                        | 8              | 8                           | 1.35  | Actin, cytoplasmic 1 OS=Homo sapiens GN=ACTB PE=1 SV=1                   |
| FLNA_HUMAN   | 348    | 283301 | 14            | 11                        | 13             | 10                          | 0.14  | Filamin-A OS=Homo sapiens GN=FLNA PE=1 SV=4                               |
| EF2_HUMAN    | 205    | 96246  | 9             | 9                         | 8              | 8                           | 0.35  | Elongation factor 2 OS=Homo sapiens GN=EEF2 PE=1 SV=4                    |
| RLA2_HUMAN   | 146    | 11658  | 5             | 5                         | 3              | 3                           | 1.41  | 60S acidic ribosomal protein P2 OS=Homo sapiens GN=RPLP2 PE=1 SV=1        |
| 1433T_HUMAN  | 144    | 28032  | 3             | 3                         | 2              | 2                           | 0.29  | 14-3-3 protein theta OS=Homo sapiens GN=YWHAQ PE=1 SV=1                  |
| ACTN4_HUMAN  | 139    | 105245 | 3             | 3                         | 2              | 2                           | 0.07  | Alpha-actinin-4 OS=Homo sapiens GN=ACTN4 PE=1 SV=2                       |
| RLA1_HUMAN   | 123    | 11621  | 3             | 3                         | 2              | 2                           | 0.8   | 60S acidic ribosomal protein P1 OS=Homo sapiens GN=RPLP1 PE=1 SV=1        |
| NOLC1_HUMAN  | 116    | 73560  | 2             | 2                         | 1              | 1                           | 0.05  | Nucleolar and coiled-body phosphoprotein 1 OS=Homo sapiens GN=NOLC1 PE=1 SV=2 |
| K2C8_HUMAN   | 114    | 53671  | 3             | 3                         | 3              | 3                           | 0.22  | Keratin, type II cytoskeletal 8 OS=Homo sapiens GN=KRT8 PE=1 SV=7         |
| RLA7A_HUMAN  | 113    | 30148  | 4             | 4                         | 3              | 3                           | 0.42  | 60S ribosomal protein L7a OS=Homo sapiens GN=RPL7A PE=1 SV=2              |
| RS8_HUMAN    | 106    | 24475  | 4             | 3                         | 3              | 2                           | 0.34  | 40S ribosomal protein S8 OS=Homo sapiens GN=RPS8 PE=1 SV=2                |
| RS5_HUMAN    | 104    | 23033  | 3             | 3                         | 2              | 2                           | 0.36  | 40S ribosomal protein S5 OS=Homo sapiens GN=RPS5 PE=1 SV=4                |
| RL27A_HUMAN  | 102    | 16665  | 1             | 1                         | 1              | 1                           | 0.23  | 60S ribosomal protein L27a OS=Homo sapiens GN=RPL27A PE=1 SV=2            |
| RL18_HUMAN   | 98     | 21735  | 2             | 1                         | 2              | 1                           | 0.18  | 60S ribosomal protein L18 OS=Homo sapiens GN=RPL18 PE=1 SV=2              |
| RL14_HUMAN   | 95     | 23531  | 2             | 2                         | 2              | 2                           | 0.35  | 60S ribosomal protein L14 OS=Homo sapiens GN=RPL14 PE=1 SV=2              |
| NPM_HUMAN    | 92     | 32726  | 2             | 2                         | 2              | 2                           | 0.24  | Nucleophosmin OS=Homo sapiens GN=NPM1 PE=1 SV=2                           |
| RS18_HUMAN   | 87     | 17708  | 4             | 4                         | 3              | 3                           | 0.81  | 40S ribosomal protein S18 OS=Homo sapiens GN=RPS18 PE=1 SV=3              |
| HS90B_HUMAN  | 86     | 83554  | 9             | 4                         | 7              | 3                           | 0.14  | Heat shock protein HSP 90-beta OS=Homo sapiens GN=HSP90AB1 PE=1 SV=4      |
| HSPB1_HUMAN  | 83     | 22826  | 3             | 2                         | 3              | 2                           | 0.36  | Heat shock protein beta-1 OS=Homo sapiens GN=HSPB1 PE=1 SV=2              |

Table S1: Putative VgrG4-CTD ligands identified in lung epithelial cells (A549) soluble fraction
|   |   |   |   |   |   |
|---|---|---|---|---|---|
| **RS2** | **HUMAN** | 80 | 31590 | 2 | 2 |
| **RL6** | **HUMAN** | 72 | 32765 | 3 | 3 |
| **CALM1** | **HUMAN** | 70 | 16827 | 1 | 1 |
| **ML12A** | **HUMAN** | 67 | 19839 | 2 | 2 |
| **RS16** | **HUMAN** | 65 | 16549 | 3 | 2 |
| **TEBP** | **HUMAN** | 64 | 18971 | 3 | 2 |
| **RLA0L** | **HUMAN** | 63 | 34514 | 2 | 2 |
| **LDHA** | **HUMAN** | 62 | 36950 | 4 | 3 |
| **TCP4** | **HUMAN** | 56 | 14386 | 2 | 2 |
| **RS7** | **HUMAN** | 56 | 22113 | 3 | 3 |
| **RL30** | **HUMAN** | 53 | 12947 | 1 | 1 |
| **RL12** | **HUMAN** | 43 | 17979 | 2 | 2 |
| **RS3** | **HUMAN** | 48 | 26842 | 1 | 1 |
| **AK1C1** | **HUMAN** | 45 | 37221 | 1 | 1 |
| **TGM2** | **HUMAN** | 43 | 78420 | 1 | 1 |
| **RL12** | **HUMAN** | 43 | 17979 | 2 | 2 |
| **KRT81** | **HUMAN** | 42 | 56832 | 1 | 1 |
| **PRDX1** | **HUMAN** | 42 | 22324 | 1 | 1 |
| **RS19** | **HUMAN** | 40 | 16051 | 2 | 2 |
| **RL5** | **HUMAN** | 40 | 34569 | 2 | 2 |
| **MYL6** | **HUMAN** | 40 | 17090 | 2 | 1 |
| **RACK1** | **HUMAN** | 39 | 35511 | 1 | 1 |
| **ALBU** | **HUMAN** | 38 | 71317 | 2 | 1 |
| **RL7** | **HUMAN** | 36 | 29264 | 1 | 1 |
| **NUCL** | **HUMAN** | 36 | 76625 | 2 | 1 |
|   | Name         | Value | Column1 | Column2 | Column3 | Column4 | Column5 | Column6 |
|---|--------------|-------|---------|---------|---------|---------|---------|---------|
| 51| RS3A_HUMAN   | 36    | 30154   | 2       | 1       | 2       | 1       | 0.13    |
| 52| RS13_HUMAN   | 34    | 17212   | 1       | 1       | 1       | 1       | 0.23    |
| 53| RS9_HUMAN    | 34    | 22635   | 2       | 2       | 2       | 2       | 0.37    |
| 54| RL22_HUMAN   | 33    | 14835   | 1       | 1       | 1       | 1       | 0.26    |
| 55| RL4_HUMAN    | 33    | 47953   | 2       | 2       | 2       | 2       | 0.16    |
| 56| RL8_HUMAN    | 32    | 28235   | 1       | 1       | 1       | 1       | 0.13    |
| 57| H2B1A_HUMAN  | 31    | 14159   | 1       | 1       | 1       | 1       | 0.28    |
| 58| RL24_HUMAN   | 31    | 17882   | 2       | 2       | 2       | 2       | 0.48    |
| 59| RS4X_HUMAN   | 29    | 29807   | 3       | 1       | 3       | 1       | 0.13    |
| 60| G3P_HUMAN    | 28    | 36201   | 1       | 1       | 1       | 1       | 0.1     |
| 61| RL23A_HUMAN  | 27    | 17684   | 1       | 1       | 1       | 1       | 0.22    |
| 62| H2A1B_HUMAN  | 26    | 14127   | 3       | 2       | 2       | 2       | 0.63    |
| 63| RS10_HUMAN   | 21    | 18886   | 2       | 1       | 1       | 1       | 0.2     |
| 64| PUR6_HUMAN   | 19    | 47790   | 1       | 1       | 1       | 1       | 0.08    |

- **40S ribosomal protein S3a OS=Homo sapiens GN=RPS3A PE=1 SV=2**
- **40S ribosomal protein S13 OS=Homo sapiens GN=RPS13 PE=1 SV=2**
- **40S ribosomal protein S9 OS=Homo sapiens GN=RPS9 PE=1 SV=3**
- **60S ribosomal protein L22 OS=Homo sapiens GN=RPL22 PE=1 SV=2**
- **60S ribosomal protein L4 OS=Homo sapiens GN=RPL4 PE=1 SV=5**
- **60S ribosomal protein L8 OS=Homo sapiens GN=RPL8 PE=1 SV=2**
- **Histone H2B type 1-A OS=Homo sapiens GN=HIST1H2BA PE=1 SV=3**
- **60S ribosomal protein L24 OS=Homo sapiens GN=RPL24 PE=1 SV=1**
- **40S ribosomal protein S4, X isoform OS=Homo sapiens GN=RPS4X PE=1 SV=2**
- **Glyceraldehyde-3-phosphate dehydrogenase OS=Homo sapiens GN=GAPDH PE=1 SV=3**
- **60S ribosomal protein L23a OS=Homo sapiens GN=RPL23A PE=1 SV=1**
- **Histone H2A type 1-B/E OS=Homo sapiens GN=HIST1H2AB PE=1 SV=2**
- **40S ribosomal protein S10 OS=Homo sapiens GN=RPS10 PE=1 SV=1**
- **Multifunctional protein ADE2 OS=Homo sapiens GN=PAICS PE=1 SV=3**
| Accession     | Score | Mass     | N° of matches | N° of significant matches | N° of sequences | N° of significant sequences | emPAI | Description                                                                 |
|---------------|-------|----------|---------------|----------------------------|----------------|-----------------------------|-------|-----------------------------------------------------------------------------|
| VIME_HUMAN    | 1095  | 53676    | 35            | 34                         | 22             | 22                          | 4.35  | Vimentin OS=Homo sapiens GN=VIM PE=1 SV=4                                   |
| KPYM_HUMAN    | 947   | 58470    | 23            | 23                         | 18             | 18                          | 2.23  | Pyruvate kinase PKM OS=Homo sapiens GN=PKM PE=1 SV=4                       |
| K1C18_HUMAN   | 939   | 48029    | 33            | 29                         | 19             | 16                          | 2.85  | Keratin, type I cytoskeletal 18 OS=Homo sapiens GN=KRT18 PE=1 SV=2         |
| K2C8_HUMAN    | 800   | 53671    | 28            | 26                         | 18             | 17                          | 2.13  | Keratin, type II cytoskeletal 8 OS=Homo sapiens GN=KRT8 PE=1 SV=7           |
| FLNA_HUMAN    | 786   | 283301   | 29            | 24                         | 19             | 15                          | 0.23  | Filamin-A OS=Homo sapiens GN=FLNA PE=1 SV=4                               |
| ACTB_HUMAN    | 714   | 42052    | 17            | 13                         | 11             | 9                           | 1.35  | Actin, cytoplasmic 1 OS=Homo sapiens GN=ACTB PE=1 SV=1                     |
| ANXA2_HUMAN   | 623   | 38808    | 17            | 16                         | 9              | 8                           | 1.29  | Annexin A2 OS=Homo sapiens GN=ANXA2 PE=1 SV=2                              |
| ACTN4_HUMAN   | 590   | 105245   | 15            | 15                         | 10             | 10                          | 0.41  | Alpha-actinin-4 OS=Homo sapiens GN=ACTN4 PE=1 SV=2                         |
| ATPB_HUMAN    | 482   | 56525    | 12            | 10                         | 8              | 8                           | 0.67  | ATP synthase subunit beta, mitochondrial OS=Homo sapiens GN=ATPSB PE=1 SV=3|
| HSP7C_HUMAN   | 460   | 71082    | 13            | 12                         | 9              | 8                           | 0.5   | Heat shock cognate 71 kDa protein OS=Homo sapiens GN=HSPA8 PE=1 SV=1       |
| CH6O_HUMAN    | 385   | 61187    | 13            | 11                         | 9              | 9                           | 0.7   | Heat shock cognate 71 kDa protein, mitochondrial OS=Homo sapiens GN=HSPD1 PE=1 SV=2 |
| HNRPK_HUMAN   | 344   | 47822    | 10            | 9                          | 4              | 4                           | 0.42  | Heterogeneous nuclear ribonucleoprotein K OS=Homo sapiens GN=HNRNPK PE=1 SV=1 |
| AL1A1_HUMAN   | 342   | 55454    | 9             | 8                          | 9              | 8                           | 0.68  | Retinal dehydrogenase 1 OS=Homo sapiens GN=ALDH1A1 PE=1 SV=2              |
| TBBS5_HUMAN   | 319   | 50095    | 9             | 9                          | 7              | 7                           | 0.65  | Tubulin beta chain OS=Homo sapiens GN=TUBB PE=1 SV=2                       |
| ANXA1_HUMAN   | 308   | 38918    | 13            | 11                         | 7              | 5                           | 0.74  | Annexin A1 OS=Homo sapiens GN=ANXA1 PE=1 SV=2                              |
| GRP75_HUMAN   | 255   | 73920    | 9             | 9                          | 7              | 7                           | 0.41  | Stress-70 protein, mitochondrial OS=Homo sapiens GN=HSPA9 PE=1 SV=2        |
| H33_HUMAN     | 217   | 15376    | 4             | 4                          | 3              | 3                           | 0.97  | Histone H3.3 OS=Homo sapiens GN=H3F3A PE=1 SV=2                            |
| PDIAG_HUMAN   | 205   | 48490    | 6             | 6                          | 3              | 3                           | 0.25  | Protein disulfide-isomerase A6 OS=Homo sapiens GN=PDIAG PE=1 SV=1           |
| H2B1C_HUMAN   | 204   | 13989    | 7             | 6                          | 3              | 3                           | 1.71  | Histone H2B type 1-C/E/F/G/I OS=Homo sapiens GN=HIST1H2BC PE=1 SV=4        |
| ENOA_HUMAN    | 198   | 47481    | 8             | 7                          | 7              | 7                           | 0.7   | Alpha-enolase OS=Homo sapiens GN=ENO1 PE=1 SV=2                            |
| EF1A1_HUMAN   | 194   | 50451    | 11            | 8                          | 7              | 5                           | 0.43  | Elongation factor 1-alpha 1 OS=Homo sapiens GN=EF1A1 PE=1 SV=1             |
| EF2_HUMAN     | 181   | 96246    | 11            | 8                          | 9              | 6                           | 0.25  | Elongation factor 2 OS=Homo sapiens GN=EF2 PE=1 SV=4                       |
| ROA2_HUMAN    | 179   | 37464    | 4             | 3                          | 4              | 3                           | 0.33  | Heterogeneous nuclear ribonucleoproteins A2/B1 OS=Homo sapiens GN=HNRNPA2B1 PE=1 SV=2 |
| AK1C2_HUMAN   | 170   | 37111    | 5             | 5                          | 5              | 5                           | 0.62  | Aldo-keto reductase family 1 member C2 OS=Homo sapiens GN=AKR1C2 PE=1 SV=3 |
| TBA1B_HUMAN   | 162   | 50804    | 4             | 4                          | 3              | 3                           | 0.24  | Tubulin alpha-1B chain OS=Homo sapiens GN=TUBA1B PE=1 SV=1                 |
| HSPB1_HUMAN   | 162   | 22826    | 5             | 5                          | 3              | 3                           | 0.59  | Heat shock protein beta-1 OS=Homo sapiens GN=HSPB1 PE=1 SV=2               |

Table S2: Putative VgrG4-CTD ligands identified in lung epithelial cells (A549) membrane-enriched fraction
| 27 | LMNA_HUMAN | 159 | 74380 | 5 | 5 | 4 | 4 | 0.28 | Prelamin-A/C OS=Homo sapiens GN=LMNA PE=1 SV=1 |
| 28 | IFSA1_HUMAN | 155 | 17049 | 5 | 4 | 4 | 3 | 0.85 | Eukaryotic translation initiation factor 5A-1 OS=Homo sapiens GN=EIFSA PE=1 SV=2 |
| 29 | 4F2_HUMAN | 150 | 68180 | 4 | 4 | 2 | 2 | 0.11 | 4F2 cell-surface antigen heavy chain OS=Homo sapiens GN=SLC3A2 PE=1 SV=3 |
| 31 | PRDX1_HUMAN | 139 | 22324 | 3 | 2 | 3 | 2 | 0.37 | Peroxiredoxin-1 OS=Homo sapiens GN=PRDX1 PE=1 SV=1 |
| 30 | PRDX6_HUMAN | 139 | 25133 | 4 | 4 | 4 | 4 | 0.76 | Peroxiredoxin-6 OS=Homo sapiens GN=PRDX6 PE=1 SV=3 |
| 32 | ANXA4_HUMAN | 136 | 36088 | 2 | 2 | 2 | 2 | 0.22 | Annexin A4 OS=Homo sapiens GN=ANXA4 PE=1 SV=4 |
| 34 | RAB10_HUMAN | 124 | 22755 | 3 | 3 | 1 | 1 | 0.17 | Ras-related protein Rab-10 OS=Homo sapiens GN=RAB10 PE=1 SV=1 |
| 33 | PDIA1_HUMAN | 124 | 57480 | 10 | 8 | 6 | 5 | 0.46 | Protein disulfide-isomerase OS=Homo sapiens GN=P4HB PE=1 SV=3 |
| 35 | SDHA_HUMAN | 120 | 73672 | 1 | 1 | 1 | 1 | 0.05 | Succinate dehydrogenase [ubiquinone] flavoprotein subunit, mitochondrial OS=Homo sapiens GN=SDHA PE=1 SV=2 |
| 36 | UGDH_HUMAN | 116 | 55674 | 3 | 3 | 3 | 3 | 0.21 | UDP-glucose 6-dehydrogenase OS=Homo sapiens GN=UGDH PE=1 SV=1 |
| 37 | RA1L2_HUMAN | 113 | 34375 | 2 | 2 | 2 | 2 | 0.23 | Heterogeneous nuclear ribonucleoprotein A1-like 2 OS=Homo sapiens GN=HNRNPA1L2 PE=2 SV=2 |
| 38 | K2C1_HUMAN | 109 | 66170 | 3 | 3 | 2 | 2 | 0.12 | Keratin, type II cytoskeletal 1 OS=Homo sapiens GN=KRT1 PE=1 SV=6 |
| 39 | TCPB_HUMAN | 108 | 57794 | 2 | 1 | 2 | 1 | 0.06 | T-complex protein 1 subunit beta OS=Homo sapiens GN=CCT2 PE=1 SV=4 |
| 40 | ACOC_HUMAN | 103 | 98850 | 2 | 2 | 1 | 1 | 0.08 | Cytoplasmic aconitase hydratase OS=Homo sapiens GN=ACO1 PE=1 SV=3 |
| 41 | RAP1A_HUMAN | 95 | 21316 | 2 | 2 | 1 | 1 | 0.18 | Ras-related protein Rap-1A OS=Homo sapiens GN=RAP1A PE=1 SV=1 |
| 42 | TNL1_HUMAN | 92 | 217766 | 2 | 2 | 2 | 2 | 0.03 | Talin-1 OS=Homo sapiens GN=TLN1 PE=1 SV=3 |
| 43 | TERA_HUMAN | 91 | 89950 | 6 | 4 | 5 | 4 | 0.18 | Transitional endoplasmic reticulum ATPase OS=Homo sapiens GN=VCP PE=1 SV=4 |
| 44 | DDX5_HUMAN | 90 | 69618 | 2 | 2 | 1 | 1 | 0.05 | Probable ATP-dependent RNA helicase DDX5 OS=Homo sapiens GN=DDX5 PE=1 SV=1 |
| 45 | H2A1D_HUMAN | 90 | 14099 | 5 | 5 | 3 | 3 | 1.09 | Histone H2A type 1 D OS=Homo sapiens GN=HIST1H2AD PE=1 SV=2 |
| 47 | LPPRC_HUMAN | 81 | 159003 | 1 | 1 | 1 | 1 | 0.02 | Leucine-rich PPR motif-containing protein, mitochondrial OS=Homo sapiens GN=LRP1C PE=1 SV=3 |
| 46 | STM2L_HUMAN | 81 | 38624 | 2 | 2 | 1 | 1 | 0.1 | Stomatolin-like protein 2, mitochondrial OS=Homo sapiens GN=STOML2 PE=1 SV=1 |
| 48 | EFI1G_HUMAN | 81 | 50429 | 2 | 2 | 2 | 2 | 0.15 | Elongation factor 1-gamma OS=Homo sapiens GN=EEF1G PE=1 SV=3 |
| 49 | CKAP4_HUMAN | 80 | 66097 | 2 | 1 | 2 | 1 | 0.06 | Cytoskeleton-associated protein 4 OS=Homo sapiens GN=CKAP4 PE=1 SV=2 |
| 50 | RSPA_HUMAN | 78 | 32947 | 1 | 1 | 1 | 1 | 0.11 | 40S ribosomal protein SA OS=Homo sapiens GN=RPSA PE=1 SV=4 |
| 51 | 1433E_HUMAN | 78 | 29326 | 3 | 3 | 3 | 3 | 0.44 | 14-3-3 protein epsilon OS=Homo sapiens GN=YWHAE PE=1 SV=1 |
| 52 | SPTN1_HUMAN | 75 | 285163 | 2 | 2 | 2 | 2 | 0.03 | Spectrin alpha chain, non-erythrocytic 1 OS=Homo sapiens GN=SPTAN1 PE=1 SV=3 |
| 54 | LDHA_HUMAN | 73 | 36950 | 2 | 1 | 2 | 1 | 0.1 | L-lactate dehydrogenase A chain OS=Homo sapiens GN=LDHA PE=1 SV=2 |
| 53 | EF1D_HUMAN | 73 | 31217 | 4 | 3 | 3 | 3 | 0.41 | Elongation factor 1-delta OS=Homo sapiens GN=EEF1D PE=1 SV=5 |
| 55 | SFQ_HUMAN | 71 | 76216 | 2 | 2 | 2 | 2 | 0.1 | Splicing factor, proline- and glutamine-rich OS=Homo sapiens GN=SFPQ PE=1 SV=2 |
| 56 | TAGL2_HUMAN | 71 | 22548 | 2 | 1 | 2 | 1 | 0.17 | Transgelin-2 OS=Homo sapiens GN=TAGLN2 PE=1 SV=3 |
| GeneSymbol | Organism | Name | Description | OS | GN | PE | SV | Score |
|------------|----------|------|-------------|----|----|----|----|-------|
| NUCL_HUMAN | Homo sapiens | Nucleolin | Nucleolin | Homo sapiens | NCL | 1 | 3 | 0.15 |
| HOOK3_HUMAN | Homo sapiens | Protein Hook homolog 3 | Protein Hook homolog 3 | Homo sapiens | HOOK3 | 1 | 2 | 0.04 |
| ADT2_HUMAN | Homo sapiens | ADP/ATP translocase 2 | ADP/ATP translocase 2 | Homo sapiens | SLC25A5 | 1 | 7 | 0.38 |
| RLA1_HUMAN | Homo sapiens | 60S acidic ribosomal protein P1 | 60S acidic ribosomal protein P1 | Homo sapiens | RPLP1 | 1 | 1 | 0.8 |
| AL3A1_HUMAN | Homo sapiens | Aldehyde dehydrogenase, dimeric NADP-preferring | Aldehyde dehydrogenase, dimeric NADP-preferring | Homo sapiens | ALDH3A1 | 1 | 3 | 0.07 |
| PDIA3_HUMAN | Homo sapiens | Protein disulfide-isomerase A3 | Protein disulfide-isomerase A3 | Homo sapiens | PDIA3 | 1 | 4 | 0.13 |
| TPM3_HUMAN | Homo sapiens | Protein Hook homolog 3 | Protein Hook homolog 3 | Homo sapiens | HOOK3 | 1 | 2 | 0.04 |
| ARP3B_HUMAN | Homo sapiens | Actin-related protein 3B | Actin-related protein 3B | Homo sapiens | ACTR3B | 1 | 1 | 0.08 |
| PRDX3_HUMAN | Homo sapiens | Thioredoxin-dependent peroxide reductase, mitochondrial | Thioredoxin-dependent peroxide reductase, mitochondrial | Homo sapiens | PRDX3 | 1 | 3 | 0.14 |
| SAP_HUMAN | Homo sapiens | Prosaposin | Prosaposin | Homo sapiens | PSAP | 1 | 2 | 0.13 |
| C1QBP_HUMAN | Homo sapiens | Complement component 1 Q subcomponent-binding protein, mitochondrial | Complement component 1 Q subcomponent-binding protein, mitochondrial | Homo sapiens | C1QBP | 1 | 1 | 0.12 |
| ATP5H_HUMAN | Homo sapiens | ATP synthase subunit d, mitochondrial | ATP synthase subunit d, mitochondrial | Homo sapiens | ATP5H | 1 | 3 | 0.46 |
| RPN2_HUMAN | Homo sapiens | Heterogeneous nuclear ribonucleoprotein L | Heterogeneous nuclear ribonucleoprotein L | Homo sapiens | HNRNPL | 1 | 2 | 0.16 |
| RPB1A_HUMAN | Homo sapiens | 3-hydroxyacyl-CoA dehydrogenase type-2 | 3-hydroxyacyl-CoA dehydrogenase type-2 | Homo sapiens | HSD17B10 | 1 | 3 | 0.14 |
| PP1A_HUMAN | Homo sapiens | Polypyrimidine tract-binding protein 1 | Polypyrimidine tract-binding protein 1 | Homo sapiens | PTBP1 | 1 | 1 | 0.06 |
| PDI3_HUMAN | Homo sapiens | Peptidyl-prolyl cis-trans isomerase A | Peptidyl-prolyl cis-trans isomerase A | Homo sapiens | PPIA | 1 | 2 | 0.21 |
| ML12A_HUMAN | Homo sapiens | Myosin regulatory light chain 12A | Myosin regulatory light chain 12A | Homo sapiens | MYL12A | 1 | 2 | 0.19 |
| HNRH1_HUMAN | Homo sapiens | Heterogeneous nuclear ribonucleoprotein H | Heterogeneous nuclear ribonucleoprotein H | Homo sapiens | HNRNPH1 | 1 | 4 | 0.16 |
| CAPR1_HUMAN | Homo sapiens | Caprin-1 | Caprin-1 | Homo sapiens | CAPR1 | 1 | 2 | 0.05 |
| Gene Name | Accession | Chromosome | Strand | Start | End | Width | Description |
|-----------|-----------|------------|--------|-------|-----|-------|-------------|
| EF1B_HUMAN | 24919 | 1 | 1 | 1 | 1 | 0.15 | Elongation factor 1-beta OS=Homo sapiens GN=EEF1B2 PE=1 SV=3 |
| GSTO1_HUMAN | 27833 | 1 | 1 | 1 | 1 | 0.14 | Glutathione S-transferase omega-1 OS=Homo sapiens GN=GSTO1 PE=1 SV=2 |
| RS4X_HUMAN | 29807 | 1 | 1 | 1 | 1 | 0.13 | 40S ribosomal protein S4, X isofrom OS=Homo sapiens GN=RPS4X PE=1 SV=2 |
| HSP74_HUMAN | 95127 | 1 | 1 | 1 | 1 | 0.04 | Heat shock 70 kDa protein 4 OS=Homo sapiens GN=HSPA4 PE=1 SV=4 |
| CLH1_HUMAN | 193260 | 1 | 1 | 1 | 1 | 0.02 | Clathrin heavy chain 1 OS=Homo sapiens GN=CLTC PE=1 SV=5 |
| PHB_HUMAN | 29843 | 1 | 1 | 1 | 1 | 0.13 | Prohibitin OS=Homo sapiens GN=PHB PE=1 SV=1 |
| MIC60_HUMAN | 84026 | 1 | 1 | 1 | 1 | 0.04 | MICOS complex subunit MIC60 OS=Homo sapiens GN=IMMT PE=1 SV=1 |
| EFTU_HUMAN | 49852 | 1 | 1 | 1 | 1 | 0.07 | Elongation factor Tu, mitochondrial OS=Homo sapiens GN=TUFM PE=1 SV=2 |
| ATPA_HUMAN | 59828 | 1 | 1 | 1 | 1 | 0.06 | ATP synthase subunit alpha, mitochondrial OS=Homo sapiens GN=ATP5A1 PE=1 SV=1 |
| MATR3_HUMAN | 95078 | 1 | 1 | 1 | 1 | 0.04 | Matrin-3 OS=Homo sapiens GN=MATR3 PE=1 SV=2 |
| RPS27A_HUMAN | 18296 | 1 | 1 | 1 | 1 | 0.21 | Ubiquitin-40S ribosomal protein S27a OS=Homo sapiens GN=RPS27A PE=1 SV=2 |
| LDHB_HUMAN | 36900 | 1 | 1 | 1 | 1 | 0.1 | L-lactate dehydrogenase B chain OS=Homo sapiens GN=LDHB PE=1 SV=2 |
| MYL6_HUMAN | 17090 | 2 | 1 | 2 | 1 | 0.23 | Myosin light polypeptide 6 OS=Homo sapiens GN=MYL6 PE=1 SV=2 |
| NP1L1_HUMAN | 45631 | 1 | 1 | 1 | 1 | 0.08 | Nucleosome assembly protein 1-like 1 OS=Homo sapiens GN=NAP1L1 PE=1 SV=1 |
| LRC59_HUMAN | 35308 | 2 | 1 | 2 | 1 | 0.11 | Leucine-rich repeat-containing protein 59 OS=Homo sapiens GN=LRRC59 PE=1 SV=1 |
| H4_HUMAN | 11360 | 1 | 1 | 1 | 1 | 0.35 | Histone H4 OS=Homo sapiens GN=HIST1H4A PE=1 SV=2 |
| RS16_HUMAN | 16549 | 1 | 1 | 1 | 1 | 0.23 | 40S ribosomal protein S16 OS=Homo sapiens GN=RPS16 PE=1 SV=2 |
| RRP1_HUMAN | 152780 | 1 | 1 | 1 | 1 | 0.02 | Ribosome-binding protein 1 OS=Homo sapiens GN=RRP1 PE=1 SV=4 |
| ENPL_HUMAN | 92696 | 1 | 1 | 1 | 1 | 0.04 | Endoplasmin OS=Homo sapiens GN=HSP90B1 PE=1 SV=1 |
| TCPG_HUMAN | 61066 | 1 | 1 | 1 | 1 | 0.06 | T-complex protein 1 subunit gamma OS=Homo sapiens GN=CCT3 PE=1 SV=4 |
| ANXA5_HUMAN | 35971 | 1 | 1 | 1 | 1 | 0.1 | Annexin A5 OS=Homo sapiens GN=ANX5 PE=1 SV=2 |
| 2B1D_HUMAN | 30331 | 1 | 1 | 1 | 1 | 0.13 | HLA class II histocompatibility antigen, DRB1-13 beta chain OS=Homo sapiens GN=HLA-DRB1 PE=1 SV=1 |
| HNRDL_HUMAN | 46580 | 1 | 1 | 1 | 1 | 0.08 | Heterogeneous nuclear ribonucleoprotein D-like OS=Homo sapiens GN=HNRNPDL PE=1 SV=3 |
| IF4A1_HUMAN | 46353 | 1 | 1 | 1 | 1 | 0.08 | Eukaryotic initiation factor 4A-1 OS=Homo sapiens GN=EIF4A1 PE=1 SV=1 |
| TALDO_HUMAN | 37688 | 1 | 1 | 1 | 1 | 0.1 | Transaldolase OS=Homo sapiens GN=TALDO1 PE=1 SV=2 |
| 6PGD_HUMAN | 53619 | 2 | 1 | 2 | 1 | 0.07 | 6-phosphogluconate dehydrogenase, decarboxylating OS=Homo sapiens GN=PGD PE=1 SV=3 |
| UBA1_HUMAN | 118858 | 2 | 1 | 2 | 1 | 0.03 | Ubiquitin-like modifier-activating enzyme 1 OS=Homo sapiens GN=UBA1 PE=1 SV=3 |
| LEG1_HUMAN | 15048 | 2 | 1 | 2 | 1 | 0.26 | Galectin-1 OS=Homo sapiens GN=LGALS1 PE=1 SV=2 |
| CNPY2_HUMAN | 20981 | 1 | 1 | 1 | 1 | 0.18 | Protein canopy homolog 2 OS=Homo sapiens GN=CNPY2 PE=1 SV=1 |
| HNRPO_HUMAN | 69788 | 1 | 1 | 1 | 1 | 0.05 | Heterogeneous nuclear ribonucleoprotein Q OS=Homo sapiens GN=SYNCRIP PE=1 SV=2 |
|   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|
|   | LBX1_HUMAN | 19 | 30430 | 1 | 1 | 1 | 1 | 0.12 | Transcription factor LBX1 OS=Homo sapiens GN=LBX1 PE=2 SV=2 |
|   | HNRPU_HUMAN | 16 | 91269 | 1 | 1 | 1 | 1 | 0.04 | Heterogeneous nuclear ribonucleoprotein U OS=Homo sapiens GN=HNRNU PE=1 SV=6 |
|   | SRSF3_HUMAN | 15 | 19546 | 2 | 1 | 1 | 1 | 0.2  | Serine/arginine-rich splicing factor 3 OS=Homo sapiens GN=SRSF3 PE=1 SV=1 |
Table S3: Putative VgrG4-CTD ligands identified in THP1 macrophages soluble fraction

| Accession     | Score | Mass     | N° of matches | N° of significant matches | N° of sequences | N° of significant sequences | emPAI | Description                                                                 |
|---------------|-------|----------|---------------|---------------------------|-----------------|----------------------------|-------|-----------------------------------------------------------------------------|
| ENOA_HUMAN    | 2362  | 47481    | 66            | 64                        | 14              | 14                         | 2.91  | Alpha-enolase OS=Homo sapiens GN=ENO1 PE=1 SV=2                             |
| G3P_HUMAN     | 986   | 36201    | 31            | 29                        | 8               | 7                          | 1.21  | Glyceraldehyde-3-phosphate dehydrogenase OS=Homo sapiens GN=GAPDH PE=1 SV=3 |
| EF1A1_HUMAN   | 923   | 50451    | 32            | 25                        | 9               | 5                          | 0.9   | Elongation factor 1-alpha 1 OS=Homo sapiens GN=EEF1A1 PE=1 SV=1             |
| ACTB_HUMAN    | 807   | 42052    | 23            | 20                        | 6               | 6                          | 0.98  | Actin, cytoplasmic 1 OS=Homo sapiens GN=ACTB PE=1 SV=1                     |
| KPYM_HUMAN    | 621   | 58470    | 26            | 23                        | 12              | 10                         | 0.85  | Pyruvate kinase PKM OS=Homo sapiens GN=PKM PE=1 SV=4                        |
| TCPB_HUMAN    | 486   | 57794    | 21            | 15                        | 8               | 6                          | 0.55  | T-complex protein 1 subunit beta OS=Homo sapiens GN=CCT2 PE=1 SV=4          |
| K2C1_HUMAN    | 435   | 66170    | 28            | 25                        | 10              | 8                          | 0.64  | Keratin, type II cytoskeletal 1 OS=Homo sapiens GN=KRT1 PE=1 SV=6           |
| RS13_HUMAN    | 315   | 17212    | 11            | 11                        | 3               | 3                          | 0.84  | 40S ribosomal protein S13 OS=Homo sapiens GN=RPS13 PE=1 SV=2               |
| RS19_HUMAN    | 315   | 16051    | 16            | 14                        | 6               | 6                          | 2.66  | 40S ribosomal protein S13 OS=Homo sapiens GN=RPS13 PE=1 SV=2               |
| PRDX6_HUMAN   | 266   | 25133    | 14            | 11                        | 5               | 3                          | 0.53  | Peroxiredoxin-6 OS=Homo sapiens GN=PRDX6 PE=1 SV=3                         |
| RS5_HUMAN     | 261   | 23033    | 9             | 9                         | 2               | 2                          | 0.36  | 40S ribosomal protein S5 OS=Homo sapiens GN=RPS5 PE=1 SV=4                 |
| K1C10_HUMAN   | 231   | 59020    | 15            | 12                        | 7               | 6                          | 0.44  | Keratin, type I cytoskeletal 10 OS=Homo sapiens GN=KRT10 PE=1 SV=6          |
| RS18_HUMAN    | 231   | 17708    | 18            | 13                        | 6               | 5                          | 1.68  | 40S ribosomal protein S18 OS=Homo sapiens GN=RPS18 PE=1 SV=3               |
| TCPZ_HUMAN    | 222   | 58444    | 10            | 5                         | 6               | 2                          | 0.13  | T-complex protein 1 subunit zeta OS=Homo sapiens GN=CCT6A PE=1 SV=3        |
| RAP1A_HUMAN   | 187   | 21316    | 5             | 5                         | 1               | 1                          | 0.18  | Ras-related protein Rap-1A OS=Homo sapiens GN=RAP1A PE=1 SV=1              |
| K1C9_HUMAN    | 183   | 62255    | 7             | 7                         | 5               | 5                          | 0.34  | Keratin, type I cytoskeletal 9 OS=Homo sapiens GN=KRT9 PE=1 SV=3            |
| RS25_HUMAN    | 172   | 13791    | 9             | 7                         | 4               | 4                          | 1.73  | 40S ribosomal protein S25 OS=Homo sapiens GN=RPS25 PE=1 SV=1               |
| RS10_HUMAN    | 167   | 18886    | 16            | 10                        | 4               | 3                          | 0.75  | 40S ribosomal protein S10 OS=Homo sapiens GN=RPS10 PE=1 SV=1               |
| RS20_HUMAN    | 162   | 13478    | 8             | 6                         | 2               | 2                          | 0.67  | 40S ribosomal protein S20 OS=Homo sapiens GN=RPS20 PE=1 SV=1               |
| HSPB1_HUMAN   | 149   | 22826    | 9             | 6                         | 4               | 3                          | 0.59  | Heat shock protein beta-1 OS=Homo sapiens GN=HSPB1 PE=1 SV=2               |
| IF4G1_HUMAN   | 147   | 176124   | 5             | 4                         | 3               | 2                          | 0.04  | Eukaryotic translation initiation factor 4 gamma 1 OS=Homo sapiens GN=EIF4G1 PE=1 SV=4 |
| RL12_HUMAN    | 138   | 17979    | 4             | 2                         | 2               | 1                          | 0.21  | 60S ribosomal protein L12 OS=Homo sapiens GN=RPL12 PE=1 SV=1               |
|    | ENSEMBL     |    |    |    |    | Size (aa) | Score | Peptide | Protein Name | Organism | Genbank | Peptide | Peptides | Score   | Description |
|----|-------------|----|----|----|----|-----------|-------|----------|--------------|----------|---------|----------|----------|---------|------------|
| 23 | TBA1B_HUMAN | 133| 50804| 11 | 7 | 5 | 2 | 0.15 | Tubulin alpha-1B chain | OS=Homo sapiens | GN=TUBA1B | PE=1 | SV=1 |        |          |
| 24 | LDHA_HUMAN  | 126| 36950| 8  | 5 | 3 | 2 | 0.21 | L-lactate dehydrogenase A chain | OS=Homo sapiens | GN=LDHA | PE=1 | SV=2 |        |          |
| 25 | RS3A_HUMAN  | 112| 30154| 5  | 3 | 3 | 2 | 0.27 | 40S ribosomal protein S3a | OS=Homo sapiens | GN=RPS3A | PE=1 | SV=2 |        |          |
| 26 | R57_HUMAN   | 107| 22113| 5  | 5 | 2 | 0.61 | 40S ribosomal protein S7 | OS=Homo sapiens | GN=RPS7 | PE=1 | SV=1 |        |          |
| 27 | HS90B_HUMAN | 95 | 83554| 8  | 2 | 5 | 2 | 0.09 | Heat shock protein HSP 90-beta | OS=Homo sapiens | GN=HSP90AB1 | PE=1 | SV=4 |        |          |
| 28 | RS14_HUMAN  | 89 | 16434| 3  | 3 | 3 | 2 | 0.24 | 40S ribosomal protein S14 | OS=Homo sapiens | GN=RPS14 | PE=1 | SV=3 |        |          |
| 29 | TCPD_HUMAN  | 89 | 58401| 7  | 4 | 4 | 2 | 0.13 | T-complex protein 1 subunit delta | OS=Homo sapiens | GN=CCT4 | PE=1 | SV=3 |        |          |
| 30 | RS4X_HUMAN  | 79 | 29807| 5  | 5 | 2 | 0.27 | 40S ribosomal protein S4, X isoform | OS=Homo sapiens | GN=RPS4X | PE=1 | SV=2 |        |          |
| 31 | RS16_HUMAN  | 78 | 16549| 5  | 4 | 1 | 1 | 0.23 | 40S ribosomal protein S16 | OS=Homo sapiens | GN=RPS16 | PE=1 | SV=2 |        |          |
| 32 | RAB1A_HUMAN | 69 | 22891| 9  | 5 | 4 | 3 | 0.59 | Ras-related protein Rab-1A | OS=Homo sapiens | GN=RAB1A | PE=1 | SV=3 |        |          |
| 33 | CALX_HUMAN  | 68 | 67982| 2  | 1 | 1 | 1 | 0.05 | Calnexin | OS=Homo sapiens | GN=CANX | PE=1 | SV=2 |        |          |
| 34 | ARF1_HUMAN  | 67 | 20741| 5  | 3 | 3 | 1 | 0.18 | ADP-ribsylation factor 1 | OS=Homo sapiens | GN=ARF1 | PE=1 | SV=2 |        |          |
| 35 | TCPE_HUMAN  | 63 | 60089| 2  | 2 | 2 | 2 | 0.13 | T-complex protein 1 subunit epsilon | OS=Homo sapiens | GN=CCT5 | PE=1 | SV=1 |        |          |
| 36 | ITB2_HUMAN  | 54 | 87976| 7  | 3 | 4 | 2 | 0.09 | Integrin beta-2 | OS=Homo sapiens | GN=ITGB2 | PE=1 | SV=2 |        |          |
| 37 | RS17_HUMAN  | 53 | 15597| 4  | 3 | 2 | 2 | 0.56 | 40S ribosomal protein S17 | OS=Homo sapiens | GN=RPS17 | PE=1 | SV=2 |        |          |
| 38 | TCPG_HUMAN  | 47 | 61066| 2  | 2 | 1 | 1 | 0.06 | T-complex protein 1 subunit gamma | OS=Homo sapiens | GN=CCT3 | PE=1 | SV=4 |        |          |
| 39 | RL11_HUMAN  | 47 | 20468| 2  | 2 | 1 | 1 | 0.19 | 60S ribosomal protein L11 | OS=Homo sapiens | GN=RPL11 | PE=1 | SV=2 |        |          |
| 40 | ARP4_HUMAN  | 47 | 19768| 5  | 4 | 3 | 3 | 0.71 | Actin-related protein 2/3 complex subunit 4 | OS=Homo sapiens | GN=ARPC4 | PE=1 | SV=3 |        |          |
| 41 | SERA_HUMAN  | 46 | 57356| 10 | 5 | 2 | 2 | 0.13 | D-3-phosphoglycerate dehydrogenase | OS=Homo sapiens | GN=PHGDH | PE=1 | SV=4 |        |          |
| 42 | AMPN_HUMAN  | 45 | 109870| 3  | 2 | 3 | 2 | 0.07 | Aminopeptidase N | OS=Homo sapiens | GN=ANPEP | PE=1 | SV=4 |        |          |
| 43 | FACE1_HUMAN | 44 | 55063| 1  | 1 | 1 | 1 | 0.07 | CAAX prenyl protease 1 homolog | OS=Homo sapiens | GN=ZMPSTE24 | PE=1 | SV=2 |        |          |
| 44 | H4_HUMAN    | 43 | 11360| 8  | 6 | 3 | 2 | 0.83 | Histone H4 | OS=Homo sapiens | GN=HIST1H4A | PE=1 | SV=2 |        |          |
| 45 | RAC2_HUMAN  | 42 | 21814| 10 | 6 | 4 | 4 | 0.91 | Ras-related C3 botulinum toxin substrate 2 | OS=Homo sapiens | GN=RAC2 | PE=1 | SV=1 |        |          |
| 46 | RS3_HUMAN   | 40 | 26842| 5  | 3 | 4 | 3 | 0.49 | 40S ribosomal protein S3 | OS=Homo sapiens | GN=RPS3 | PE=1 | SV=2 |        |          |
| 47 | USO1_HUMAN  | 39 | 108740| 3  | 2 | 1 | 1 | 0.03 | General vesicular transport factor p115 | OS=Homo sapiens | GN=USO1 | PE=1 | SV=2 |        |          |
| 48 | CDC42_HUMAN | 39 | 21587| 3  | 2 | 1 | 1 | 0.39 | Cell division control protein 42 homolog | OS=Homo sapiens | GN=CDC42 | PE=1 | SV=2 |        |          |
| Protein | Species | Accession | Mass | Charge | Intensity | Function | Description |
|---------|---------|-----------|------|--------|-----------|----------|-------------|
| Galectin-1 | Homo sapiens | LGALS1 | 15048 | 4 | 2 | 2 | 0.58 | Galectin-1 OS=Homo sapiens GN=LGALS1 PE=1 SV=2 |
| Cofilin-1 | Homo sapiens | CFL1 | 18719 | 2 | 1 | 2 | 1 | 0.21 | Cofilin-1 OS=Homo sapiens GN=CFL1 PE=1 SV=3 |
| 60S ribosomal protein L31 | Homo sapiens | RPL31 | 14454 | 1 | 1 | 1 | 1 | 0.27 | 60S ribosomal protein L31 OS=Homo sapiens GN=RPL31 PE=1 SV=1 |
| 60S ribosomal protein L30 | Homo sapiens | RPL30 | 12947 | 1 | 1 | 1 | 1 | 0.3 | 60S ribosomal protein L30 OS=Homo sapiens GN=RPL30 PE=1 SV=2 |
| Multifunctional protein ADE2 | Homo sapiens | PAICS | 47790 | 4 | 2 | 1 | 1 | 0.08 | Multifunctional protein ADE2 OS=Homo sapiens GN=PAICS PE=1 SV=3 |
| 60S ribosomal protein L27a | Homo sapiens | RPL27A | 16665 | 4 | 2 | 1 | 1 | 0.23 | 60S ribosomal protein L27a OS=Homo sapiens GN=RPL27A PE=1 SV=2 |
| T-complex protein 1 subunit alpha | Homo sapiens | TCP1 | 60819 | 4 | 3 | 2 | 2 | 0.13 | T-complex protein 1 subunit alpha OS=Homo sapiens GN=TCP1 PE=1 SV=1 |
| 60S ribosomal protein L23a | Homo sapiens | RPL23A | 17684 | 1 | 1 | 1 | 1 | 0.22 | 60S ribosomal protein L23a OS=Homo sapiens GN=RPL23A PE=1 SV=1 |
| ADP/ATP translocase 1 | Homo sapiens | SLC25A4 | 33271 | 3 | 3 | 1 | 1 | 0.11 | ADP/ATP translocase 1 OS=Homo sapiens GN=SLC25A4 PE=1 SV=4 |
| 60S ribosomal protein L36 | Homo sapiens | RPL36 | 12303 | 3 | 1 | 3 | 1 | 0.32 | 60S ribosomal protein L36 OS=Homo sapiens GN=RPL36 PE=1 SV=3 |
| Tubulin beta-2A chain | Homo sapiens | TUBB2A | 50274 | 1 | 1 | 1 | 1 | 0.07 | Tubulin beta-2A chain OS=Homo sapiens GN=TUBB2A PE=1 SV=1 |
| Stromal membrane-associated protein 2 | Homo sapiens | SMAP2 | 47097 | 4 | 2 | 4 | 2 | 0.17 | Stromal membrane-associated protein 2 OS=Homo sapiens GN=SMAP2 PE=1 SV=1 |
| Cytoplastic dynein 2 heavy chain 1 | Homo sapiens | DYNC2H1 | 495790 | 7 | 2 | 2 | 1 | 0.01 | Cytoplastic dynein 2 heavy chain 1 OS=Homo sapiens GN=DYNC2H1 PE=1 SV=4 |
| Protein disulfide-isomerase A6 | Homo sapiens | PDIA6 | 48490 | 1 | 1 | 1 | 1 | 0.08 | Protein disulfide-isomerase A6 OS=Homo sapiens GN=PDIA6 PE=1 SV=1 |
| 4F2 cell-surface antigen heavy chain | Homo sapiens | SLC3A2 | 68180 | 1 | 1 | 1 | 1 | 0.05 | 4F2 cell-surface antigen heavy chain OS=Homo sapiens GN=SLC3A2 PE=1 SV=3 |
| L-lactate dehydrogenase B chain | Homo sapiens | LDHB | 36900 | 1 | 1 | 1 | 1 | 0.1 | L-lactate dehydrogenase B chain OS=Homo sapiens GN=LDHB PE=1 SV=2 |
| Annexin A11 | Homo sapiens | ANXA11 | 54697 | 1 | 1 | 1 | 1 | 0.07 | Annexin A11 OS=Homo sapiens GN=ANXA11 PE=1 SV=1 |
| EH domain-containing protein 4 | Homo sapiens | EHD4 | 61365 | 1 | 1 | 1 | 1 | 0.06 | EH domain-containing protein 4 OS=Homo sapiens GN=EHD4 PE=1 SV=1 |
| 40S ribosomal protein S11 | Homo sapiens | RPS11 | 18590 | 3 | 1 | 1 | 1 | 0.22 | 40S ribosomal protein S11 OS=Homo sapiens GN=RPS11 PE=1 SV=3 |
| Monocarboxylate transporter 4 | Homo sapiens | SLC16A3 | 50064 | 2 | 1 | 1 | 1 | 0.07 | Monocarboxylate transporter 4 OS=Homo sapiens GN=SLC16A3 PE=1 SV=1 |
Table S4: Putative VgrG4-CTD ligands identified in THP1 macrophages membrane-enriched fraction

| Accession | Score | Mass | N° of matches | N° of significant matches | N° of sequences | N° of significant sequences | emPAI | Description |
|-----------|-------|------|---------------|---------------------------|----------------|-----------------------------|-------|-------------|
| K1C10_HUMAN | 1229 | 59020 | 46 | 41 | 18 | 16 | 1.83 | Keratin, type I cytoskeletal 10 OS=Homo sapiens GN=KRT10 PE=1 SV=6 |
| K1C9_HUMAN | 1034 | 62255 | 35 | 32 | 12 | 11 | 1.13 | Keratin, type I cytoskeletal 9 OS=Homo sapiens GN=KRT9 PE=1 SV=3 |
| K2C1_HUMAN | 1009 | 66170 | 38 | 35 | 11 | 11 | 0.82 | Keratin, type II cytoskeletal 1 OS=Homo sapiens GN=KRT1 PE=1 SV=6 |
| PDA1_HUMAN | 532 | 57480 | 28 | 23 | 12 | 12 | 0.99 | Protein disulfide-isomerase OS=Homo sapiens GN=P4HB PE=1 SV=3 |
| H2B1C_HUMAN | 462 | 13898 | 11 | 8 | 4 | 3 | 1.11 | Histone H2B type 1-C/F/G/I OS=Homo sapiens GN=HIST1H2BC PE=1 SV=4 |
| G3P_HUMAN | 385 | 36201 | 12 | 11 | 6 | 6 | 1 | Glyceraldehyde-3-phosphate dehydrogenase OS=Homo sapiens GN=GAPDH PE=1 SV=3 |
| PDA6_HUMAN | 371 | 48490 | 11 | 8 | 4 | 3 | 0.25 | Protein disulfide-isomerase A6 OS=Homo sapiens GN=PDA6 PE=1 SV=1 |
| ACTB_HUMAN | 338 | 40252 | 16 | 12 | 7 | 7 | 0.82 | Actin, cytoplasmic 1 OS=Homo sapiens GN=ACTB PE=1 SV=1 |
| GRP78_HUMAN | 322 | 72402 | 13 | 9 | 5 | 5 | 0.28 | 78 kDa glucose-regulated protein OS=Homo sapiens GN=HSPA5 PE=1 SV=2 |
| ATPB_HUMAN | 318 | 56525 | 17 | 13 | 8 | 6 | 0.47 | ATP synthase subunit beta, mitochondrial OS=Homo sapiens GN=ATP5B PE=1 SV=3 |
| CALX_HUMAN | 287 | 67982 | 11 | 9 | 6 | 5 | 0.3 | Calnexin OS=Homo sapiens GN=CANX PE=1 SV=2 |
| H4_HUMAN | 255 | 11360 | 15 | 13 | 4 | 3 | 2.34 | Histone H4 OS=Homo sapiens GN=HIST1H4A PE=1 SV=2 |
| TBA1B_HUMAN | 247 | 50804 | 9 | 7 | 4 | 3 | 0.24 | Tubulin alpha-1B chain OS=Homo sapiens GN=TUBA1B PE=1 SV=1 |
| TBB5_HUMAN | 231 | 50095 | 9 | 5 | 5 | 3 | 0.33 | Tubulin beta chain OS=Homo sapiens GN=TUBB PE=1 SV=2 |
| GRP75_HUMAN | 200 | 73920 | 7 | 5 | 3 | 3 | 0.16 | Stress-70 protein, mitochondrial OS=Homo sapiens GN=HSPA9 PE=1 SV=2 |
| ENPL_HUMAN | 190 | 92696 | 14 | 8 | 10 | 6 | 0.26 | Endoplasmin OS=Homo sapiens GN=HSP90B1 PE=1 SV=1 |
| H32_HUMAN | 185 | 15436 | 3 | 3 | 1 | 1 | 0.25 | Histone H3.2 OS=Homo sapiens GN=HIST2H3A PE=1 SV=3 |
| H2A1B_HUMAN | 184 | 14127 | 11 | 10 | 2 | 2 | 1.09 | Histone H2A type 1-B/E OS=Homo sapiens GN=HIST1H2AB PE=1 SV=2 |
| RPN2_HUMAN | 168 | 69355 | 7 | 5 | 4 | 3 | 0.17 | Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit 2 OS=Homo sapiens GN=RPN2 PE=1 SV=3 |
| CH60_HUMAN | 167 | 61187 | 4 | 2 | 4 | 2 | 0.11 | 60 kDa heat shock protein, mitochondrial OS=Homo sapiens GN=HSPD1 PE=1 SV=2 |
| EST1_HUMAN | 164 | 62766 | 10 | 7 | 5 | 4 | 0.26 | Liver carboxylesterase 1 OS=Homo sapiens GN=CES1 PE=1 SV=2 |
| RAB1A_HUMAN | 152 | 22891 | 6 | 5 | 4 | 4 | 0.86 | Ras-related protein Rab-1A OS=Homo sapiens GN=RAB1A PE=1 SV=3 |
| ANXA2_HUMAN | 150 | 38808 | 3 | 3 | 2 | 2 | 0.2 | Annexin A2 OS=Homo sapiens GN=ANXA2 PE=1 SV=2 |
| ILF2_HUMAN | 141 | 43263 | 3 | 3 | 2 | 2 | 0.18 | Interleukin enhancer-binding factor 2 OS=Homo sapiens GN=ILF2 PE=1 SV=2 |
| HNRH1_HUMAN | 139 | 49484 | 4 | 4 | 2 | 2 | 0.16 | Heterogeneous nuclear ribonucleoprotein H OS=Homo sapiens GN=HNRH1 PE=1 SV=4 |
| ROA2_HUMAN | 133 | 37464 | 7 | 3 | 4 | 1 | 0.1 | Heterogeneous nuclear ribonucleoproteins A2/B1 OS=Homo sapiens GN=HNRPA2B1 PE=1 SV=2 |
| HNRPK_HUMAN | 131 | 51230 | 2 | 2 | 1 | 1 | 0.07 | Heterogeneous nuclear ribonucleoprotein K OS=Homo sapiens GN=HNRPK PE=1 SV=1 |
| ATPA_HUMAN | 129 | 59828 | 8 | 6 | 5 | 4 | 0.27 | ATP synthase subunit alpha, mitochondrial OS=Homo sapiens GN=ATP5A1 PE=1 SV=1 |
| CAP1_HUMAN | 129 | 52325 | 14 | 9 | 8 | 5 | 0.41 | Adenylyl cyclase-associated protein 1 OS=Homo sapiens GN=CAP1 PE=1 SV=5 |
| ADT3_HUMAN | 124 | 33073 | 7 | 7 | 2 | 2 | 0.24 | ADP/ATP translocase 3 OS=Homo sapiens GN=SLC25A6 PE=1 SV=4 |
| RPN1_HUMAN | 120 | 68641 | 9 | 6 | 6 | 4 | 0.23 | Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit 1 OS=Homo sapiens GN=RPN1 PE=1 SV=1 |
| Gene               | Accession | Description                                      | Score | Homo sapiens | Length | PE | SV | Score |
|--------------------|-----------|--------------------------------------------------|-------|--------------|--------|----|----|-------|
| PLD3_HUMAN         | 110       | Phospholipase D3 OS=Homo sapiens GN=PLD3 PE=1 SV=1 |
| PPIB_HUMAN         | 110       | Peptidyl-prolyl cis-trans isomerase B OS=Homo sapiens GN=PPIB PE=1 SV=2 |
| RAP1A_HUMAN        | 105       | Ras-related protein Rap-1A OS=Homo sapiens GN=RAP1A PE=1 SV=1 |
| COMT_HUMAN         | 103       | Catechol O-methyltransferase OS=Homo sapiens GN=COMT PE=1 SV=2 |
| HSPB1_HUMAN        | 102       | Heat shock protein beta-1 OS=Homo sapiens GN=HSPB1 PE=1 SV=2 |
| EF1A1_HUMAN        | 97        | Elongation factor 1-alpha 1 OS=Homo sapiens GN=EF1A1 PE=1 SV=1 |
| ROA1_HUMAN         | 95        | Heterogeneous nuclear ribonucleoprotein A1 OS=Homo sapiens GN=HNRPA1 PE=1 SV=5 |
| VDAC3_HUMAN        | 91        | Voltage-dependent anion-selective channel protein 3 OS=Homo sapiens GN=VDAC3 PE=1 SV=1 |
| ALBU_HUMAN         | 88        | Serum albumin OS=Homo sapiens GN=ALB PE=1 SV=2 |
| PDIA3_HUMAN        | 87        | Protein disulfide-isomerase A3 OS=Homo sapiens GN=PDIA3 PE=1 SV=4 |
| H33_HUMAN          | 84        | Histone H3.3 OS=Homo sapiens GN=H3F3A PE=1 SV=2 |
| HNRPU_HUMAN        | 82        | Heterogeneous nuclear ribonucleoprotein U OS=Homo sapiens GN=HNRNP U=1 SV=6 |
| TPP1_HUMAN         | 81        | Tryptophanase 1 OS=Homo sapiens GN=TPP1 PE=1 SV=2 |
| DHE3_HUMAN         | 78        | Glutamate dehydrogenase 1, mitochondrial OS=Homo sapiens GN=GLUD1 PE=1 SV=2 |
| PPIA_HUMAN         | 77        | Peptidyl-prolyl cis-trans isomerase A OS=Homo sapiens GN=PPIA PE=1 SV=2 |
| CALR_HUMAN         | 77        | Calreticulin OS=Homo sapiens GN=CALR PE=1 SV=1 |
| PTBP1_HUMAN        | 71        | Polyubiquitin-binding protein 1 OS=Homo sapiens GN=PTBP1 PE=1 SV=1 |
| ITB2_HUMAN         | 69        | Integrin beta-2 OS=Homo sapiens GN=ITGB2 PE=1 SV=2 |
| CATD_HUMAN         | 67        | Cathepsin D OS=Homo sapiens GN=CTSD PE=1 SV=1 |
| PRDX3_HUMAN        | 61        | Thioredoxin-dependent peroxide reductase, mitochondrial OS=Homo sapiens GN=PRDX3 PE=1 SV=3 |
| COF1_HUMAN         | 60        | Coflin-1 OS=Homo sapiens GN=CFL1 PE=1 SV=3 |
| RAB7A_HUMAN        | 60        | Ras-related protein Rab-7a OS=Homo sapiens GN=RAB7A PE=1 SV=1 |
| DECR_HUMAN         | 59        | 2,4-dienoyl-CoA reductase, mitochondrial OS=Homo sapiens GN=DECR1 PE=1 SV=1 |
| LMNA_HUMAN         | 59        | Prealbumin-A/C OS=Homo sapiens GN=LMNA PE=1 SV=1 |
| DHB12_HUMAN        | 58        | Very-long-chain 3-oxoacyl-CoA reductase OS=Homo sapiens GN=HSD17B12 PE=1 SV=2 |
| HNRPM_HUMAN        | 57        | Heterogeneous nuclear ribonucleoprotein M OS=Homo sapiens GN=HNRMPM PE=1 SV=3 |
| RL14_HUMAN         | 53        | 16S ribosomal protein L14 OS=Homo sapiens GN=RPL14 PE=1 SV=4 |
| GLYM_HUMAN         | 53        | Serine hydroxymethyltransferase, mitochondrial OS=Homo sapiens GN=SHMT2 PE=1 SV=3 |
| CLU1_HUMAN         | 53        | Clathrin heavy chain 1 OS=Homo sapiens GN=CLTC PE=1 SV=5 |
| SEL5_HUMAN         | 51        | Gelsolin OS=Homo sapiens GN=GSN PE=1 SV=1 |
| ARP3B_HUMAN        | 50        | Actin-related protein 3B OS=Homo sapiens GN=ACTR3B PE=2 SV=1 |
| CATB_HUMAN         | 49        | Cathepsin B OS=Homo sapiens GN=CTSB PE=1 SV=3 |
| LMMB1_HUMAN        | 48        | Lamin-B1 OS=Homo sapiens GN=LMMB1 PE=1 SV=2 |
| APEX1_HUMAN        | 46        | DNA-(apurinic or apyrimidinic site) lyase OS=Homo sapiens GN=APEX1 PE=1 SV=2 |
| APOC2_HUMAN        | 46        | Apolipoprotein C-II OS=Homo sapiens GN=APOC2 PE=1 SV=1 |
| Gene Name                        | Accession | Chromosome | Start Position | End Position | Strand | Gene Name                        | Accession | Chromosome | Start Position | End Position | Strand |
|---------------------------------|-----------|------------|----------------|--------------|--------|---------------------------------|-----------|------------|----------------|--------------|--------|
| RS27A_HUMAN                     | 24        | 18         | 18942193       | 18942193     |        | Actin-related protein 2/3 complex subunit 4 | ARPC4     | 24         | 18942193       | 18942193     |        |
| Dock2                            | 8         | 12         | 12345678       | 12345678     |        | Dock2                           | 8         | 12         | 12345678       | 12345678     |        |
| Dock2                            | 8         | 12         | 12345678       | 12345678     |        | Dock2                           | 8         | 12         | 12345678       | 12345678     |        |
| Dock2                            | 8         | 12         | 12345678       | 12345678     |        | Dock2                           | 8         | 12         | 12345678       | 12345678     |        |
| Dock2                            | 8         | 12         | 12345678       | 12345678     |        | Dock2                           | 8         | 12         | 12345678       | 12345678     |        |
| Dock2                            | 8         | 12         | 12345678       | 12345678     |        | Dock2                           | 8         | 12         | 12345678       | 12345678     |        |
| Dock2                            | 8         | 12         | 12345678       | 12345678     |        | Dock2                           | 8         | 12         | 12345678       | 12345678     |        |
| Dock2                            | 8         | 12         | 12345678       | 12345678     |        | Dock2                           | 8         | 12         | 12345678       | 12345678     |        |
| Dock2                            | 8         | 12         | 12345678       | 12345678     |        | Dock2                           | 8         | 12         | 12345678       | 12345678     |        |
| Dock2                            | 8         | 12         | 12345678       | 12345678     |        | Dock2                           | 8         | 12         | 12345678       | 12345678     |        |
| Dock2                            | 8         | 12         | 12345678       | 12345678     |        | Dock2                           | 8         | 12         | 12345678       | 12345678     |        |
| Gene Symbol | ID | Value1 | Value2 | Value3 | Value4 | Description |
|-------------|----|--------|--------|--------|--------|-------------|
| HEXB_HUMAN  | 19 | 63527  | 1      | 1      | 1      | 0.06        |
|             |    |        |        |        |        | Beta-hexosaminidase subunit beta OS=Homo sapiens GN=HEXB PE=1 SV=3 |
| ALDOA_HUMAN | 19 | 39851  | 1      | 1      | 1      | 0.09        |
|             |    |        |        |        |        | Fructose-bisphosphate aldolase A OS=Homo sapiens GN=ALDOA PE=1 SV=2 |
| CISY_HUMAN  | 16 | 51908  | 3      | 1      | 3      | 0.07        |
|             |    |        |        |        |        | Citrate synthase, mitochondrial OS=Homo sapiens GN=CS PE=1 SV=2 |
| DIJB11_HUMAN| 15 | 40774  | 1      | 1      | 1      | 0.09        |
|             |    |        |        |        |        | DnaJ homolog subfamily B member 11 OS=Homo sapiens GN=DNJB11 PE=1 SV=1 |
| MCPH_PUMAN  | 15 | 40525  | 1      | 1      | 1      | 0.09        |
|             |    |        |        |        |        | Phosphate carrier protein, mitochondrial OS=Homo sapiens GN=SLC25A3 PE=1 SV=2 |
| ECHA_HUMAN  | 15 | 83688  | 1      | 1      | 1      | 0.04        |
|             |    |        |        |        |        | Trifunctional enzyme subunit alpha, mitochondrial OS=Homo sapiens GN=HADHA PE=1 SV=2 |
| LPPRC_HUMAN | 15 | 159003 | 3      | 1      | 3      | 0.02        |
|             |    |        |        |        |        | Leucine-rich PPR motif-containing protein, mitochondrial OS=Homo sapiens GN=LRPPRC PE=1 SV=3 |
| ODP2_HUMAN  | 14 | 69466  | 1      | 1      | 1      | 0.05        |
|             |    |        |        |        |        | Dihydrolipoyllysine-residue acetyltransferase component of pyruvate dehydrogenase complex, mitochondrial OS=Homo sapiens GN=DLAT PE=1 SV=3 |
| ETHE1_HUMAN | 14 | 28368  | 4      | 2      | 3      | 0.28        |
|             |    |        |        |        |        | Persulfide dioxygenase ETHE1, mitochondrial OS=Homo sapiens GN=ETHE1 PE=1 SV=2 |
| HM13_HUMAN  | 13 | 41747  | 1      | 1      | 1      | 0.09        |
|             |    |        |        |        |        | Minor histocompatibility antigen H13 OS=Homo sapiens GN=HM13 PE=1 SV=1 |