

**Table S4:** Nesprin2 $\beta$  hot spots**NES2-SR51**

| Cluster centre | Conservation | SASA (Å <sup>2</sup> ) | neighbours | Conservation | SASA (Å <sup>2</sup> ) | Distance Å |
|----------------|--------------|------------------------|------------|--------------|------------------------|------------|
| ASN 6029       | 9            | 53.31                  | GLN 6024   | 8            | 48.28                  | 8.672      |
| ASN 6029       | 9            | 53.31                  | ASP 6027   | 8            | 47.27                  | 5.399      |
| ASN 6029       | 9            | 53.31                  | ASN 6032   | 9            | 53.36                  | 5.356      |
| ASN 6029       | 9            | 53.31                  | ARG 6034   | 8            | 150.92                 | 8.51       |
| ASN 6029       | 9            | 53.31                  | SER 6081   | 9            | 49.64                  | 9.753      |
|                |              |                        |            |              |                        |            |
| ARG 6034       | 8            | 150.92                 | LYS 6028   | 8            | 108.57                 | 9.831      |
| ARG 6034       | 8            | 150.92                 | ASN 6029   | 9            | 53.31                  | 8.51       |
| ARG 6034       | 8            | 150.92                 | ASN 6032   | 9            | 53.36                  | 5.339      |
| ARG 6034       | 8            | 150.92                 | THR 6108   | 9            | 33.15                  | 9.858      |
| ARG 6034       | 8            | 150.92                 | ASP 6113   | 8            | 39.96                  | 9.708      |
| ARG 6034       | 8            | 150.92                 | ARG 6115   | 8            | 102.34                 | 7.501      |
|                |              |                        |            |              |                        |            |
| TYR 6050       | 7            | 94.99                  | LYS 6046   | 8            | 99.21                  | 8.39       |
| TYR 6050       | 7            | 94.99                  | PRO 6047   | 8            | 102.17                 | 5.514      |
| TYR 6050       | 7            | 94.99                  | VAL 6048   | 9            | 51.38                  | 5.414      |
| TYR 6050       | 7            | 94.99                  | CYS 6053   | 7            | 118.61                 | 8.707      |
| TYR 6050       | 7            | 94.99                  | ARG 6127   | 8            | 145.74                 | 9.93       |
| TYR 6050       | 7            | 94.99                  | GLU 6131   | 8            | 61.09                  | 8.832      |
| TYR 6050       | 7            | 94.99                  | GLU 6132   | 8            | 101.53                 | 8.202      |
| TYR 6050       | 7            | 94.99                  | LEU 6136   | 7            | 103.92                 | 9.586      |
|                |              |                        |            |              |                        |            |
| LEU 6068       | 7            | 47.84                  | GLU 6043   | 8            | 85.29                  | 8.814      |
| LEU 6068       | 7            | 47.84                  | GLU 6064   | 8            | 61.06                  | 6.071      |
| LEU 6068       | 7            | 47.84                  | GLN 6066   | 8            | 86.07                  | 5.37       |
| LEU 6068       | 7            | 47.84                  | ASP 6071   | 8            | 59.56                  | 5.148      |
| LEU 6068       | 7            | 47.84                  | GLU 6073   | 8            | 113.27                 | 8.325      |
|                |              |                        |            |              |                        |            |
| ASP 6092       | 8            | 85.96                  | ASP 6094   | 8            | 62.84                  | 5.341      |
| ASP 6092       | 8            | 85.96                  | CYS 6096   | 7            | 63.29                  | 8.813      |
| ASP 6092       | 8            | 85.96                  | ASP 6103   | 8            | 101.51                 | 9.76       |
| ASP 6092       | 8            | 85.96                  | GLN 6106   | 8            | 74.76                  | 6.829      |
| ASP 6092       | 8            | 85.96                  | GLN 6107   | 8            | 136.46                 | 9.999      |
|                |              |                        |            |              |                        |            |
| ASP 6094       | 8            | 62.84                  | HIS 6091   | 9            | 56.7                   | 4.897      |
| ASP 6094       | 8            | 62.84                  | ASP 6092   | 8            | 85.96                  | 5.341      |
| ASP 6094       | 8            | 62.84                  | CYS 6096   | 7            | 63.29                  | 5.097      |
| ASP 6094       | 8            | 62.84                  | ASP 6103   | 8            | 101.51                 | 8.935      |
| ASP 6094       | 8            | 62.84                  | GLN 6106   | 8            | 74.76                  | 8.985      |
|                |              |                        |            |              |                        |            |
| ASP 6103       | 8            | 101.51                 | HIS 6091   | 9            | 56.7                   | 9.609      |
| ASP 6103       | 8            | 101.51                 | ASP 6092   | 8            | 85.96                  | 9.76       |
| ASP 6103       | 8            | 101.51                 | ASP 6094   | 8            | 62.84                  | 8.935      |
| ASP 6103       | 8            | 101.51                 | GLU 6101   | 8            | 48.84                  | 5.412      |
| ASP 6103       | 8            | 101.51                 | GLN 6106   | 8            | 74.76                  | 5.274      |
| ASP 6103       | 8            | 101.51                 | GLN 6107   | 8            | 136.46                 | 6.846      |
| ASP 6103       | 8            | 101.51                 | THR 6108   | 9            | 33.15                  | 9.106      |
|                |              |                        |            |              |                        |            |
| GLN 6106       | 8            | 74.76                  | HIS 6091   | 9            | 56.7                   | 7.221      |

|          |   |        |          |   |        |       |
|----------|---|--------|----------|---|--------|-------|
| GLN 6106 | 8 | 74.76  | ASP 6092 | 8 | 85.96  | 6.829 |
| GLN 6106 | 8 | 74.76  | ASP 6094 | 8 | 62.84  | 8.985 |
| GLN 6106 | 8 | 74.76  | GLU 6101 | 8 | 48.84  | 8.698 |
| GLN 6106 | 8 | 74.76  | ASP 6103 | 8 | 101.51 | 5.274 |
| GLN 6106 | 8 | 74.76  | SER 6104 | 9 | 49.99  | 5.175 |
| GLN 6106 | 8 | 74.76  | THR 6108 | 9 | 33.15  | 5.422 |
| THR 6108 | 9 | 33.15  | ASP 6027 | 8 | 47.27  | 8.097 |
| THR 6108 | 9 | 33.15  | ARG 6034 | 8 | 150.92 | 9.858 |
| THR 6108 | 9 | 33.15  | ASP 6103 | 8 | 101.51 | 9.106 |
| THR 6108 | 9 | 33.15  | SER 6104 | 9 | 49.99  | 6.388 |
| THR 6108 | 9 | 33.15  | GLN 6106 | 8 | 74.76  | 5.422 |
| THR 6108 | 9 | 33.15  | ASP 6113 | 8 | 39.96  | 8.618 |
| ASP 6113 | 8 | 39.96  | ARG 6034 | 8 | 150.92 | 9.708 |
| ASP 6113 | 8 | 39.96  | GLN 6107 | 8 | 136.46 | 9.848 |
| ASP 6113 | 8 | 39.96  | THR 6108 | 9 | 33.15  | 8.618 |
| ASP 6113 | 8 | 39.96  | ARG 6115 | 8 | 102.34 | 5.411 |
| ASP 6113 | 8 | 39.96  | ARG 6117 | 8 | 117.59 | 6.029 |
| ASP 6113 | 8 | 39.96  | ASN 6118 | 9 | 66.17  | 8.351 |
| ARG 6127 | 8 | 145.74 | TYR 6050 | 7 | 94.99  | 9.93  |
| ARG 6127 | 8 | 145.74 | GLN 6066 | 8 | 86.07  | 7.553 |
| ARG 6127 | 8 | 145.74 | GLU 6125 | 8 | 98.65  | 5.398 |
| ARG 6127 | 8 | 145.74 | GLU 6131 | 8 | 61.09  | 6.152 |
| ARG 6127 | 8 | 145.74 | GLU 6132 | 8 | 101.53 | 8.605 |
| GLU 6131 | 8 | 61.09  | TYR 6050 | 7 | 94.99  | 8.832 |
| GLU 6131 | 8 | 61.09  | GLN 6059 | 8 | 88.71  | 8.485 |
| GLU 6131 | 8 | 61.09  | ARG 6127 | 8 | 145.74 | 6.152 |
| GLU 6131 | 8 | 61.09  | ARG 6135 | 8 | 139.86 | 6.427 |
| GLU 6131 | 8 | 61.09  | LEU 6136 | 7 | 103.92 | 8.816 |

## NES2-SR52

| Cluster centre | Conservation | SASA (Å2) | neighbours | Conservation | SASA (Å2) | Distance Å |
|----------------|--------------|-----------|------------|--------------|-----------|------------|
| TYR 6168       | 8            | 150.99    | VAL 6166   | 9            | 105.96    | 7.035      |
| TYR 6168       | 8            | 150.99    | LYS 6172   | 9            | 84.48     | 6.34       |
| TYR 6168       | 8            | 150.99    | GLU 6173   | 9            | 100.75    | 8.641      |
| TYR 6168       | 8            | 150.99    | GLU 6174   | 9            | 44.24     | 9.927      |
| TYR 6168       | 8            | 150.99    | PHE 6242   | 8            | 60.8      | 6.982      |
| THR 6169       | 9            | 71.17     | VAL 6166   | 9            | 105.96    | 8.32       |
| THR 6169       | 9            | 71.17     | LYS 6172   | 9            | 84.48     | 5.025      |
| THR 6169       | 9            | 71.17     | GLU 6173   | 9            | 100.75    | 6.254      |
| THR 6169       | 9            | 71.17     | GLU 6174   | 9            | 44.24     | 8.769      |
| THR 6169       | 9            | 71.17     | PHE 6242   | 8            | 60.8      | 9.457      |
| GLU 6174       | 9            | 44.24     | TYR 6168   | 8            | 150.99    | 9.927      |
| GLU 6174       | 9            | 44.24     | THR 6169   | 9            | 71.17     | 8.769      |
| GLU 6174       | 9            | 44.24     | LYS 6172   | 9            | 84.48     | 5.557      |
| GLU 6174       | 9            | 44.24     | GLU 6179   | 9            | 68.05     | 8.35       |
| GLU 6174       | 9            | 44.24     | LEU 6236   | 8            | 31.73     | 9.878      |

|          |   |        |          |   |        |       |
|----------|---|--------|----------|---|--------|-------|
| GLU 6174 | 9 | 44.24  | PHE 6242 | 8 | 60.8   | 9.567 |
| GLN 6182 | 9 | 48.78  | GLU 6179 | 9 | 68.05  | 4.966 |
| GLN 6182 | 9 | 48.78  | HIS 6186 | 9 | 145.82 | 6.152 |
| GLN 6182 | 9 | 48.78  | GLU 6187 | 9 | 106.44 | 8.445 |
| GLN 6182 | 9 | 48.78  | GLN 6229 | 9 | 71.71  | 9.237 |
| GLN 6182 | 9 | 48.78  | LEU 6236 | 8 | 31.73  | 8.6   |
| GLU 6193 | 9 | 85.36  | LEU 6189 | 8 | 59.72  | 6.416 |
| GLU 6193 | 9 | 85.36  | THR 6190 | 9 | 81.03  | 5.298 |
| GLU 6193 | 9 | 85.36  | ASN 6196 | 9 | 60.7   | 5.09  |
| GLU 6193 | 9 | 85.36  | GLN 6198 | 9 | 84.18  | 8.255 |
| GLU 6193 | 9 | 85.36  | ASN 6222 | 9 | 63.51  | 9.395 |
| ASN 6196 | 9 | 60.7   | GLU 6193 | 9 | 85.36  | 5.09  |
| ASN 6196 | 9 | 60.7   | GLN 6198 | 9 | 84.18  | 5.467 |
| ASN 6196 | 9 | 60.7   | ARG 6200 | 9 | 189.39 | 6.594 |
| ASN 6196 | 9 | 60.7   | ARG 6201 | 9 | 188.41 | 9.074 |
| ASN 6196 | 9 | 60.7   | HIS 6219 | 9 | 111.54 | 8.789 |
| ASN 6196 | 9 | 60.7   | ASN 6222 | 9 | 63.51  | 7.449 |
| SER 6212 | 9 | 52.3   | ASN 6206 | 9 | 43.49  | 8.661 |
| SER 6212 | 9 | 52.3   | ARG 6207 | 9 | 261.39 | 7.202 |
| SER 6212 | 9 | 52.3   | THR 6208 | 9 | 42.75  | 6.198 |
| SER 6212 | 9 | 52.3   | ASP 6209 | 9 | 121.61 | 4.817 |
| SER 6212 | 9 | 52.3   | MET 6217 | 9 | 68.43  | 8.578 |
| HIS 6219 | 9 | 111.54 | ASN 6196 | 9 | 60.7   | 8.789 |
| HIS 6219 | 9 | 111.54 | ARG 6200 | 9 | 189.39 | 9.912 |
| HIS 6219 | 9 | 111.54 | MET 6217 | 9 | 68.43  | 5.299 |
| HIS 6219 | 9 | 111.54 | ASN 6222 | 9 | 63.51  | 5.278 |
| HIS 6219 | 9 | 111.54 | GLN 6223 | 9 | 80.77  | 6.422 |
| ASN 6222 | 9 | 63.51  | GLU 6193 | 9 | 85.36  | 9.395 |
| ASN 6222 | 9 | 63.51  | ASN 6196 | 9 | 60.7   | 7.449 |
| ASN 6222 | 9 | 63.51  | MET 6217 | 9 | 68.43  | 8.851 |
| ASN 6222 | 9 | 63.51  | HIS 6219 | 9 | 111.54 | 5.278 |
| ASN 6222 | 9 | 63.51  | ASP 6226 | 9 | 64.22  | 6.276 |
| GLN 6229 | 9 | 71.71  | GLN 6182 | 9 | 48.78  | 9.237 |
| GLN 6229 | 9 | 71.71  | HIS 6186 | 9 | 145.82 | 9.757 |
| GLN 6229 | 9 | 71.71  | LEU 6189 | 8 | 59.72  | 9.998 |
| GLN 6229 | 9 | 71.71  | GLN 6223 | 9 | 80.77  | 9.939 |
| GLN 6229 | 9 | 71.71  | ASP 6226 | 9 | 64.22  | 5.283 |
| GLN 6229 | 9 | 71.71  | ARG 6231 | 9 | 141.29 | 5.46  |
| GLN 6229 | 9 | 71.71  | ALA 6234 | 9 | 40.87  | 8.63  |
| ARG 6231 | 9 | 141.29 | ALA 6159 | 9 | 40.68  | 7.152 |
| ARG 6231 | 9 | 141.29 | ASP 6226 | 9 | 64.22  | 8.687 |
| ARG 6231 | 9 | 141.29 | GLN 6229 | 9 | 71.71  | 5.46  |
| ARG 6231 | 9 | 141.29 | ALA 6234 | 9 | 40.87  | 5.108 |

|          |   |        |          |   |        |       |
|----------|---|--------|----------|---|--------|-------|
| ARG 6231 | 9 | 141.29 | LEU 6236 | 8 | 31.73  | 8.35  |
| LEU 6236 | 8 | 31.73  | GLU 6174 | 9 | 44.24  | 9.878 |
| LEU 6236 | 8 | 31.73  | GLU 6179 | 9 | 68.05  | 8.327 |
| LEU 6236 | 8 | 31.73  | GLN 6182 | 9 | 48.78  | 8.6   |
| LEU 6236 | 8 | 31.73  | ARG 6231 | 9 | 141.29 | 8.35  |
| LEU 6236 | 8 | 31.73  | ALA 6234 | 9 | 40.87  | 5.373 |
| LEU 6236 | 8 | 31.73  | ARG 6238 | 9 | 92.59  | 5.402 |
| PHE 6242 | 8 | 60.8   | TYR 6168 | 8 | 150.99 | 6.982 |
| PHE 6242 | 8 | 60.8   | THR 6169 | 9 | 71.17  | 9.457 |
| PHE 6242 | 8 | 60.8   | LYS 6172 | 9 | 84.48  | 7.467 |
| PHE 6242 | 8 | 60.8   | GLU 6174 | 9 | 44.24  | 9.567 |
| PHE 6242 | 8 | 60.8   | ARG 6238 | 9 | 92.59  | 8.391 |

### NES2-SR53

| Cluster centre | Conservation | SASA (Å <sup>2</sup> ) | neighbours | Conservation | SASA (Å <sup>2</sup> ) | Distance Å |
|----------------|--------------|------------------------|------------|--------------|------------------------|------------|
| LEU 6257       | 8            | 46.35                  | THR 6261   | 9            | 36.65                  | 6.097      |
| LEU 6257       | 8            | 46.35                  | GLU 6262   | 9            | 118.24                 | 8.595      |
| LEU 6257       | 8            | 46.35                  | GLU 6324   | 9            | 63.04                  | 9.011      |
| LEU 6257       | 8            | 46.35                  | GLU 6327   | 9            | 71.07                  | 8.721      |
| LEU 6257       | 8            | 46.35                  | TYR 6331   | 8            | 89.01                  | 8.744      |
| THR 6261       | 9            | 36.65                  | LEU 6257   | 8            | 46.35                  | 6.097      |
| THR 6261       | 9            | 36.65                  | VAL 6258   | 9            | 46.8                   | 5.087      |
| THR 6261       | 9            | 36.65                  | LEU 6265   | 8            | 92.36                  | 6.378      |
| THR 6261       | 9            | 36.65                  | GLN 6266   | 9            | 83.25                  | 8.848      |
| THR 6261       | 9            | 36.65                  | TYR 6331   | 8            | 89.01                  | 8.065      |
| GLU 6262       | 9            | 118.24                 | LEU 6257   | 8            | 46.35                  | 8.595      |
| GLU 6262       | 9            | 118.24                 | VAL 6258   | 9            | 46.8                   | 6.173      |
| GLU 6262       | 9            | 118.24                 | LEU 6265   | 8            | 92.36                  | 5.02       |
| GLU 6262       | 9            | 118.24                 | GLN 6266   | 9            | 83.25                  | 6.367      |
| GLU 6262       | 9            | 118.24                 | THR 6268   | 9            | 61.02                  | 9.762      |
| THR 6268       | 9            | 61.02                  | GLU 6262   | 9            | 118.24                 | 9.762      |
| THR 6268       | 9            | 61.02                  | LEU 6265   | 8            | 92.36                  | 4.979      |
| THR 6268       | 9            | 61.02                  | GLN 6266   | 9            | 83.25                  | 5.502      |
| THR 6268       | 9            | 61.02                  | GLU 6271   | 9            | 103.07                 | 9.898      |
| THR 6268       | 9            | 61.02                  | ARG 6338   | 9            | 144.83                 | 7.874      |
| LYS 6298       | 9            | 86.95                  | THR 6293   | 9            | 75.68                  | 9.569      |
| LYS 6298       | 9            | 86.95                  | LEU 6294   | 8            | 106.9                  | 7.755      |
| LYS 6298       | 9            | 86.95                  | ASP 6300   | 9            | 69.61                  | 5.403      |
| LYS 6298       | 9            | 86.95                  | ILE 6303   | 9            | 50.52                  | 8.613      |
| LYS 6298       | 9            | 86.95                  | VAL 6304   | 9            | 61.85                  | 9.993      |
| ILE 6303       | 9            | 50.52                  | LYS 6298   | 9            | 86.95                  | 8.613      |
| ILE 6303       | 9            | 50.52                  | ASP 6300   | 9            | 69.61                  | 5.118      |
| ILE 6303       | 9            | 50.52                  | GLU 6307   | 9            | 90.61                  | 6.278      |
| ILE 6303       | 9            | 50.52                  | LEU 6309   | 8            | 41.89                  | 9.957      |
| ILE 6303       | 9            | 50.52                  | GLU 6326   | 9            | 67.63                  | 8.821      |

|          |   |        |          |   |        |       |
|----------|---|--------|----------|---|--------|-------|
| GLU 6307 | 9 | 90.61  | ILE 6303 | 9 | 50.52  | 6.278 |
| GLU 6307 | 9 | 90.61  | VAL 6304 | 9 | 61.85  | 5.314 |
| GLU 6307 | 9 | 90.61  | LEU 6309 | 8 | 41.89  | 5.474 |
| GLU 6307 | 9 | 90.61  | GLN 6311 | 9 | 83.97  | 5.868 |
| GLU 6307 | 9 | 90.61  | GLU 6322 | 9 | 49.68  | 7.759 |
| GLU 6307 | 9 | 90.61  | GLU 6326 | 9 | 67.63  | 9.877 |
| LEU 6309 | 8 | 41.89  | ARG 6246 | 9 | 190.12 | 7.719 |
| LEU 6309 | 8 | 41.89  | ILE 6303 | 9 | 50.52  | 9.957 |
| LEU 6309 | 8 | 41.89  | VAL 6304 | 9 | 61.85  | 8.86  |
| LEU 6309 | 8 | 41.89  | GLU 6307 | 9 | 90.61  | 5.474 |
| LEU 6309 | 8 | 41.89  | GLN 6311 | 9 | 83.97  | 5.618 |
| LEU 6309 | 8 | 41.89  | SER 6313 | 9 | 39.32  | 7.442 |
| LEU 6309 | 8 | 41.89  | GLU 6322 | 9 | 49.68  | 9.052 |
| GLU 6322 | 9 | 49.68  | GLU 6307 | 9 | 90.61  | 7.759 |
| GLU 6322 | 9 | 49.68  | LEU 6309 | 8 | 41.89  | 9.052 |
| GLU 6322 | 9 | 49.68  | GLN 6311 | 9 | 83.97  | 9.147 |
| GLU 6322 | 9 | 49.68  | SER 6313 | 9 | 39.32  | 9.798 |
| GLU 6322 | 9 | 49.68  | ASP 6317 | 9 | 83.34  | 8.583 |
| GLU 6322 | 9 | 49.68  | GLU 6324 | 9 | 63.04  | 5.36  |
| GLU 6322 | 9 | 49.68  | GLU 6326 | 9 | 67.63  | 6.376 |
| GLU 6322 | 9 | 49.68  | GLU 6327 | 9 | 71.07  | 8.861 |
| GLU 6326 | 9 | 67.63  | ILE 6303 | 9 | 50.52  | 8.821 |
| GLU 6326 | 9 | 67.63  | GLU 6307 | 9 | 90.61  | 9.877 |
| GLU 6326 | 9 | 67.63  | GLU 6322 | 9 | 49.68  | 6.376 |
| GLU 6326 | 9 | 67.63  | GLU 6324 | 9 | 63.04  | 5.345 |
| GLU 6326 | 9 | 67.63  | TYR 6331 | 8 | 89.01  | 8.586 |
| GLU 6327 | 9 | 71.07  | LEU 6257 | 8 | 46.35  | 8.721 |
| GLU 6327 | 9 | 71.07  | GLU 6322 | 9 | 49.68  | 8.861 |
| GLU 6327 | 9 | 71.07  | GLU 6324 | 9 | 63.04  | 5.163 |
| GLU 6327 | 9 | 71.07  | TYR 6331 | 8 | 89.01  | 5.909 |
| GLU 6327 | 9 | 71.07  | GLN 6333 | 9 | 127.95 | 9.887 |
| TYR 6331 | 8 | 89.01  | LEU 6257 | 8 | 46.35  | 8.744 |
| TYR 6331 | 8 | 89.01  | THR 6261 | 9 | 36.65  | 8.065 |
| TYR 6331 | 8 | 89.01  | GLU 6326 | 9 | 67.63  | 8.586 |
| TYR 6331 | 8 | 89.01  | GLU 6327 | 9 | 71.07  | 5.909 |
| TYR 6331 | 8 | 89.01  | GLN 6333 | 9 | 127.95 | 5.384 |
| TYR 6331 | 8 | 89.01  | GLU 6334 | 9 | 66.77  | 5.025 |
| TYR 6331 | 8 | 89.01  | PHE 6336 | 8 | 108    | 8.557 |
| PHE 6336 | 8 | 108    | THR 6293 | 9 | 75.68  | 9.657 |
| PHE 6336 | 8 | 108    | TYR 6331 | 8 | 89.01  | 8.557 |
| PHE 6336 | 8 | 108    | GLN 6333 | 9 | 127.95 | 5.456 |
| PHE 6336 | 8 | 108    | GLU 6334 | 9 | 66.77  | 5.47  |
| PHE 6336 | 8 | 108    | ARG 6338 | 9 | 144.83 | 5.414 |
| PHE 6336 | 8 | 108    | ARG 6341 | 9 | 185.3  | 8.788 |
| ARG 6338 | 9 | 144.83 | THR 6268 | 9 | 61.02  | 7.874 |

|          |   |        |          |   |        |       |
|----------|---|--------|----------|---|--------|-------|
| ARG 6338 | 9 | 144.83 | GLN 6333 | 9 | 127.95 | 8.736 |
| ARG 6338 | 9 | 144.83 | GLU 6334 | 9 | 66.77  | 6.073 |
| ARG 6338 | 9 | 144.83 | PHE 6336 | 8 | 108    | 5.414 |
| ARG 6338 | 9 | 144.83 | ARG 6341 | 9 | 185.3  | 5.242 |
| ARG 6338 | 9 | 144.83 | HIS 6343 | 9 | 90.67  | 8.531 |
| HIS 6343 | 9 | 90.67  | MET 6282 | 9 | 67.03  | 7.972 |
| HIS 6343 | 9 | 90.67  | ARG 6338 | 9 | 144.83 | 8.531 |
| HIS 6343 | 9 | 90.67  | ARG 6341 | 9 | 185.3  | 5.433 |
| HIS 6343 | 9 | 90.67  | ARG 6345 | 9 | 158    | 5.419 |
| HIS 6343 | 9 | 90.67  | SER 6348 | 9 | 73.84  | 8.753 |

## NES2-SR56

| Cluster centre | Conservation | SASA (Å <sup>2</sup> ) | neighbours | Conservation | SASA (Å <sup>2</sup> ) | Distance Å |
|----------------|--------------|------------------------|------------|--------------|------------------------|------------|
| LEU 6682       | 8            | 74.61                  | LEU 6678   | 8            | 110.32                 | 6.407      |
| LEU 6682       | 8            | 74.61                  | CYS 6685   | 8            | 37.9                   | 4.894      |
| LEU 6682       | 8            | 74.61                  | GLN 6686   | 7            | 96.65                  | 5.798      |
| LEU 6682       | 8            | 74.61                  | ASP 6687   | 7            | 62.63                  | 8.575      |
| LEU 6682       | 8            | 74.61                  | SER 6749   | 8            | 33.14                  | 9.814      |
| CYS 6685       | 8            | 37.9                   | LEU 6682   | 8            | 74.61                  | 4.894      |
| CYS 6685       | 8            | 37.9                   | ASP 6687   | 7            | 62.63                  | 5.541      |
| CYS 6685       | 8            | 37.9                   | HIS 6689   | 9            | 63.68                  | 6.915      |
| CYS 6685       | 8            | 37.9                   | LEU 6745   | 8            | 33.49                  | 8.624      |
| CYS 6685       | 8            | 37.9                   | GLN 6746   | 7            | 49.26                  | 8.684      |
| CYS 6685       | 8            | 37.9                   | ILE 6748   | 8            | 79.45                  | 9.907      |
| CYS 6685       | 8            | 37.9                   | SER 6749   | 8            | 33.14                  | 6.877      |
| CYS 6685       | 8            | 37.9                   | ASP 6760   | 7            | 81.14                  | 8.415      |
| LYS 6703       | 7            | 84.19                  | TRP 6698   | 7            | 65.45                  | 8.331      |
| LYS 6703       | 7            | 84.19                  | ARG 6705   | 7            | 137.42                 | 5.495      |
| LYS 6703       | 7            | 84.19                  | LYS 6774   | 9            | 105.7                  | 9.463      |
| LYS 6703       | 7            | 84.19                  | LEU 6775   | 8            | 64.74                  | 9.538      |
| LYS 6703       | 7            | 84.19                  | GLN 6777   | 7            | 84.8                   | 7.489      |
| LEU 6745       | 8            | 33.49                  | CYS 6685   | 8            | 37.9                   | 8.624      |
| LEU 6745       | 8            | 33.49                  | ASP 6687   | 7            | 62.63                  | 8.491      |
| LEU 6745       | 8            | 33.49                  | GLU 6747   | 7            | 81.79                  | 5.224      |
| LEU 6745       | 8            | 33.49                  | ILE 6748   | 8            | 79.45                  | 4.915      |
| LEU 6745       | 8            | 33.49                  | SER 6749   | 8            | 33.14                  | 5.821      |
| GLN 6746       | 7            | 49.26                  | CYS 6685   | 8            | 37.9                   | 8.684      |
| GLN 6746       | 7            | 49.26                  | ILE 6748   | 8            | 79.45                  | 5.75       |
| GLN 6746       | 7            | 49.26                  | SER 6749   | 8            | 33.14                  | 5.421      |
| GLN 6746       | 7            | 49.26                  | ASP 6760   | 7            | 81.14                  | 9.673      |
| GLN 6746       | 7            | 49.26                  | VAL 6768   | 7            | 51                     | 7.662      |
| GLN 6746       | 7            | 49.26                  | HIS 6769   | 8            | 149.61                 | 9.906      |
| SER 6749       | 8            | 33.14                  | LEU 6682   | 8            | 74.61                  | 9.814      |
| SER 6749       | 8            | 33.14                  | CYS 6685   | 8            | 37.9                   | 6.877      |
| SER 6749       | 8            | 33.14                  | LEU 6745   | 8            | 33.49                  | 5.821      |
| SER 6749       | 8            | 33.14                  | GLN 6746   | 7            | 49.26                  | 5.421      |

|          |   |       |          |   |        |       |
|----------|---|-------|----------|---|--------|-------|
| SER 6749 | 8 | 33.14 | GLU 6747 | 7 | 81.79  | 5.236 |
| SER 6749 | 8 | 33.14 | GLY 6758 | 8 | 38.98  | 9.726 |
| SER 6749 | 8 | 33.14 | GLU 6759 | 7 | 178.29 | 9.582 |
| SER 6749 | 8 | 33.14 | ASP 6760 | 7 | 81.14  | 8.254 |
| LYS 6767 | 9 | 58.75 | GLU 6763 | 9 | 63.54  | 6.565 |
| LYS 6767 | 9 | 58.75 | ALA 6764 | 9 | 59.09  | 5.186 |
| LYS 6767 | 9 | 58.75 | HIS 6769 | 8 | 149.61 | 5.514 |
| LYS 6767 | 9 | 58.75 | VAL 6770 | 9 | 41.67  | 4.937 |
| LYS 6767 | 9 | 58.75 | LYS 6774 | 9 | 105.7  | 9.58  |
| VAL 6770 | 9 | 41.67 | ALA 6764 | 9 | 59.09  | 9.453 |
| VAL 6770 | 9 | 41.67 | LYS 6767 | 9 | 58.75  | 4.937 |
| VAL 6770 | 9 | 41.67 | VAL 6768 | 7 | 51     | 5.69  |
| VAL 6770 | 9 | 41.67 | LYS 6774 | 9 | 105.7  | 6.435 |
| VAL 6770 | 9 | 41.67 | LEU 6775 | 8 | 64.74  | 8.772 |
| VAL 6770 | 9 | 41.67 | LYS 6776 | 7 | 68.56  | 9.551 |
| LYS 6774 | 9 | 105.7 | LEU 6697 | 8 | 120.79 | 9.922 |
| LYS 6774 | 9 | 105.7 | TRP 6698 | 7 | 65.45  | 9.991 |
| LYS 6774 | 9 | 105.7 | LYS 6703 | 7 | 84.19  | 9.463 |
| LYS 6774 | 9 | 105.7 | LYS 6767 | 9 | 58.75  | 9.58  |
| LYS 6774 | 9 | 105.7 | HIS 6769 | 8 | 149.61 | 9.613 |
| LYS 6774 | 9 | 105.7 | VAL 6770 | 9 | 41.67  | 6.435 |
| LYS 6774 | 9 | 105.7 | LYS 6776 | 7 | 68.56  | 5.29  |
| LYS 6774 | 9 | 105.7 | GLN 6777 | 7 | 84.8   | 5.014 |