

Supplementary Materials

**Table S1.** Summary of all 3 QSAR models along with their descriptors and important validation parameters.

| Equation | Model   | Descriptors                                                                     | $R^2$ | $Q^2$ | $R^2_{pred}$ | $\overline{r^2_{m(Overall)}}$ | $\Delta r^2_{m(Overall)}$ | $^c R^2_p$ |
|----------|---------|---------------------------------------------------------------------------------|-------|-------|--------------|-------------------------------|---------------------------|------------|
| 1        | 2D-QSAR | S_aasN<br>Atype_N_69<br>D/Dtr05<br>Atype_C_43<br>S_sCl                          | 0.73  | 0.70  | 0.675        | 0.59                          | 0.197                     | 0.712      |
| 2        | G-QSAR  | R3-SsClE-index<br>R2-chi5chain<br>R2-SsNH2count<br>R1-k1alpha<br>R1-chi3Cluster | 0.72  | 0.69  | 0.695        | 0.57                          | 0.19                      | 0.70       |
| 3        | QAAR    | Jurs-FPSA-2<br>R2-chi3Cluster<br>R3-<br>Electronegativity<br>Count              | 0.86  | 0.79  | -            | -                             | -                         | 0.78       |

**Table S2.** 2D-QSAR results consisting of compound names, values of important descriptors, observed, calculated and LOO predicted activity values and Glide docking scores.

| Training set compounds |        |            |         |            |        |                                |                                |                                |                     |
|------------------------|--------|------------|---------|------------|--------|--------------------------------|--------------------------------|--------------------------------|---------------------|
| Name <sup>a</sup>      | S_aasN | Atype_N_69 | D/Dtr05 | Atype_C_43 | S_sCl  | pIC <sub>50</sub> <sup>b</sup> | pIC <sub>50</sub> <sup>c</sup> | pIC <sub>d</sub> <sup>50</sup> | gScore <sup>e</sup> |
| B1a                    | 1.277  | 1          | 105.723 | 1          | 5.380  | 6.409                          | 6.678                          | 6.712                          | -6.128              |
| B1b                    | 1.292  | 1          | 97.819  | 1          | 0.000  | 7.319                          | 6.531                          | 6.433                          | -7.175              |
| B1c                    | 1.296  | 1          | 130.127 | 1          | 0.000  | 6.201                          | 6.590                          | 6.629                          | -6.751              |
| B2d                    | 1.376  | 0          | 236.690 | 1          | 5.374  | 6.335                          | 6.439                          | 6.441                          | -6.084              |
| B2f                    | 1.413  | 0          | 147.737 | 1          | 0.000  | 6.241                          | 6.161                          | 6.159                          | -5.325              |
| B2g                    | 1.417  | 0          | 180.045 | 1          | 0.000  | 6.049                          | 6.220                          | 6.223                          | -5.679              |
| B2h                    | 1.416  | 0          | 194.538 | 1          | 5.491  | 6.171                          | 6.388                          | 6.391                          | -5.021              |
| B2j                    | 1.392  | 0          | 118.089 | 1          | 0.000  | 6.223                          | 6.099                          | 6.092                          | -5.533              |
| B2l                    | 1.391  | 0          | 134.548 | 1          | 0.000  | 6.361                          | 6.127                          | 6.117                          | -5.909              |
| B4a                    | 1.426  | 0          | 186.348 | 1          | 11.351 | 6.250                          | 6.532                          | 6.541                          | -6.765              |
| B4d                    | 1.440  | 0          | 194.902 | 1          | 5.875  | 6.371                          | 6.411                          | 6.411                          | -6.739              |
| B4e                    | 1.539  | 0          | 163.609 | 1          | 5.723  | 6.182                          | 6.402                          | 6.410                          | -6.123              |
| B4f                    | 1.467  | 0          | 170.625 | 1          | 0.000  | 6.403                          | 6.229                          | 6.226                          | -6.472              |

|     |       |   |         |   |        |       |       |       |        |
|-----|-------|---|---------|---|--------|-------|-------|-------|--------|
| B4h | 1.466 | 0 | 187.084 | 1 | 0.000  | 6.312 | 6.257 | 6.256 | -7.099 |
| B4i | 1.431 | 0 | 148.882 | 1 | 5.430  | 6.382 | 6.314 | 6.313 | -6.226 |
| B4j | 1.446 | 0 | 140.978 | 1 | 0.000  | 6.334 | 6.166 | 6.161 | -6.364 |
| B4l | 1.446 | 0 | 157.437 | 1 | 0.000  | 6.193 | 6.195 | 6.195 | -6.070 |
| B5b | 1.405 | 0 | 194.452 | 1 | 5.882  | 6.420 | 6.392 | 6.392 | -7.497 |
| B5c | 1.409 | 0 | 226.760 | 1 | 5.917  | 6.538 | 6.452 | 6.451 | -6.548 |
| B5d | 1.404 | 0 | 210.910 | 1 | 5.889  | 6.252 | 6.421 | 6.423 | -7.674 |
| B5e | 1.412 | 0 | 164.195 | 1 | 0.000  | 6.171 | 6.190 | 6.190 | -6.444 |
| B5f | 1.431 | 0 | 186.634 | 1 | 0.000  | 6.231 | 6.238 | 6.239 | -6.864 |
| B5g | 1.435 | 0 | 218.942 | 1 | 0.000  | 6.439 | 6.297 | 6.294 | -6.381 |
| B5i | 1.482 | 0 | 150.656 | 1 | 5.677  | 6.158 | 6.350 | 6.355 | -6.091 |
| B5j | 1.410 | 0 | 156.987 | 1 | 0.000  | 6.331 | 6.176 | 6.172 | -6.816 |
| B5k | 1.414 | 0 | 189.295 | 1 | 0.000  | 6.223 | 6.235 | 6.235 | -5.611 |
| B5l | 1.410 | 0 | 173.445 | 1 | 0.000  | 6.127 | 6.205 | 6.207 | -6.508 |
| B6a | 1.377 | 1 | 202.356 | 1 | 11.368 | 7.357 | 7.053 | 7.031 | -9.224 |
| B6b | 1.392 | 1 | 194.452 | 1 | 5.877  | 7.143 | 6.904 | 6.892 | -9.233 |
| B6c | 1.396 | 1 | 226.760 | 1 | 5.912  | 7.469 | 6.963 | 6.931 | -9.267 |
| B6d | 1.391 | 1 | 210.910 | 1 | 5.885  | 7.194 | 6.932 | 6.918 | -8.469 |
| B6e | 1.403 | 1 | 194.538 | 1 | 5.488  | 6.609 | 6.899 | 6.915 | -8.208 |
| B6f | 1.418 | 1 | 186.634 | 1 | 0.000  | 6.706 | 6.750 | 6.752 | -6.877 |
| B6g | 1.422 | 1 | 218.942 | 1 | 0.000  | 6.572 | 6.808 | 6.824 | -8.189 |
| B6i | 1.382 | 1 | 164.891 | 1 | 5.437  | 6.697 | 6.836 | 6.843 | -6.716 |
| B6j | 1.397 | 1 | 156.987 | 1 | 0.000  | 6.618 | 6.688 | 6.691 | -6.825 |
| B6k | 1.401 | 1 | 189.295 | 1 | 0.000  | 6.730 | 6.746 | 6.747 | -6.291 |
| B6l | 1.397 | 1 | 173.445 | 1 | 0.000  | 6.025 | 6.716 | 6.753 | -6.521 |
| B7a | 1.351 | 0 | 227.433 | 1 | 11.396 | 6.333 | 6.567 | 6.577 | -8.918 |
| B7b | 1.525 | 0 | 184.593 | 1 | 0.000  | 6.193 | 6.282 | 6.284 | -6.572 |
| B7e | 1.467 | 0 | 191.888 | 1 | 0.000  | 6.194 | 6.266 | 6.267 | -7.704 |
| B7f | 1.370 | 0 | 256.203 | 1 | 5.928  | 6.272 | 6.484 | 6.491 | -6.581 |
| B7g | 1.427 | 0 | 226.676 | 1 | 5.910  | 6.315 | 6.461 | 6.463 | -5.731 |
| B7h | 1.369 | 0 | 272.662 | 1 | 5.935  | 6.572 | 6.513 | 6.510 | -7.979 |
| B7i | 1.336 | 0 | 235.954 | 1 | 16.771 | 6.650 | 6.715 | 6.721 | -7.709 |
| B7k | 1.355 | 0 | 260.358 | 1 | 11.327 | 6.469 | 6.625 | 6.632 | -8.248 |
| B7l | 1.493 | 1 | 168.716 | 1 | 0.000  | 6.745 | 6.756 | 6.757 | -6.996 |
| B7m | 1.377 | 0 | 219.615 | 1 | 5.500  | 6.449 | 6.412 | 6.412 | -8.466 |
| B7n | 1.392 | 0 | 211.711 | 1 | 0.000  | 6.266 | 6.263 | 6.263 | -5.997 |
| B7p | 1.391 | 0 | 228.169 | 1 | 0.000  | 6.326 | 6.291 | 6.290 | -7.246 |
| B7r | 1.396 | 0 | 248.385 | 1 | 0.000  | 6.376 | 6.329 | 6.327 | -6.717 |
| B7t | 1.396 | 0 | 264.844 | 1 | 0.000  | 6.365 | 6.357 | 6.357 | -8.004 |
| B7x | 1.386 | 0 | 172.013 | 1 | 5.840  | 6.335 | 6.343 | 6.343 | -9.060 |

|      |       |   |         |   |        |       |       |       |        |
|------|-------|---|---------|---|--------|-------|-------|-------|--------|
| B7y  | 1.356 | 0 | 189.968 | 1 | 5.449  | 6.451 | 6.349 | 6.346 | -6.184 |
| B7za | 1.375 | 0 | 214.372 | 1 | 0.000  | 6.192 | 6.259 | 6.261 | -7.396 |
| B7zb | 1.371 | 0 | 198.522 | 1 | 0.000  | 6.334 | 6.229 | 6.226 | -6.101 |
| B7zd | 1.375 | 0 | 218.738 | 1 | 0.000  | 6.361 | 6.266 | 6.264 | -5.695 |
| B7ze | 1.379 | 0 | 251.046 | 1 | 0.000  | 6.384 | 6.325 | 6.322 | -8.010 |
| B7zf | 1.375 | 0 | 235.197 | 1 | 0.000  | 6.322 | 6.295 | 6.294 | -6.842 |
| B7zh | 1.356 | 0 | 190.584 | 1 | 5.318  | 6.322 | 6.346 | 6.347 | -6.477 |
| B7zj | 1.356 | 0 | 207.043 | 1 | 5.324  | 6.578 | 6.375 | 6.371 | -6.799 |
| B8a  | 1.401 | 0 | 255.703 | 1 | 11.472 | 7.377 | 6.644 | 6.616 | -6.335 |
| B8b  | 1.416 | 0 | 247.798 | 1 | 5.935  | 7.523 | 6.493 | 6.473 | -7.230 |
| B8d  | 1.416 | 0 | 264.257 | 1 | 5.943  | 6.623 | 6.522 | 6.519 | -7.649 |
| B8e  | 1.517 | 0 | 218.453 | 1 | 0.000  | 6.331 | 6.337 | 6.337 | -6.613 |
| B8f  | 1.442 | 0 | 239.981 | 1 | 0.000  | 6.314 | 6.337 | 6.338 | -6.862 |
| B8g  | 1.447 | 0 | 272.289 | 1 | 0.000  | 6.305 | 6.396 | 6.400 | -5.784 |
| B8h  | 1.442 | 0 | 256.439 | 1 | 0.000  | 6.279 | 6.366 | 6.369 | -7.475 |
| B8i  | 1.407 | 0 | 218.238 | 1 | 5.483  | 6.271 | 6.425 | 6.427 | -5.118 |
| B8j  | 1.422 | 0 | 210.333 | 1 | 0.000  | 6.334 | 6.275 | 6.274 | -6.889 |
| B8k  | 1.427 | 0 | 247.885 | 1 | 5.534  | 6.331 | 6.488 | 6.491 | -7.283 |
| B8l  | 1.421 | 0 | 226.792 | 1 | 0.000  | 6.197 | 6.304 | 6.306 | -7.360 |
| B9a  | 2.715 | 1 | 329.160 | 2 | 11.454 | 5.487 | 5.487 | 5.488 | -5.400 |
| B9b  | 2.737 | 1 | 317.248 | 2 | 5.926  | 5.126 | 5.333 | 5.349 | -7.383 |
| B9e  | 2.751 | 1 | 317.693 | 2 | 5.525  | 5.156 | 5.331 | 5.343 | -6.185 |
| B9f  | 2.773 | 1 | 305.782 | 2 | 0.000  | 5.185 | 5.177 | 5.176 | -6.978 |
| B9h  | 2.768 | 1 | 330.417 | 2 | 0.000  | 5.320 | 5.217 | 5.209 | -7.175 |
| B9i  | 2.726 | 1 | 273.203 | 2 | 5.474  | 5.334 | 5.239 | 5.231 | -6.752 |
| B9j  | 2.748 | 1 | 261.292 | 2 | 0.000  | 5.280 | 5.086 | 5.069 | -6.928 |
| B9k  | 2.754 | 1 | 311.567 | 2 | 0.000  | 5.198 | 5.177 | 5.176 | -6.128 |
| C10a | 2.827 | 1 | 315.216 | 2 | 11.772 | 5.544 | 5.528 | 5.526 | -7.088 |
| C10b | 2.853 | 1 | 306.943 | 2 | 5.994  | 5.195 | 5.376 | 5.388 | -5.271 |
| C10c | 2.861 | 1 | 343.889 | 2 | 6.033  | 5.484 | 5.445 | 5.442 | -6.264 |
| C10e | 2.864 | 1 | 304.265 | 2 | 5.774  | 5.209 | 5.370 | 5.382 | -6.781 |
| C10f | 2.890 | 1 | 295.992 | 2 | 0.000  | 5.191 | 5.218 | 5.220 | -4.994 |
| C10g | 2.897 | 1 | 332.937 | 2 | 0.000  | 5.338 | 5.286 | 5.282 | -6.072 |
| C10h | 2.889 | 1 | 313.789 | 2 | 0.000  | 5.302 | 5.249 | 5.244 | -5.365 |
| C10j | 2.865 | 1 | 253.563 | 2 | 0.000  | 5.289 | 5.132 | 5.119 | -5.679 |
| C10k | 2.872 | 1 | 290.508 | 2 | 0.000  | 5.212 | 5.200 | 5.199 | -6.736 |
| C2b  | 1.382 | 1 | 91.335  | 1 | 0.000  | 6.413 | 6.566 | 6.579 | -7.483 |
| C3a  | 1.458 | 0 | 150.204 | 1 | 11.597 | 6.465 | 6.492 | 6.493 | -7.397 |
| C3b  | 1.477 | 0 | 144.832 | 1 | 5.900  | 6.337 | 6.343 | 6.343 | -4.906 |
| C3d  | 1.480 | 0 | 156.555 | 1 | 5.909  | 6.340 | 6.365 | 6.365 | -4.094 |

|      |       |   |         |   |        |       |       |       |        |
|------|-------|---|---------|---|--------|-------|-------|-------|--------|
| C3e  | 1.485 | 0 | 142.901 | 1 | 5.694  | 6.124 | 6.338 | 6.345 | -4.729 |
| C3f  | 1.503 | 0 | 137.529 | 1 | 0.000  | 6.243 | 6.189 | 6.187 | -7.232 |
| C3g  | 1.508 | 0 | 160.961 | 1 | 0.000  | 6.050 | 6.233 | 6.237 | -7.659 |
| C3h  | 1.506 | 0 | 149.252 | 1 | 0.000  | 6.171 | 6.211 | 6.212 | -5.488 |
| C3i  | 1.464 | 0 | 115.315 | 1 | 5.636  | 6.162 | 6.278 | 6.283 | -8.071 |
| C3j  | 1.482 | 0 | 109.943 | 1 | 0.000  | 6.234 | 6.130 | 6.125 | -6.245 |
| C3k  | 1.487 | 0 | 133.375 | 1 | 0.000  | 6.209 | 6.174 | 6.172 | -7.195 |
| C5c  | 1.536 | 0 | 188.972 | 1 | 5.974  | 6.259 | 6.452 | 6.457 | -5.734 |
| C5e  | 1.452 | 0 | 178.530 | 1 | 5.480  | 6.182 | 6.378 | 6.380 | -6.667 |
| C5h  | 1.561 | 0 | 169.960 | 1 | 0.000  | 5.312 | 6.275 | 6.313 | -6.436 |
| C5i  | 1.469 | 1 | 150.656 | 1 | 5.674  | 7.215 | 6.861 | 6.839 | -6.456 |
| C5j  | 1.536 | 0 | 130.651 | 1 | 0.000  | 6.339 | 6.194 | 6.187 | -6.868 |
| C5k  | 1.542 | 0 | 154.083 | 1 | 0.000  | 6.249 | 6.237 | 6.237 | -6.626 |
| C6a  | 1.477 | 0 | 185.545 | 1 | 11.689 | 6.354 | 6.565 | 6.573 | -6.787 |
| C6b  | 1.500 | 0 | 145.284 | 1 | 0.000  | 6.410 | 6.201 | 6.195 | -6.378 |
| C6c  | 1.500 | 0 | 203.605 | 1 | 5.989  | 6.533 | 6.459 | 6.458 | -6.606 |
| C6d  | 1.498 | 0 | 191.896 | 1 | 5.958  | 6.267 | 6.437 | 6.440 | -7.027 |
| C6e  | 1.503 | 0 | 178.242 | 1 | 5.736  | 6.167 | 6.410 | 6.415 | -6.359 |
| C6g  | 1.526 | 0 | 196.302 | 1 | 0.000  | 6.452 | 6.304 | 6.299 | -6.473 |
| C6h  | 1.366 | 0 | 219.529 | 1 | 5.893  | 6.193 | 6.417 | 6.422 | -6.468 |
| C6i  | 1.395 | 0 | 164.891 | 1 | 5.441  | 6.158 | 6.324 | 6.328 | -5.507 |
| C6j  | 1.495 | 0 | 180.173 | 1 | 5.949  | 6.410 | 6.415 | 6.415 | -6.187 |
| C6k  | 1.506 | 0 | 168.716 | 1 | 0.000  | 6.246 | 6.245 | 6.245 | -6.386 |
| C7a  | 1.464 | 1 | 185.545 | 1 | 11.681 | 7.409 | 7.076 | 7.046 | -5.440 |
| C7b  | 1.482 | 1 | 180.173 | 1 | 5.945  | 7.194 | 6.926 | 6.909 | -4.697 |
| C7f  | 1.508 | 1 | 172.870 | 1 | 0.000  | 6.717 | 6.771 | 6.775 | -4.767 |
| C7g  | 1.513 | 1 | 196.302 | 1 | 0.000  | 6.578 | 6.815 | 6.833 | -6.440 |
| C7h  | 1.512 | 1 | 184.593 | 1 | 0.000  | 6.342 | 6.794 | 6.827 | -7.027 |
| C7i  | 1.518 | 0 | 136.023 | 1 | 5.665  | 7.215 | 6.342 | 6.304 | -6.715 |
| C7k  | 1.350 | 0 | 244.508 | 1 | 11.278 | 6.745 | 6.593 | 6.587 | -7.446 |
| C8aa | 1.355 | 0 | 264.107 | 1 | 11.459 | 6.194 | 6.635 | 6.657 | -6.820 |
| C8ab | 1.465 | 0 | 180.179 | 1 | 0.000  | 6.437 | 6.244 | 6.241 | -5.626 |
| C8ac | 1.447 | 0 | 208.171 | 1 | 5.718  | 6.440 | 6.434 | 6.433 | -6.162 |
| C8af | 1.469 | 0 | 214.522 | 1 | 0.000  | 6.322 | 6.306 | 6.306 | -6.529 |
| C8ag | 1.428 | 0 | 181.745 | 1 | 11.059 | 6.345 | 6.517 | 6.523 | -5.921 |
| C8ah | 1.446 | 0 | 176.373 | 1 | 5.369  | 6.324 | 6.369 | 6.369 | -5.862 |
| C8ai | 1.452 | 0 | 199.805 | 1 | 5.400  | 6.446 | 6.413 | 6.413 | -5.285 |
| C8aj | 1.450 | 0 | 188.096 | 1 | 5.376  | 6.577 | 6.391 | 6.389 | -5.515 |
| C8b  | 1.456 | 0 | 203.346 | 1 | 5.961  | 6.193 | 6.436 | 6.438 | -6.092 |
| C8d  | 1.460 | 0 | 215.068 | 1 | 5.970  | 6.453 | 6.458 | 6.459 | -6.291 |

|     |       |   |         |   |        |       |       |       |        |
|-----|-------|---|---------|---|--------|-------|-------|-------|--------|
| C8e | 1.442 | 0 | 243.060 | 1 | 11.776 | 6.210 | 6.650 | 6.666 | -8.004 |
| C8f | 1.460 | 0 | 237.688 | 1 | 5.995  | 6.280 | 6.499 | 6.502 | -6.702 |
| C8i | 1.423 | 0 | 216.634 | 1 | 17.136 | 6.640 | 6.734 | 6.742 | -5.740 |
| C8j | 1.441 | 0 | 211.262 | 1 | 11.383 | 6.585 | 6.584 | 6.584 | -7.087 |
| C8k | 1.446 | 0 | 234.694 | 1 | 11.454 | 6.469 | 6.629 | 6.634 | -5.259 |
| C8l | 1.445 | 0 | 222.985 | 1 | 11.399 | 6.733 | 6.607 | 6.603 | -7.702 |
| C8m | 1.464 | 0 | 201.415 | 1 | 5.745  | 6.456 | 6.431 | 6.431 | -8.363 |
| C8o | 1.487 | 0 | 219.475 | 1 | 0.000  | 6.249 | 6.324 | 6.326 | -7.610 |
| C8q | 1.468 | 0 | 235.757 | 1 | 5.776  | 6.330 | 6.494 | 6.496 | -7.264 |
| C8r | 1.486 | 0 | 230.385 | 1 | 0.000  | 6.384 | 6.343 | 6.342 | -5.824 |
| C8s | 1.492 | 0 | 253.817 | 1 | 0.000  | 6.332 | 6.386 | 6.389 | -5.118 |
| C8t | 1.490 | 0 | 242.108 | 1 | 0.000  | 6.363 | 6.365 | 6.365 | -6.107 |
| C8u | 1.449 | 0 | 209.331 | 1 | 11.168 | 6.274 | 6.579 | 6.588 | -7.638 |
| C8v | 1.467 | 0 | 203.959 | 1 | 5.419  | 6.192 | 6.429 | 6.431 | -6.114 |
| C8w | 1.473 | 0 | 227.391 | 1 | 5.451  | 6.262 | 6.473 | 6.476 | -6.808 |
| C8y | 1.443 | 0 | 173.829 | 1 | 5.687  | 6.343 | 6.371 | 6.371 | -5.698 |
| C8z | 1.461 | 0 | 168.457 | 1 | 0.000  | 6.485 | 6.222 | 6.217 | -7.186 |
| C9a | 1.488 | 0 | 235.283 | 1 | 11.789 | 7.456 | 6.660 | 6.626 | -4.567 |
| C9b | 1.507 | 0 | 229.911 | 1 | 6.003  | 6.672 | 6.509 | 6.505 | -8.047 |
| C9c | 1.512 | 0 | 253.342 | 1 | 6.042  | 6.664 | 6.554 | 6.550 | -6.565 |
| C9d | 1.510 | 0 | 241.633 | 1 | 6.012  | 6.588 | 6.531 | 6.530 | -6.829 |
| C9e | 1.514 | 0 | 227.980 | 1 | 5.783  | 7.495 | 6.504 | 6.479 | -8.491 |
| C9f | 1.533 | 0 | 222.608 | 1 | 0.000  | 6.415 | 6.353 | 6.350 | -7.209 |
| C9g | 1.538 | 0 | 246.039 | 1 | 0.000  | 6.362 | 6.396 | 6.398 | -7.857 |
| C9h | 1.536 | 0 | 234.330 | 1 | 0.000  | 6.573 | 6.375 | 6.367 | -3.818 |
| C9i | 1.494 | 0 | 200.393 | 1 | 5.725  | 6.474 | 6.444 | 6.443 | -6.385 |
| C9k | 1.426 | 0 | 242.642 | 1 | 0.000  | 6.331 | 6.334 | 6.334 | -7.072 |

#### Test set compounds

| Name <sup>a</sup> | S_aasN | Atype_N_69 | D/Dtr05 | Atype_C_43 | S_sCl | pIC <sub>50</sub> <sup>b</sup> | pIC <sub>50</sub> <sup>c</sup> | pIC <sub>d</sub> <sup>50</sup> | gScore <sup>e</sup> |
|-------------------|--------|------------|---------|------------|-------|--------------------------------|--------------------------------|--------------------------------|---------------------|
| B1d               | 1.292  | 1          | 114.277 | 1          | 0.000 | 6.578                          | 6.560                          | -                              | -7.467              |
| B2a               | 1.377  | 0          | 220.231 | 1          | 5.368 | 6.192                          | 6.410                          | -                              | -4.779              |
| B2b               | 1.386  | 0          | 155.555 | 1          | 5.832 | 6.335                          | 6.314                          | -                              | -5.145              |
| B2c               | 1.390  | 0          | 187.863 | 1          | 5.867 | 6.730                          | 6.373                          | -                              | -5.807              |
| B2e               | 1.398  | 0          | 155.641 | 1          | 5.455 | 6.119                          | 6.310                          | -                              | -5.059              |
| B2i               | 1.377  | 0          | 125.994 | 1          | 5.405 | 6.165                          | 6.246                          | -                              | -5.669              |
| B2k               | 1.396  | 0          | 150.398 | 1          | 0.000 | 6.212                          | 6.157                          | -                              | -6.405              |
| B4b               | 1.441  | 0          | 178.443 | 1          | 5.867 | 7.208                          | 6.382                          | -                              | -7.767              |
| B4c               | 1.445  | 0          | 210.751 | 1          | 5.902 | 7.194                          | 6.442                          | -                              | -6.638              |

|      |       |   |         |   |        |       |       |   |         |
|------|-------|---|---------|---|--------|-------|-------|---|---------|
| B4g  | 1.471 | 0 | 202.934 | 1 | 0.000  | 6.305 | 6.287 | - | -6.724  |
| B4k  | 1.450 | 0 | 173.286 | 1 | 0.000  | 6.241 | 6.225 | - | -6.679  |
| B5a  | 1.390 | 0 | 202.356 | 1 | 11.376 | 6.357 | 6.542 | - | -6.864  |
| B5h  | 1.430 | 0 | 203.092 | 1 | 0.000  | 6.188 | 6.267 | - | -7.451  |
| B6h  | 1.417 | 1 | 203.092 | 1 | 0.000  | 6.333 | 6.778 | - | -7.422  |
| B7c  | 1.370 | 0 | 251.837 | 1 | 5.928  | 6.469 | 6.476 | - | -10.732 |
| B7d  | 1.365 | 0 | 235.987 | 1 | 5.901  | 6.453 | 6.446 | - | -6.259  |
| B7j  | 1.351 | 0 | 228.049 | 1 | 11.264 | 6.585 | 6.565 | - | -7.249  |
| B7o  | 1.396 | 0 | 244.019 | 1 | 0.000  | 6.249 | 6.321 | - | -9.204  |
| B7q  | 1.381 | 0 | 256.290 | 1 | 5.528  | 6.331 | 6.479 | - | -10.095 |
| B7s  | 1.400 | 0 | 280.694 | 1 | 0.000  | 6.334 | 6.387 | - | -5.986  |
| B7u  | 1.362 | 0 | 228.136 | 1 | 10.871 | 6.276 | 6.560 | - | -6.999  |
| B7v  | 1.371 | 0 | 163.459 | 1 | 11.291 | 6.192 | 6.463 | - | -7.110  |
| B7w  | 1.381 | 0 | 252.540 | 1 | 5.396  | 6.266 | 6.469 | - | -9.535  |
| B7z  | 1.371 | 0 | 182.064 | 1 | 0.000  | 6.416 | 6.200 | - | -5.960  |
| B7zc | 1.360 | 0 | 226.642 | 1 | 5.477  | 6.438 | 6.416 | - | -6.613  |
| B7zg | 1.341 | 0 | 198.489 | 1 | 10.770 | 6.335 | 6.495 | - | -6.300  |
| B7zi | 1.360 | 0 | 222.893 | 1 | 5.346  | 6.449 | 6.406 | - | -6.311  |
| B8c  | 1.420 | 0 | 280.107 | 1 | 5.970  | 6.609 | 6.552 | - | -6.955  |
| B9c  | 2.743 | 1 | 367.524 | 2 | 5.961  | 5.498 | 5.425 | - | -6.286  |
| B9d  | 2.732 | 1 | 341.884 | 2 | 5.934  | 5.177 | 5.374 | - | -7.521  |
| B9g  | 2.779 | 1 | 356.057 | 2 | 0.000  | 5.332 | 5.267 | - | -6.359  |
| B9l  | 2.743 | 1 | 285.927 | 2 | 0.000  | 5.193 | 5.127 | - | -6.677  |
| C10d | 2.852 | 1 | 324.741 | 2 | 6.003  | 5.233 | 5.406 | - | -7.069  |
| C10i | 2.839 | 1 | 261.835 | 2 | 5.716  | 5.394 | 5.282 | - | -7.128  |
| C10l | 2.864 | 1 | 271.360 | 2 | 0.000  | 5.207 | 5.162 | - | -7.050  |
| C2a  | 1.364 | 1 | 96.707  | 1 | 5.606  | 7.367 | 6.712 | - | -7.438  |
| C2c  | 1.388 | 1 | 114.767 | 1 | 0.000  | 6.207 | 6.609 | - | -8.810  |
| C2d  | 1.386 | 1 | 103.058 | 1 | 0.000  | 6.572 | 6.588 | - | -7.495  |
| C3c  | 1.482 | 0 | 168.264 | 1 | 5.939  | 6.738 | 6.387 | - | -5.626  |
| C3l  | 1.485 | 0 | 121.666 | 1 | 0.000  | 6.364 | 6.152 | - | -8.189  |
| C5a  | 1.513 | 0 | 170.912 | 1 | 11.662 | 7.237 | 6.557 | - | -5.009  |
| C5b  | 1.531 | 0 | 165.540 | 1 | 5.935  | 6.382 | 6.407 | - | -4.452  |
| C5d  | 1.535 | 0 | 177.263 | 1 | 5.944  | 6.375 | 6.430 | - | -7.242  |
| C5f  | 1.557 | 0 | 158.237 | 1 | 0.000  | 6.406 | 6.253 | - | -5.180  |
| C5g  | 1.563 | 0 | 181.669 | 1 | 0.000  | 6.313 | 6.296 | - | -4.091  |
| C5l  | 1.540 | 0 | 142.374 | 1 | 0.000  | 6.193 | 6.216 | - | -5.650  |
| C6f  | 1.521 | 0 | 172.870 | 1 | 0.000  | 6.238 | 6.260 | - | -5.831  |
| C6l  | 1.504 | 0 | 157.007 | 1 | 0.000  | 6.135 | 6.223 | - | -5.958  |
| C7c  | 1.487 | 1 | 203.605 | 1 | 5.984  | 6.627 | 6.971 | - | -5.008  |

|      |       |   |         |   |        |       |       |   |        |
|------|-------|---|---------|---|--------|-------|-------|---|--------|
| C7d  | 1.485 | 1 | 191.896 | 1 | 5.954  | 6.697 | 6.949 | - | -7.308 |
| C7e  | 1.490 | 1 | 178.242 | 1 | 5.732  | 7.432 | 6.921 | - | -5.504 |
| C7j  | 1.487 | 1 | 145.284 | 1 | 0.000  | 6.604 | 6.713 | - | -6.523 |
| C7l  | 1.491 | 1 | 157.007 | 1 | 0.000  | 6.031 | 6.735 | - | -6.787 |
| C8a  | 1.438 | 0 | 208.718 | 1 | 11.710 | 6.330 | 6.586 | - | -6.040 |
| C8ad | 1.466 | 0 | 202.799 | 1 | 0.000  | 6.361 | 6.284 | - | -4.987 |
| C8ae | 1.471 | 0 | 226.231 | 1 | 0.000  | 6.386 | 6.328 | - | -8.514 |
| C8c  | 1.461 | 0 | 226.777 | 1 | 6.000  | 6.498 | 6.481 | - | -6.864 |
| C8g  | 1.465 | 0 | 261.120 | 1 | 6.035  | 6.316 | 6.544 | - | -5.993 |
| C8h  | 1.464 | 0 | 249.411 | 1 | 6.004  | 6.567 | 6.521 | - | -7.308 |
| C8n  | 1.482 | 0 | 196.043 | 1 | 0.000  | 6.261 | 6.281 | - | -6.977 |
| C8p  | 1.486 | 0 | 207.766 | 1 | 0.000  | 6.331 | 6.303 | - | -6.815 |
| C8x  | 1.471 | 0 | 215.682 | 1 | 5.426  | 6.441 | 6.451 | - | -7.620 |
| C9j  | 1.512 | 0 | 195.021 | 1 | 0.000  | 6.344 | 6.294 | - | -4.774 |
| C9l  | 1.515 | 0 | 206.744 | 1 | 0.000  | 6.272 | 6.316 | - | -4.817 |

<sup>a</sup>Compound names

<sup>b</sup>Observed activity

<sup>c</sup>Calculated activity using 2D-QSAR model

<sup>d</sup>LOO predicted activity

<sup>e</sup>Glide docking score (gScore)

**Table S3.** G-QSAR results consisting of compound names, values of important descriptors, and observed, calculated and LOO predicted activity values.

| Training set compounds |                        |                  |                   |            |                    |                                |                                |                                |
|------------------------|------------------------|------------------|-------------------|------------|--------------------|--------------------------------|--------------------------------|--------------------------------|
| Name <sup>a</sup>      | R3-<br>SsClE-<br>index | R2-<br>chi5chain | R2-<br>SsNH2count | R1-k1alpha | R1-<br>chi3Cluster | pIC <sub>50</sub> <sup>b</sup> | pIC <sub>50</sub> <sup>c</sup> | pIC <sub>50</sub> <sup>d</sup> |
| B1a                    | 0.780                  | 0.000            | 0                 | 0.000      | 0.000              | 6.409                          | 6.728                          | 6.790                          |
| B1b                    | 0.000                  | 0.000            | 0                 | 0.000      | 0.000              | 7.319                          | 6.622                          | 6.499                          |
| B1c                    | 0.000                  | 0.000            | 0                 | 0.000      | 0.000              | 6.201                          | 6.622                          | 6.696                          |
| B2d                    | 0.000                  | 0.000            | 0                 | 6.302      | 0.493              | 6.335                          | 6.505                          | 6.509                          |
| B2f                    | 0.000                  | 0.000            | 0                 | 5.035      | 0.204              | 6.241                          | 6.267                          | 6.267                          |
| B2g                    | 0.000                  | 0.000            | 0                 | 5.035      | 0.204              | 6.049                          | 6.267                          | 6.271                          |
| B2h                    | 0.000                  | 0.000            | 0                 | 5.035      | 0.204              | 6.171                          | 6.267                          | 6.269                          |
| B2j                    | 0.000                  | 0.000            | 0                 | 2.670      | 0.000              | 6.223                          | 6.285                          | 6.286                          |
| B2l                    | 0.000                  | 0.000            | 0                 | 2.670      | 0.000              | 6.361                          | 6.285                          | 6.283                          |
| B4a                    | 0.780                  | 0.000            | 0                 | 6.302      | 0.493              | 6.250                          | 6.611                          | 6.624                          |
| B4d                    | 0.000                  | 0.000            | 0                 | 6.302      | 0.493              | 6.371                          | 6.505                          | 6.508                          |
| B4e                    | 0.780                  | 0.000            | 0                 | 5.035      | 0.204              | 6.182                          | 6.373                          | 6.379                          |

|     |       |       |   |       |       |       |       |       |
|-----|-------|-------|---|-------|-------|-------|-------|-------|
| B4f | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.403 | 6.267 | 6.265 |
| B4h | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.312 | 6.267 | 6.266 |
| B4i | 0.780 | 0.000 | 0 | 2.670 | 0.000 | 6.382 | 6.391 | 6.391 |
| B4j | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.334 | 6.285 | 6.284 |
| B4l | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.193 | 6.285 | 6.286 |
| B5b | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.420 | 6.505 | 6.507 |
| B5c | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.538 | 6.505 | 6.504 |
| B5d | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.252 | 6.505 | 6.511 |
| B5e | 0.780 | 0.000 | 0 | 5.035 | 0.204 | 6.171 | 6.373 | 6.380 |
| B5f | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.231 | 6.267 | 6.268 |
| B5g | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.439 | 6.267 | 6.264 |
| B5i | 0.780 | 0.000 | 0 | 2.670 | 0.000 | 6.158 | 6.391 | 6.399 |
| B5j | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.331 | 6.285 | 6.284 |
| B5k | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.223 | 6.285 | 6.286 |
| B5l | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.127 | 6.285 | 6.288 |
| B6a | 0.780 | 0.000 | 1 | 6.302 | 0.493 | 7.357 | 7.080 | 7.055 |
| B6b | 0.000 | 0.000 | 1 | 6.302 | 0.493 | 7.143 | 6.974 | 6.961 |
| B6c | 0.000 | 0.000 | 1 | 6.302 | 0.493 | 7.469 | 6.974 | 6.936 |
| B6d | 0.000 | 0.000 | 1 | 6.302 | 0.493 | 7.194 | 6.974 | 6.957 |
| B6e | 0.780 | 0.000 | 1 | 5.035 | 0.204 | 6.609 | 6.842 | 6.861 |
| B6f | 0.000 | 0.000 | 1 | 5.035 | 0.204 | 6.706 | 6.736 | 6.738 |
| B6g | 0.000 | 0.000 | 1 | 5.035 | 0.204 | 6.572 | 6.736 | 6.747 |
| B6i | 0.780 | 0.000 | 1 | 2.670 | 0.000 | 6.697 | 6.860 | 6.874 |
| B6j | 0.000 | 0.000 | 1 | 2.670 | 0.000 | 6.618 | 6.754 | 6.764 |
| B6k | 0.000 | 0.000 | 1 | 2.670 | 0.000 | 6.730 | 6.754 | 6.756 |
| B6l | 0.000 | 0.000 | 1 | 2.670 | 0.000 | 6.025 | 6.754 | 6.806 |
| B7a | 0.780 | 0.000 | 0 | 6.302 | 0.493 | 6.333 | 6.611 | 6.621 |
| B7b | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.193 | 6.505 | 6.512 |
| B7e | 0.780 | 0.000 | 0 | 6.302 | 0.493 | 6.194 | 6.611 | 6.627 |
| B7f | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.272 | 6.505 | 6.510 |
| B7g | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.315 | 6.505 | 6.509 |
| B7h | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.572 | 6.505 | 6.503 |
| B7i | 0.780 | 0.000 | 0 | 6.302 | 0.493 | 6.650 | 6.611 | 6.609 |
| B7k | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.469 | 6.505 | 6.506 |
| B7l | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.745 | 6.505 | 6.499 |
| B7m | 0.780 | 0.000 | 0 | 5.035 | 0.204 | 6.449 | 6.373 | 6.370 |
| B7n | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.266 | 6.267 | 6.267 |
| B7p | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.326 | 6.267 | 6.266 |
| B7r | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.376 | 6.267 | 6.265 |
| B7t | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.365 | 6.267 | 6.265 |

|      |       |       |   |       |       |       |       |       |
|------|-------|-------|---|-------|-------|-------|-------|-------|
| B7x  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.335 | 6.267 | 6.266 |
| B7y  | 0.780 | 0.000 | 0 | 2.670 | 0.000 | 6.451 | 6.391 | 6.389 |
| B7za | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.192 | 6.285 | 6.286 |
| B7zb | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.334 | 6.285 | 6.284 |
| B7zd | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.361 | 6.285 | 6.283 |
| B7ze | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.384 | 6.285 | 6.283 |
| B7zf | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.322 | 6.285 | 6.284 |
| B7zh | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.322 | 6.285 | 6.284 |
| B7zj | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.578 | 6.285 | 6.279 |
| B8a  | 0.780 | 0.000 | 0 | 6.302 | 0.493 | 7.377 | 6.611 | 6.582 |
| B8b  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 7.523 | 6.505 | 6.480 |
| B8d  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.623 | 6.505 | 6.502 |
| B8e  | 0.780 | 0.000 | 0 | 5.035 | 0.204 | 6.331 | 6.373 | 6.374 |
| B8f  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.314 | 6.267 | 6.266 |
| B8g  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.305 | 6.267 | 6.266 |
| B8h  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.279 | 6.267 | 6.267 |
| B8i  | 0.780 | 0.000 | 0 | 2.670 | 0.000 | 6.271 | 6.391 | 6.395 |
| B8j  | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.334 | 6.285 | 6.284 |
| B8k  | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.331 | 6.285 | 6.284 |
| B8l  | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.197 | 6.285 | 6.286 |
| B9a  | 0.780 | 0.096 | 1 | 6.302 | 0.493 | 5.487 | 5.522 | 5.526 |
| B9b  | 0.000 | 0.096 | 1 | 6.302 | 0.493 | 5.126 | 5.416 | 5.440 |
| B9e  | 0.780 | 0.096 | 1 | 5.035 | 0.204 | 5.156 | 5.284 | 5.295 |
| B9f  | 0.000 | 0.096 | 1 | 5.035 | 0.204 | 5.185 | 5.178 | 5.178 |
| B9h  | 0.000 | 0.096 | 1 | 5.035 | 0.204 | 5.320 | 5.178 | 5.168 |
| B9i  | 0.780 | 0.096 | 1 | 2.670 | 0.000 | 5.334 | 5.302 | 5.299 |
| B9j  | 0.000 | 0.096 | 1 | 2.670 | 0.000 | 5.280 | 5.196 | 5.190 |
| B9k  | 0.000 | 0.096 | 1 | 2.670 | 0.000 | 5.198 | 5.196 | 5.196 |
| C10a | 0.813 | 0.096 | 1 | 6.302 | 0.493 | 5.544 | 5.527 | 5.525 |
| C10b | 0.000 | 0.096 | 1 | 6.302 | 0.493 | 5.195 | 5.416 | 5.434 |
| C10c | 0.000 | 0.096 | 1 | 6.302 | 0.493 | 5.484 | 5.416 | 5.411 |
| C10e | 0.813 | 0.096 | 1 | 5.035 | 0.204 | 5.209 | 5.289 | 5.296 |
| C10f | 0.000 | 0.096 | 1 | 5.035 | 0.204 | 5.191 | 5.178 | 5.178 |
| C10g | 0.000 | 0.096 | 1 | 5.035 | 0.204 | 5.338 | 5.178 | 5.167 |
| C10h | 0.000 | 0.096 | 1 | 5.035 | 0.204 | 5.302 | 5.178 | 5.170 |
| C10j | 0.000 | 0.096 | 1 | 2.670 | 0.000 | 5.289 | 5.196 | 5.189 |
| C10k | 0.000 | 0.096 | 1 | 2.670 | 0.000 | 5.212 | 5.196 | 5.195 |
| C2b  | 0.000 | 0.000 | 0 | 0.000 | 0.000 | 6.413 | 6.622 | 6.659 |
| C3a  | 0.813 | 0.000 | 0 | 6.302 | 0.493 | 6.465 | 6.615 | 6.621 |
| C3b  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.337 | 6.505 | 6.509 |

|      |       |       |   |       |       |       |       |       |
|------|-------|-------|---|-------|-------|-------|-------|-------|
| C3d  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.340 | 6.505 | 6.509 |
| C3e  | 0.813 | 0.000 | 0 | 5.035 | 0.204 | 6.124 | 6.377 | 6.386 |
| C3f  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.243 | 6.267 | 6.267 |
| C3g  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.050 | 6.267 | 6.271 |
| C3h  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.171 | 6.267 | 6.269 |
| C3i  | 0.813 | 0.000 | 0 | 2.670 | 0.000 | 6.162 | 6.395 | 6.404 |
| C3j  | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.234 | 6.285 | 6.286 |
| C3k  | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.209 | 6.285 | 6.286 |
| C5c  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.259 | 6.505 | 6.511 |
| C5e  | 0.813 | 0.000 | 0 | 5.035 | 0.204 | 6.182 | 6.377 | 6.384 |
| C5h  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 5.312 | 6.267 | 6.284 |
| C5i  | 0.813 | 0.000 | 0 | 2.670 | 0.000 | 7.215 | 6.395 | 6.366 |
| C5j  | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.339 | 6.285 | 6.284 |
| C5k  | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.249 | 6.285 | 6.285 |
| C6a  | 0.813 | 0.000 | 0 | 6.302 | 0.493 | 6.354 | 6.615 | 6.626 |
| C6b  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.410 | 6.505 | 6.507 |
| C6c  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.533 | 6.505 | 6.504 |
| C6d  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.267 | 6.505 | 6.510 |
| C6e  | 0.813 | 0.000 | 0 | 5.035 | 0.204 | 6.167 | 6.377 | 6.385 |
| C6g  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.452 | 6.267 | 6.264 |
| C6h  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.193 | 6.267 | 6.268 |
| C6i  | 0.813 | 0.000 | 0 | 2.670 | 0.000 | 6.158 | 6.395 | 6.404 |
| C6j  | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.410 | 6.285 | 6.283 |
| C6k  | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.246 | 6.285 | 6.285 |
| C7a  | 0.813 | 0.000 | 1 | 6.302 | 0.493 | 7.409 | 7.084 | 7.054 |
| C7b  | 0.000 | 0.000 | 1 | 6.302 | 0.493 | 7.194 | 6.974 | 6.957 |
| C7f  | 0.000 | 0.000 | 1 | 5.035 | 0.204 | 6.717 | 6.736 | 6.737 |
| C7g  | 0.000 | 0.000 | 1 | 5.035 | 0.204 | 6.578 | 6.736 | 6.747 |
| C7h  | 0.000 | 0.000 | 1 | 5.035 | 0.204 | 6.342 | 6.736 | 6.763 |
| C7i  | 0.813 | 0.000 | 1 | 2.670 | 0.000 | 7.215 | 6.864 | 6.833 |
| C7k  | 0.000 | 0.000 | 1 | 2.670 | 0.000 | 6.745 | 6.754 | 6.754 |
| C8aa | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.194 | 6.285 | 6.286 |
| C8ab | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.437 | 6.285 | 6.282 |
| C8ac | 0.813 | 0.000 | 0 | 2.670 | 0.000 | 6.440 | 6.395 | 6.394 |
| C8af | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.322 | 6.285 | 6.284 |
| C8ag | 0.813 | 0.000 | 0 | 2.670 | 0.000 | 6.345 | 6.395 | 6.397 |
| C8ah | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.324 | 6.285 | 6.284 |
| C8ai | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.446 | 6.285 | 6.282 |
| C8aj | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.577 | 6.285 | 6.280 |
| C8b  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.193 | 6.505 | 6.512 |

|     |       |       |   |       |       |       |       |       |
|-----|-------|-------|---|-------|-------|-------|-------|-------|
| C8d | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.453 | 6.505 | 6.506 |
| C8e | 0.813 | 0.000 | 0 | 6.302 | 0.493 | 6.210 | 6.615 | 6.631 |
| C8f | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.280 | 6.505 | 6.510 |
| C8i | 0.813 | 0.000 | 0 | 6.302 | 0.493 | 6.640 | 6.615 | 6.614 |
| C8j | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.585 | 6.505 | 6.503 |
| C8k | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.469 | 6.505 | 6.506 |
| C8l | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.733 | 6.505 | 6.499 |
| C8m | 0.813 | 0.000 | 0 | 5.035 | 0.204 | 6.456 | 6.377 | 6.375 |
| C8o | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.249 | 6.267 | 6.267 |
| C8q | 0.813 | 0.000 | 0 | 5.035 | 0.204 | 6.330 | 6.377 | 6.379 |
| C8r | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.384 | 6.267 | 6.265 |
| C8s | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.332 | 6.267 | 6.266 |
| C8t | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.363 | 6.267 | 6.265 |
| C8u | 0.813 | 0.000 | 0 | 5.035 | 0.204 | 6.274 | 6.377 | 6.381 |
| C8v | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.192 | 6.267 | 6.268 |
| C8w | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.262 | 6.267 | 6.267 |
| C8y | 0.813 | 0.000 | 0 | 2.670 | 0.000 | 6.343 | 6.395 | 6.397 |
| C8z | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.485 | 6.285 | 6.281 |
| C9a | 0.813 | 0.000 | 0 | 6.302 | 0.493 | 7.456 | 6.615 | 6.582 |
| C9b | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.672 | 6.505 | 6.501 |
| C9c | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.664 | 6.505 | 6.501 |
| C9d | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.588 | 6.505 | 6.503 |
| C9e | 0.813 | 0.000 | 0 | 5.035 | 0.204 | 7.495 | 6.377 | 6.338 |
| C9f | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.415 | 6.267 | 6.264 |
| C9g | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.362 | 6.267 | 6.265 |
| C9h | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.573 | 6.267 | 6.261 |
| C9i | 0.813 | 0.000 | 0 | 2.670 | 0.000 | 6.474 | 6.395 | 6.392 |
| C9k | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.331 | 6.285 | 6.284 |

**Test set compounds**

| Name <sup>a</sup> | R3-<br>SsCIE-<br>index | R2-<br>chi5chain | R2-<br>SsNH2count | R1-k1alpha | R1-<br>chi3Cluster | pIC <sub>50</sub> <sup>b</sup> | pIC <sub>50</sub> <sup>c</sup> | pIC <sub>50</sub> <sup>d</sup> |
|-------------------|------------------------|------------------|-------------------|------------|--------------------|--------------------------------|--------------------------------|--------------------------------|
| B1d               | 0.000                  | 0.000            | 0                 | 0.000      | 0.000              | 6.578                          | 6.622                          | -                              |
| B2a               | 0.780                  | 0.000            | 0                 | 6.302      | 0.493              | 6.192                          | 6.611                          | -                              |
| B2b               | 0.000                  | 0.000            | 0                 | 6.302      | 0.493              | 6.335                          | 6.505                          | -                              |
| B2c               | 0.000                  | 0.000            | 0                 | 6.302      | 0.493              | 6.730                          | 6.505                          | -                              |
| B2e               | 0.780                  | 0.000            | 0                 | 5.035      | 0.204              | 6.119                          | 6.373                          | -                              |
| B2i               | 0.780                  | 0.000            | 0                 | 2.670      | 0.000              | 6.165                          | 6.391                          | -                              |
| B2k               | 0.000                  | 0.000            | 0                 | 2.670      | 0.000              | 6.212                          | 6.285                          | -                              |
| B4b               | 0.000                  | 0.000            | 0                 | 6.302      | 0.493              | 7.208                          | 6.505                          | -                              |

|      |       |       |   |       |       |       |       |   |
|------|-------|-------|---|-------|-------|-------|-------|---|
| B4c  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 7.194 | 6.505 | - |
| B4g  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.305 | 6.267 | - |
| B4k  | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.241 | 6.285 | - |
| B5a  | 0.780 | 0.000 | 0 | 6.302 | 0.493 | 6.357 | 6.611 | - |
| B5h  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.188 | 6.267 | - |
| B6h  | 0.000 | 0.000 | 1 | 5.035 | 0.204 | 6.333 | 6.736 | - |
| B7c  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.469 | 6.505 | - |
| B7d  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.453 | 6.505 | - |
| B7j  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.585 | 6.505 | - |
| B7o  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.249 | 6.267 | - |
| B7q  | 0.780 | 0.000 | 0 | 5.035 | 0.204 | 6.331 | 6.373 | - |
| B7s  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.334 | 6.267 | - |
| B7u  | 0.780 | 0.000 | 0 | 5.035 | 0.204 | 6.276 | 6.373 | - |
| B7v  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.192 | 6.267 | - |
| B7w  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.266 | 6.267 | - |
| B7z  | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.416 | 6.285 | - |
| B7zc | 0.780 | 0.000 | 0 | 2.670 | 0.000 | 6.438 | 6.391 | - |
| B7zg | 0.780 | 0.000 | 0 | 2.670 | 0.000 | 6.335 | 6.391 | - |
| B7zi | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.449 | 6.285 | - |
| B8c  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.609 | 6.505 | - |
| B9c  | 0.000 | 0.096 | 1 | 6.302 | 0.493 | 5.498 | 5.416 | - |
| B9d  | 0.000 | 0.096 | 1 | 6.302 | 0.493 | 5.177 | 5.416 | - |
| B9g  | 0.000 | 0.096 | 1 | 5.035 | 0.204 | 5.332 | 5.178 | - |
| B9l  | 0.000 | 0.096 | 1 | 2.670 | 0.000 | 5.193 | 5.196 | - |
| C10d | 0.000 | 0.096 | 1 | 6.302 | 0.493 | 5.233 | 5.416 | - |
| C10i | 0.813 | 0.096 | 1 | 2.670 | 0.000 | 5.394 | 5.307 | - |
| C10l | 0.000 | 0.096 | 1 | 2.670 | 0.000 | 5.207 | 5.196 | - |
| C2a  | 0.813 | 0.000 | 0 | 0.000 | 0.000 | 7.367 | 6.732 | - |
| C2c  | 0.000 | 0.000 | 0 | 0.000 | 0.000 | 6.207 | 6.622 | - |
| C2d  | 0.000 | 0.000 | 0 | 0.000 | 0.000 | 6.572 | 6.622 | - |
| C3c  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.738 | 6.505 | - |
| C3l  | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.364 | 6.285 | - |
| C5a  | 0.813 | 0.000 | 0 | 6.302 | 0.493 | 7.237 | 6.615 | - |
| C5b  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.382 | 6.505 | - |
| C5d  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.375 | 6.505 | - |
| C5f  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.406 | 6.267 | - |
| C5g  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.313 | 6.267 | - |
| C5l  | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.193 | 6.285 | - |
| C6f  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.238 | 6.267 | - |
| C6l  | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.135 | 6.285 | - |

|      |       |       |   |       |       |       |       |   |
|------|-------|-------|---|-------|-------|-------|-------|---|
| C7c  | 0.000 | 0.000 | 1 | 6.302 | 0.493 | 6.627 | 6.974 | - |
| C7d  | 0.000 | 0.000 | 1 | 6.302 | 0.493 | 6.697 | 6.974 | - |
| C7e  | 0.813 | 0.000 | 1 | 5.035 | 0.204 | 7.432 | 6.846 | - |
| C7j  | 0.000 | 0.000 | 1 | 2.670 | 0.000 | 6.604 | 6.754 | - |
| C7l  | 0.000 | 0.000 | 1 | 2.670 | 0.000 | 6.031 | 6.754 | - |
| C8a  | 0.813 | 0.000 | 0 | 6.302 | 0.493 | 6.330 | 6.615 | - |
| C8ad | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.361 | 6.285 | - |
| C8ae | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.386 | 6.285 | - |
| C8c  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.498 | 6.505 | - |
| C8g  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.316 | 6.505 | - |
| C8h  | 0.000 | 0.000 | 0 | 6.302 | 0.493 | 6.567 | 6.505 | - |
| C8n  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.261 | 6.267 | - |
| C8p  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.331 | 6.267 | - |
| C8x  | 0.000 | 0.000 | 0 | 5.035 | 0.204 | 6.441 | 6.267 | - |
| C9j  | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.344 | 6.285 | - |
| C9l  | 0.000 | 0.000 | 0 | 2.670 | 0.000 | 6.272 | 6.285 | - |

<sup>a</sup>Compound names

<sup>b</sup>Observed activity

<sup>c</sup>Calculated activity using G-QSAR model

<sup>d</sup>LOO predicted activity

**Table S4.** QAAR results consisting of compound names, values of important descriptors, and observed, calculated and LOO predicted activity values.

| Name <sup>a</sup> | Jurs-FPSA-2 | R2-chi3Cluster | R3-ElectronegativityCount | pIC <sub>50</sub> <sup>b</sup> | pIC <sub>50</sub> <sup>c</sup> | pIC <sub>50</sub> <sup>d</sup> |
|-------------------|-------------|----------------|---------------------------|--------------------------------|--------------------------------|--------------------------------|
| B1b               | 0.925       | 0.000          | 0.662                     | 0.018                          | 0.173                          | 0.244                          |
| B4b               | 1.175       | 0.000          | 0.662                     | 1.265                          | 1.138                          | 1.106                          |
| B4c               | 1.261       | 0.000          | 0.638                     | 1.321                          | 1.333                          | 1.336                          |
| B6a               | 1.606       | 0.408          | 0.735                     | 1.306                          | 1.419                          | 1.480                          |
| B6b               | 1.629       | 0.408          | 0.662                     | 0.938                          | 1.094                          | 1.108                          |
| B6c               | 1.639       | 0.408          | 0.638                     | 1.139                          | 0.996                          | 0.987                          |
| B6d               | 1.887       | 0.408          | 0.668                     | 1.996                          | 2.121                          | 2.186                          |
| B8a               | 1.487       | 0.612          | 0.735                     | 0.085                          | 0.062                          | 0.040                          |
| B8b               | 1.792       | 0.612          | 0.662                     | 1.232                          | 0.824                          | 0.748                          |
| C2a               | 0.985       | 0.000          | 0.597                     | 0.083                          | 0.038                          | 0.010                          |
| C5a               | 1.302       | 0.000          | 0.597                     | 1.292                          | 1.259                          | 1.252                          |
| C5i               | 1.320       | 0.000          | 0.597                     | 1.335                          | 1.327                          | 1.327                          |
| C7a               | 1.705       | 0.408          | 0.597                     | 1.312                          | 1.020                          | 0.986                          |
| C7b               | 1.761       | 0.408          | 0.555                     | 0.963                          | 0.998                          | 1.008                          |

|     |       |       |       |       |       |       |
|-----|-------|-------|-------|-------|-------|-------|
| C7e | 1.832 | 0.408 | 0.597 | 1.120 | 1.509 | 1.568 |
| C7i | 1.894 | 0.408 | 0.597 | 1.992 | 1.747 | 1.694 |
| C9a | 1.836 | 0.612 | 0.597 | 0.137 | 0.628 | 0.782 |
| C9e | 1.956 | 0.612 | 0.597 | 1.243 | 1.090 | 1.054 |

<sup>a</sup>Compound names

<sup>b</sup>Observed activity<sup>(CDK5-CDK2)</sup>

<sup>c</sup>Calculated activity<sup>(CDK5-CDK2)</sup> using QAAR model

<sup>d</sup>LOO predicted activity<sup>(CDK5-CDK2)</sup>