

### Additional File 3: Cluster Evaluation for Data Set #9

Table 1: Comparison of the results for Pfam domain families with more than 1000 representations in data set #9 to the output of coreClust and comparison of these coreClust clusters to their matching families based on PClust.

| Pfam Family | $ Pfam $ | $ coreClust $ | $\frac{ Pfam \cap CoReCl }{ Pfam }$ | $\frac{ Pfam \cap CoReCl }{ CoReCl }$ | $ PClust $ | $\frac{ PClust \cap CoReCl }{ PClust }$ | $\frac{ PClust \cap CoReCl }{ CoReCl }$ |
|-------------|----------|---------------|-------------------------------------|---------------------------------------|------------|-----------------------------------------|-----------------------------------------|
| PF00397.23  | 9898     | 4504          | 0.45                                | 0.999                                 | 5159       | 0.87                                    | 0.99                                    |
| PF00109.23  | 9872     | 5185          | 0.52                                | 0.99                                  | 11         | 1                                       | 0.002                                   |
|             |          |               |                                     |                                       | 17         | 0.47                                    | 0.001                                   |
|             |          |               |                                     |                                       | 108        | 0.75                                    | 0.01                                    |
|             |          |               |                                     |                                       | 5149       | 0.92                                    | 0.91                                    |
| PF02801.19  | 9861     | 5516          | 0.55                                | 0.98                                  | 27         | 0.07                                    | 0.0003                                  |
|             |          |               |                                     |                                       | 51         | 0.94                                    | 0.008                                   |
|             |          |               |                                     |                                       | 39         | 0.02                                    | 0.0001                                  |
|             |          |               |                                     |                                       | 10         | 0.3                                     | 0.0005                                  |
|             |          |               |                                     |                                       | 5602       | 0.95                                    | 0.96                                    |
| PF00400.29  | 7671     | 5566          | 0.71                                | 0.98                                  | 36         | 0.78                                    | 0.005                                   |
|             |          |               |                                     |                                       | 38         | 0.03                                    | 0.0001                                  |
|             |          |               |                                     |                                       | 27         | 1                                       | 0.004                                   |
|             |          |               |                                     |                                       | 11         | 1                                       | 0.001                                   |
|             |          |               |                                     |                                       | 6781       | 0.80                                    | 0.97                                    |
| PF13472.3   | 6708     | 957           | 0.12                                | 0.84                                  | 10         | 1                                       | 0.01                                    |
|             |          |               |                                     |                                       | 12         | 0.67                                    | 0.01                                    |
|             |          |               |                                     |                                       | 460        | 0.64                                    | 0.31                                    |
|             |          |               |                                     |                                       | 51         | 0.72                                    | 0.04                                    |
|             |          |               |                                     |                                       | 441        | 0.85                                    | 0.39                                    |
|             |          |               |                                     |                                       | 257        | 0.42                                    | 0.11                                    |
| PF05729.9   | 6568     | 1351          | 0.20                                | 0.997                                 | 43         | 0.98                                    | 0.03                                    |
|             |          |               |                                     |                                       | 11         | 0.36                                    | 0.002                                   |
|             |          |               |                                     |                                       | 24         | 0.75                                    | 0.01                                    |
|             |          |               |                                     |                                       | 1322       | 0.96                                    | 0.94                                    |
| PF16363.2   | 6325     | 3000          | 0.43                                | 0.90                                  | 1725       | 0.98                                    | 0.56                                    |
|             |          |               |                                     |                                       | 932        | 0.98                                    | 0.30                                    |
| PF13516.3   | 6323     | 3206          | 0.50                                | 0.996                                 | 3745       | 0.83                                    | 0.97                                    |
| PF00550.22  | 6016     | 1486          | 0.23                                | 0.94                                  | 14         | 0.5                                     | 0.004                                   |
|             |          |               |                                     |                                       | 2125       | 0.61                                    | 0.88                                    |
|             |          |               |                                     |                                       | 55         | 1                                       | 0.04                                    |
| PF00053.21  | 5360     | 4422          | 0.75                                | 0.91                                  | 4745       | 0.74                                    | 0.79                                    |
|             |          |               |                                     |                                       | 112        | 0.98                                    | 0.02                                    |
|             |          |               |                                     |                                       | 11         | 1                                       | 0.002                                   |
|             |          |               |                                     |                                       | 41         | 0.76                                    | 0.01                                    |
|             |          |               |                                     |                                       | 526        | 0.95                                    | 0.11                                    |
| PF16197.2   | 4661     | 3762          | 0.78                                | 0.97                                  | 11         | 0.09                                    | 0.0002                                  |
|             |          |               |                                     |                                       | 10         | 0.4                                     | 0.001                                   |
|             |          |               |                                     |                                       | 32         | 0.12                                    | 0.001                                   |
|             |          |               |                                     |                                       | 24         | 0.96                                    | 0.006                                   |
|             |          |               |                                     |                                       | 10         | 1                                       | 0.002                                   |
|             |          |               |                                     |                                       | 228        | 0.88                                    | 0.05                                    |
|             |          |               |                                     |                                       | 14         | 0.07                                    | 0.0002                                  |
|             |          |               |                                     |                                       | 2752       | 0.86                                    | 0.63                                    |
|             |          |               |                                     |                                       | 11         | 0.91                                    | 0.002                                   |

|            |      |      |      |       |      |      |        |
|------------|------|------|------|-------|------|------|--------|
|            |      |      |      |       | 1050 | 0.86 | 0.24   |
| PF00698.18 | 4510 | 3402 | 0.68 | 0.91  | 62   | 0.92 | 0.02   |
|            |      |      |      |       | 29   | 0.72 | 0.006  |
|            |      |      |      |       | 13   | 0.08 | 0.0002 |
|            |      |      |      |       | 18   | 0.5  | 0.002  |
|            |      |      |      |       | 1122 | 0.88 | 0.29   |
|            |      |      |      |       | 299  | 0.62 | 0.05   |
|            |      |      |      |       | 15   | 0.67 | 0.002  |
|            |      |      |      |       | 19   | 0.05 | 0.0002 |
|            |      |      |      |       | 24   | 0.62 | 0.004  |
|            |      |      |      |       | 34   | 0.5  | 0.004  |
|            |      |      |      |       | 131  | 0.43 | 0.01   |
|            |      |      |      |       | 1967 | 0.82 | 0.48   |
|            |      |      |      |       | 148  | 0.66 | 0.03   |
| PF08659.7  | 3841 | 2606 | 0.62 | 0.92  | 13   | 0.61 | 0.003  |
|            |      |      |      |       | 10   | 0.6  | 0.002  |
|            |      |      |      |       | 32   | 1    | 0.01   |
|            |      |      |      |       | 18   | 0.28 | 0.001  |
|            |      |      |      |       | 23   | 0.65 | 0.005  |
|            |      |      |      |       | 23   | 0.04 | 0.0003 |
|            |      |      |      |       | 30   | 0.6  | 0.006  |
|            |      |      |      |       | 10   | 0.2  | 0.0007 |
|            |      |      |      |       | 61   | 0.87 | 0.02   |
|            |      |      |      |       | 3248 | 0.70 | 0.88   |
| PF04397.12 | 3705 | 463  | 0.12 | 0.99  | 12   | 0.08 | 0.002  |
|            |      |      |      |       | 10   | 0.4  | 0.008  |
|            |      |      |      |       | 587  | 0.36 | 0.46   |
|            |      |      |      |       | 584  | 0.26 | 0.33   |
|            |      |      |      |       | 12   | 0.33 | 0.008  |
| PF03106.12 | 3527 | 3422 | 0.97 | 0.999 | 145  | 1    | 0.04   |
|            |      |      |      |       | 3352 | 0.97 | 0.95   |
| PF14765.3  | 3472 | 684  | 0.19 | 0.98  | 15   | 0.53 | 0.01   |
|            |      |      |      |       | 28   | 0.71 | 0.03   |
|            |      |      |      |       | 613  | 0.79 | 0.71   |
|            |      |      |      |       | 177  | 0.56 | 0.14   |
|            |      |      |      |       | 19   | 0.68 | 0.02   |
|            |      |      |      |       | 10   | 0.3  | 0.004  |
|            |      |      |      |       | 11   | 0.09 | 0.001  |
|            |      |      |      |       | 10   | 0.7  | 0.01   |
|            |      |      |      |       | 12   | 1    | 0.02   |
| PF13191.3  | 3400 | 468  | 0.11 | 0.79  | 27   | 0.92 | 0.05   |
|            |      |      |      |       | 235  | 0.25 | 0.13   |
|            |      |      |      |       | 28   | 1    | 0.06   |
|            |      |      |      |       | 35   | 0.71 | 0.05   |
|            |      |      |      |       | 375  | 0.73 | 0.58   |
| PF00054.20 | 3094 | 202  | 0.06 | 1     | 50   | 0.9  | 0.22   |
|            |      |      |      |       | 208  | 0.71 | 0.73   |
| PF00072.21 | 2966 | 1630 | 0.47 | 0.86  | 10   | 0.4  | 0.002  |
|            |      |      |      |       | 22   | 0.5  | 0.006  |
|            |      |      |      |       | 2151 | 0.65 | 0.86   |
|            |      |      |      |       | 51   | 1    | 0.03   |
| PF00008.24 | 2768 | 2141 | 0.66 | 0.85  | 31   | 0.77 | 0.01   |
|            |      |      |      |       | 19   | 1    | 0.008  |

|            |      |      |      |       |      |        |       |
|------------|------|------|------|-------|------|--------|-------|
|            |      |      |      |       | 30   | 0.87   | 0.01  |
|            |      |      |      |       | 2727 | 0.67   | 0.85  |
|            |      |      |      |       | 11   | 1      | 0.005 |
|            |      |      |      |       | 11   | 0.90   | 0.004 |
| PF01176.16 | 2710 | 1724 | 0.63 | 0.99  | 1739 | 0.98   | 0.99  |
|            |      |      |      |       | 24   | 0.83   | 0.01  |
| PF01846.16 | 2523 | 671  | 0.25 | 0.95  | 402  | 0.75   | 0.45  |
|            |      |      |      |       | 40   | 0.75   | 0.04  |
|            |      |      |      |       | 365  | 0.92   | 0.50  |
| PF02772.13 | 2447 | 2405 | 0.97 | 0.99  | 2416 | 0.97   | 0.98  |
|            |      |      |      |       | 13   | 1      | 0.005 |
| PF00168.27 | 2441 | 933  | 0.36 | 0.94  | 824  | 0.93   | 0.82  |
|            |      |      |      |       | 109  | 0.98   | 0.11  |
|            |      |      |      |       | 38   | 1      | 0.04  |
| PF02773.13 | 2416 | 2422 | 0.99 | 0.99  | 20   | 1      | 0.008 |
|            |      |      |      |       | 2389 | 0.996  | 0.98  |
| PF00438.17 | 2412 | 2353 | 0.97 | 0.999 | 2381 | 0.98   | 0.99  |
|            |      |      |      |       | 18   | 1      | 0.007 |
| PF00081.19 | 2351 | 2212 | 0.93 | 0.99  | 2292 | 0.94   | 0.98  |
| PF02777.15 | 2324 | 2333 | 0.95 | 0.94  | 51   | 0.82   | 0.02  |
|            |      |      |      |       | 2297 | 0.95   | 0.94  |
|            |      |      |      |       | 42   | 1      | 0.02  |
|            |      |      |      |       | 15   | 0.47   | 0.003 |
| PF07983.10 | 2180 | 1949 | 0.88 | 0.98  | 18   | 0.94   | 0.008 |
|            |      |      |      |       | 12   | 0.42   | 0.002 |
|            |      |      |      |       | 1822 | 0.94   | 0.88  |
|            |      |      |      |       | 20   | 0.5    | 0.005 |
|            |      |      |      |       | 301  | 0.55   | 0.08  |
| PF02210.21 | 2170 | 188  | 0.09 | 1     | 198  | 0.95   | 1     |
| PF03168.10 | 1974 | 342  | 0.17 | 0.98  | 271  | 0.52   | 0.41  |
|            |      |      |      |       | 233  | 0.80   | 0.54  |
| PF00479.19 | 1891 | 1805 | 0.94 | 0.98  | 27   | 0.18   | 0.002 |
|            |      |      |      |       | 1764 | 0.95   | 0.93  |
|            |      |      |      |       | 69   | 0.97   | 0.04  |
| PF02781.13 | 1887 | 1686 | 0.89 | 0.99  | 1762 | 0.91   | 0.95  |
|            |      |      |      |       | 65   | 0.89   | 0.03  |
| PF12796.4  | 1818 | 568  | 0.25 | 0.80  | 18   | 0.11   | 0.003 |
|            |      |      |      |       | 878  | 0.50   | 0.77  |
|            |      |      |      |       | 10   | 0.7    | 0.01  |
| PF04383.10 | 1802 | 1013 | 0.56 | 1     | 1072 | 0.94   | 0.999 |
| PF05383.14 | 1779 | 1596 | 0.86 | 0.96  | 1707 | 0.89   | 0.96  |
|            |      |      |      |       | 56   | 0.71   | 0.02  |
| PF08529.8  | 1662 | 1080 | 0.64 | 0.98  | 12   | 0.33   | 0.003 |
|            |      |      |      |       | 109  | 0.80   | 0.08  |
|            |      |      |      |       | 106  | 0.99   | 0.10  |
|            |      |      |      |       | 1098 | 0.79   | 0.80  |
| PF00095.18 | 1637 | 366  | 0.20 | 0.89  | 1289 | 0.25   | 0.88  |
|            |      |      |      |       | 32   | 0.9375 | 0.08  |
| PF00057.15 | 1608 | 1085 | 0.67 | 0.999 | 1567 | 0.69   | 0.999 |
| PF13184.3  | 1555 | 1530 | 0.96 | 0.97  | 1553 | 0.96   | 0.97  |
|            |      |      |      |       | 36   | 0.97   | 0.02  |
| PF00957.18 | 1506 | 603  | 0.38 | 0.96  | 613  | 0.91   | 0.92  |
| PF00595.21 | 1447 | 311  | 0.21 | 1     | 39   | 0.97   | 0.12  |

|            |      |      |      |      |      |       |       |
|------------|------|------|------|------|------|-------|-------|
|            |      |      |      |      | 286  | 0.95  | 0.88  |
| PF00005.24 | 1367 | 957  | 0.67 | 0.96 | 10   | 0.1   | 0.001 |
|            |      |      |      |      | 921  | 0.99  | 0.95  |
|            |      |      |      |      | 39   | 1     | 0.04  |
| PF01221.15 | 1350 | 843  | 0.62 | 0.99 | 976  | 0.85  | 0.98  |
| PF16113.2  | 1340 | 1318 | 0.78 | 0.79 | 138  | 0.51  | 0.05  |
|            |      |      |      |      | 44   | 0.82  | 0.03  |
|            |      |      |      |      | 16   | 0.87  | 0.01  |
|            |      |      |      |      | 1125 | 0.87  | 0.75  |
| PF01220.16 | 1314 | 1469 | 0.96 | 0.86 | 24   | 0.46  | 0.00  |
|            |      |      |      |      | 1309 | 0.97  | 0.86  |
| PF02735.13 | 1294 | 168  | 0.13 | 0.99 | 79   | 0.80  | 0.37  |
|            |      |      |      |      | 104  | 0.94  | 0.58  |
| PF14484.3  | 1245 | 1199 | 0.84 | 0.88 | 1108 | 0.95  | 0.88  |
|            |      |      |      |      | 19   | 0.10  | 0.001 |
| PF00041.18 | 1205 | 68   | 0.06 | 1    | 69   | 0.97  | 0.98  |
| PF16653.2  | 1190 | 905  | 0.39 | 0.51 | 10   | 0.1   | 0.001 |
|            |      |      |      |      | 482  | 0.89  | 0.48  |
|            |      |      |      |      | 499  | 0.88  | 0.49  |
|            |      |      |      |      | 23   | 0.17  | 0.004 |
| PF09383.7  | 1139 | 106  | 0.09 | 1    | 232  | 0.45  | 0.99  |
| PF03435.15 | 1137 | 373  | 0.33 | 1    | 371  | 1     | 0.99  |
| PF10544.6  | 1125 | 653  | 0.58 | 1    | 651  | 1     | 0.996 |
| PF00632.22 | 1085 | 1081 | 0.99 | 0.99 | 1077 | 0.99  | 0.99  |
| PF13855.3  | 1085 | 726  | 0.48 | 0.72 | 13   | 1     | 0.02  |
|            |      |      |      |      | 27   | 0.63  | 0.02  |
|            |      |      |      |      | 619  | 0.83  | 0.71  |
| PF07677.11 | 1073 | 380  | 0.35 | 0.99 | 632  | 0.57  | 0.95  |
| PF08242.9  | 1054 | 1050 | 0.78 | 0.79 | 30   | 0.07  | 0.001 |
|            |      |      |      |      | 1038 | 0.80  | 0.79  |
|            |      |      |      |      | 196  | 0.88  | 0.16  |
|            |      |      |      |      | 28   | 0.11  | 0.002 |
| PF07678.11 | 1049 | 751  | 0.56 | 0.78 | 32   | 1     | 0.04  |
|            |      |      |      |      | 33   | 0.18  | 0.007 |
|            |      |      |      |      | 604  | 0.81  | 0.65  |
|            |      |      |      |      | 70   | 1     | 0.09  |
|            |      |      |      |      | 18   | 1     | 0.02  |
| PF02198.13 | 1046 | 168  | 0.16 | 0.99 | 176  | 0.94  | 0.98  |
| PF00332.15 | 1029 | 491  | 0.47 | 0.98 | 562  | 0.78  | 0.89  |
|            |      |      |      |      | 30   | 0.9   | 0.05  |
| PF15901.2  | 1008 | 565  | 0.56 | 1    | 16   | 0.125 | 0.003 |
|            |      |      |      |      | 149  | 0.86  | 0.23  |
|            |      |      |      |      | 115  | 0.67  | 0.14  |
|            |      |      |      |      | 203  | 0.98  | 0.35  |
|            |      |      |      |      | 193  | 0.76  | 0.26  |
| PF00069.22 | 1008 | 365  | 0.30 | 0.83 | 462  | 0.64  | 0.81  |
|            |      |      |      |      | 59   | 1     | 0.16  |