Supplementary Material for "Alchemical Grid Dock (AlGDock) calculations in the D3R Grand Challenge 3: Binding Free Energies between Flexible Ligands and Rigid Receptors"

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1 Supplementary Methods

1.1 Homologous Structures

The following structures were identified as having greater than 90% sequence homology to the template sequences and were downloaded from the Protein Data Bank.

Cathepsin S: 1GLO, 1MS6, 1NPZ, 1NQC, 2C0Y, 2F1G, 2FQ9, 2FRA, 2FRQ, 2FT2, 2FUD, 2FYE, 2G6D, 2G7Y, 2H7J, 2HH5, 2HHN, 2HXZ, 2OP3, 2R9M, 2R9N, 2R9O, 3IEJ, 3KWN, 3MPE, 3MPF, 3N3G, 3N4C, 3OVX.

VEGFR2: 1VR2, 1Y6A, 1Y6B, 1YWN, 2OH4, 2P2H, 2P2I, 2QU5, 2QU6, 2RL5, 2XIR, 3B8Q, 3B8R, 3BE2, 3C7Q, 3CJF, 3CJG, 3CP9, 3CPB, 3CPC, 3DTW, 3EFL, 3EWH, 3U6J, 3VHE, 3VHK, 3VID, 3VNT, 3VO3, 4AG8, 4AGC, 4AGD, 4ASD, 4ASE.

JAK2: 2B7A, 2W1I, 2XA4, 3E62, 3E63, 3E64, 3FUP, 3IO7, 3IOK, 3JY9, 3KCK, 3KRR, 3LPB, 3Q32, 3RVG, 3TJC, 3TJD, 3UGZ, 3ZMM, 4AQC, 4BBE, 4BBF, 4E4M, 4E6D, 4E6Q, 4F08, 4F09, 4GFM, 4GL9, 4GMY, 4HGE, 4IVA, 4JI9, 4JIA.

p38-α: 1A9U, 1BL6, 1BL7, 1BMK, 1DI9, 1IAN, 1KV1, 1KV2, 1LEW, 1LEZ, 1M7Q, 1OUK, 1OUY, 1OVE, 1OZ1, 1P38, 1R39, 1R3C, 1W7H, 1W82, 1W83, 1W84, 1WBN, 1WBO, 1WBS, 1WBT, 1WBV, 1WBW, 1WFC, 1YQJ, 1YW2, 1YWR, 1ZYJ, 1ZZ2, 1ZZL, 2BAJ, 2BAK, 2BAL, 2BAQ, 2EWA, 2FSL, 2FSM, 2FSO, 2FST, 2GFS, 2GHL, 2GHM, 2GTM, 2GTN, 2I0H, 2LGC, 2NPQ, 2OKR, 2ONL, 2OZA, 2PUU, 2QD9, 2RG5, 2RG6, 2Y8O, 2YIS, 2YIW, 2YIX, 2ZAZ, 2ZB0, 2ZB1, 3BV2, 3BV3, 3BX5, 3C5U, 3CTQ, 3D7Z, 3D83, 3DS6, 3DT1, 3E92, 3E93, 3FC1, 3FI4, 3FKL, 3FKN, 3FKO, 3FL4, 3FLN, 3FLQ, 3FLS, 3FLW, 3FLY, 3FLZ, 3FMH, 3FMJ, 3FMK, 3FML, 3FMM, 3FMN, 3FSF, 3FSK, 3GC7, 3GCP, 3GCQ, 3GCS, 3GCU, 3GCV, 3GFE, 3GI3, 3HA8, 3HEC, 3HEG, 3HL7, 3HLL, 3HP2, 3HP5, 3HRB, 3HUB, 3HUC, 3HV3, 3HV4, 3HV5, 3HV6, 3HV7. 3HVC, 3IPH, 3ITZ, 3IW5, 3IW6, 3IW7, 3IW8, 3K3I, 3K3J, 3KF7, 3KQ7, 3L8S, 3L8X, 3LFA, 3LFB, 3LFC, 3LFD, 3LFE, 3LFF, 3LHJ, 3MGY, 3MH0, 3MH1, 3MH2, 3MH3, 3MPA, 3MPT, 3MVL, 3MVM, 3MW1, 3NEW, 3NNU, 3NNV, 3NNW, 3NNX, 3NWW, 3O8P, 3O8T, 3O8U, 3OBG, 3OBJ, 3OC1, 3OCG, 3OD6, 3ODY, 3ODZ, 3OEF, 3P4K, 3P5K, 3P78, 3P79, 3P7A, 3P7B, 3P7C, 3PG3, 3PY3, 3QUD, 3QUE, 3RIN, 3ROC, 3S3I, 3S4Q, 3TG1, 3U8W, 3UVP, 3UVQ, 3UVR, 3ZS5, 3ZSG, 3ZSH, 3ZSI, 3ZYA, 4A9Y, 4AA0, 4AA4, 4AA5, 4AAC, 4DLI, 4DLJ, 4E5A, 4E5B, 4E6A, 4E6C, 4E8A, 4EH2, 4EH3, 4EH4, 4EH5, 4EH6, 4EH7, 4EH8, 4EH9, 4EHV, 4EWQ, 4F9W, 4F9Y, 4FA2, 4GEO, 4KA3, 4KIN, 4KIP, 4KIQ, 4LOO, 4LOP, 4LOQ.

1.2 Binding Site Residues

The following residues in the template structure were identified as being in the binding site of each receptor.

Cathepsin S: 23 25 26 67 68 69 70 71 161 162 163 164 165

VEGFR2: 840 848 865 866 867 868 869 885 898 899 900 914 915 916 917 918 919 922 923 924 1031 1032 1033 1034 1035 1036 1044 1046

JAK2: 858 859 860 867 869 884 933 935 936 937 939 940 984 987 997 998

p38-α: 40 41 42 43 59 60 61 62 63 64 75 80 83 92 93 94 95 108 109 110 111 112 113 224 225 226 227 228 229 230 231 232 233 234 235 236 237 238 239 240 241 242 243 244 245

1.3 Molecular Docking Parameters

grid_spacing	0.25
energy_cutoff_distance	9999
attractive_exponent	6
repulsive_exponent	12
distance_dielectric	yes
dielectric_factor	4
bump_filter	yes
bump_overlap	0.75

Table 1: Parameters for showbox

max_orientations	5000
flexible_ligand	yes
min_anchor_size	40
pruning_max_orients	1000
pruning_clustering_cutoff	1000
pruning_conformer_score_cutoff	25.0
max_bumps_anchor	12
max_bumps_growth	12
num_scored_conformers	1000
cluster_conformations	yes
cluster_rmsd_threshold	2.0

Table 2: Parameters for UCSF DOCK 6