

In Silico Methods for Identification of Potential Active Sites of Therapeutic Targets

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Table S1 Ligand-specific methods in the identification of binding sites

| Names | Year | Methods | Predicted type of binding site | URL | Available |
|--------------------|------|------------|---|---|-----------|
| CHED [1] | 2007 | Web server | Metal-binding site | http://ligin.weizmann.ac.il/ched/ | NA |
| FINDSITE-metal [2] | 2011 | Web server | Metal-binding site | http://cssb.biology.gatech.edu/findsite-metal/ | FOSS |
| IonCom [3] | 2016 | Web server | Metal-binding site and acid radical ion-binding site | http://zhanglab.ccmb.med.umich.edu/IonCom/ | FOSS |
| ATPint [4] | 2009 | Web server | ATP -binding site | http://www.imtech.res.in/raghava/atpint/ | NA |
| ATPsite [5] | 2011 | Web server | ATP -binding site | http://biomine.ece.ualberta.ca/ATPsite/ | NA |
| TargetATPsite [6] | 2013 | Web server | ATP -binding site | http://www.csbio.sjtu.edu.cn/bioinf/TargetATPsite/ | Free |
| ATPbind [7] | 2018 | Web server | ATP-binding site | http://zhanglab.ccmb.med.umich.edu/ATPbind/ | Free |
| MetaDBSite [8] | 2011 | Web server | DNA-binding site | http://sysbio.zju.edu.cn/metadbsite/ | Free |
| DNABR [9] | 2012 | Web server | DNA-binding site | http://www.cbi.seu.edu.cn/DNABR/ | Free |
| TargetDNA [10] | 2016 | Web server | DNA-binding site | http://202.119.84.36:3079/TargetDNA/ | Free |
| DRNApred [11] | 2017 | Web server | DNA/RNA-binding site | http://biomine.cs.vcu.edu/servers/DRNApred/ | Free |
| NsitePred [12] | 2012 | Web server | Nucleotides-binding site | http://biomine.ece.ualberta.ca/nSITEpred/ | NA |
| TargetS [13] | 2013 | Web server | Nucleotides-binding site | http://www.csbio.sjtu.edu.cn/bioinf/TargetS/ | Free |
| TargetSOS [14] | 2014 | Web server | Nucleotides-binding site | http://www.csbio.sjtu.edu.cn/bioinf/TargetSOS/ | Free |
| TargetNUCs [15] | 2016 | Web server | Nucleotides-binding site | http://csbio.njust.edu.cn/bioinf/TargetNUCs/ | Free |
| SXGBsite [16] | 2019 | Software | Nucleotide-binding site, DNA-binding site, Mg ²⁺ -binding site | https://github.com/Lightness7/SXGBsite/ | FOSS |
| GraphBind [17] | 2021 | Web server | Nucleic-acid-binding site | http://www.csbio.sjtu.edu.cn/bioinf/GraphBind/ | FOSS |
| DRAF [18] | 2018 | Web server | TF-binding site | https://www.cbrc.kaust.edu.sa/DRAF/index.php/ | FOSS |
| MTTFsite [19] | 2019 | Web server | TF-binding site | http://hlt.hitsz.edu.cn/MTTFsite/ | FOSS |
| Anchor [20] | 2019 | Software | TF-binding site | https://github.com/GuanLab/Anchor/ | FOSS |
| FactorNet [21] | 2019 | Software | TF-binding site | http://github.com/ucicbcl/FactorNet/ | FOSS |
| Leopard [22] | 2021 | Software | TF-binding site | https://github.com/GuanLab/Leopard/ | FOSS |
| DeepGRN [23] | 2021 | Software | TF-binding site | https://github.com/jianlin-cheng/DeepGRN/ | FOSS |
| RBinds [24] | 2020 | Web server | RNA-binding site | http://zhaoserver.com.cn/RBinds/RBinds.html/ | Free |
| iCircRBP-DHN [25] | 2021 | Software | RNA-binding site | https://github.com/houzl3416/iCircRBP-DHN/ | FOSS |
| TargetM6A [26] | 2016 | Web server | N6-methyladenosine-binding site | http://csbio.njust.edu.cn/bioinf/TargetM6A/ | Free |
| TS-m6A-DL [27] | 2021 | Web server | N6-methyladenosine-binding site | http://nscibio.jbnu.ac.kr/tools/TS-m6A-DL/ | NA |
| VitaPred [28] | 2013 | Web server | Vitamin interacting residues | http://crdd.osdd.net/raghava/vitapred/ | Free |
| GTP-TP-RBF [29] | 2016 | Web server | GTP-binding site | http://140.138.155.226/~kahn/gtp-tp/ | NA |
| FAD-ETC-RBF [30] | 2016 | Web server | FAD(flavin adenine dinucleotide)-binding site | http://140.138.155.226/~kahn/Bioinformatics/ | NA |
| HEMEsPred [31] | 2018 | Web server | Heme-binding site | http://www.inforstation.com/HEMEsPred/ | Free |
| SAMBinder [32] | 2020 | Web server | S-adenosyl-L-methionine (SAM) | https://webs.iiitd.edu.in/raghava/sambinder/ | FOSS |

Table S2 General-purpose methods in the identification of binding sites

| Names | Year | Methods | Types | URL | Available |
|----------------------|------|------------------|---------------------|---|-----------|
| ConCavity [33] | 2009 | Sequence-based | Web server | http://compbio.cs.princeton.edu/concavity/ | FOSS |
| MPLs-Pred [34] | 2019 | Sequence-based | Web server | http://icdtools.nenu.edu.cn/ | Free |
| FunFOLD [35] | 2011 | Template-based | Web server | http://www.reading.ac.uk/bioinf/FunFOLD/ | FOSS |
| COFACTOR [36] | 2012 | Template-based | Web server | https://zhanglab.ccmb.med.umich.edu/COFACTOR/ | Free |
| WebPDBinder [37] | 2013 | Template-based | Web server | http://pdbinder.bio.uniroma2.it/PDBinder | FOSS |
| GalaxySite [38] | 2014 | Template-based | Web server | http://galaxy.seoklab.org/site/ | Free |
| LIBRA [39] | 2015 | Template-based | Web server | http://www.computationalbiology.it/software/LIBRAv1.zip/ | FOSS |
| LIBRA-WA [40] | 2017 | Template-based | Web server | http://biochimica3.bio.uniroma3.it/LIBRAWA/ | NA |
| Sitemap [41] | 2009 | Geometric-based | Software | https://www.schrodinger.com/products/sitemap/ | FOSS |
| MSPocket [42] | 2010 | Geometric-based | Web server | http://appserver.biotec.tu-dresden.de/MSPocket/ | FOSS |
| Fpocket [43] | 2010 | Geometric-based | Web server/software | http://www.sourceforge.net/projects/fpocket/ | FOSS |
| LISE [44] | 2013 | Geometric-based | Web server | http://lise.ibms.sinica.edu.tw/ | Free |
| Patch-Surfer2.0 [45] | 2014 | Geometric-based | Web server | http://kiharalab.org/patchsurfer2.0/ | NA |
| CB-Dock [46] | 2019 | Geometric-based | Web server | http://cao.labshare.cn/cb-dock/ | Free |
| SITEHOUND [47] | 2009 | Energetic-based | Web server | http://sitehound.sanchezlab.org/ | NA |
| FTSite [48] | 2012 | Energetic-based | Web server | https://ftsites.bu.edu/ | Free |
| SiteComp [49] | 2012 | Energetic-based | Web server | http://sitecomp.sanchezlab.org/ | Free |
| MetaPocket 2.0 [50] | 2011 | Consensus-based | Web server | http://projects.biotec.tu-dresden.de/metapocket/ | Free |
| COACH [51] | 2013 | Consensus-based | Web server | http://zhanglab.ccmb.med.umich.edu/COACH/ | FOSS |
| DeepSite [52] | 2017 | Machine learning | Web server | https://playmolecule.com/deepsite/ | Free |
| COACH-D [53] | 2018 | Machine learning | Web server | http://yanglab.nankai.edu.cn/COACH-D/ | Free |
| P2Rank [54] | 2018 | Machine learning | Web server | http://siret.ms.mff.cuni.cz/p2rank/ | FOSS |
| BIPSPI [55] | 2018 | Machine learning | Web server | http://bipsi.cnb.csic.es/ | FOSS |
| Taba [56] | 2019 | Machine learning | Web server | https://github.com/azevedolab/taab/ | FOSS |
| DeepBind [57] | 2015 | Deep learning | Web server | http://tools.genes.toronto.edu/deepbind/ | FOSS |
| DeepDTA [58] | 2018 | Deep learning | Web server | https://github.com/hkmztrk/DeepDTA/ | FOSS |
| KDEEP [59] | 2018 | Deep learning | Web server | https://playmolecule.com/Kdeep/ | NA |
| DeepCSeqSite [60] | 2019 | Deep learning | Web server | https://github.com/yfCuiFaith/DeepCSeqSite/ | FOSS |
| DeepConv-DTI [61] | 2019 | Deep learning | Web server | https://github.com/GIST-CSBL/DeepConv-DTI/ | FOSS |
| DeepDrug3D [62] | 2019 | Deep learning | Web server | https://github.com/pulimeng/DeepDrug3D/ | FOSS |
| Onionnet [63] | 2019 | Deep learning | Web server | http://github.com/zhenglz/onionnet/ | FOSS |
| PUResNet [64] | 2021 | Deep learning | Web server | https://github.com/jivankandel/PUResNet/ | FOSS |

Table S3 Software or tools in the assessment of druggability

| Name | Methods | Types | Pocket search method | Druggable criteria | URL | Available |
|--------------------|------------------|------------|--|--|---|-----------|
| PockDrug [65] | Structured-based | Web server | Prox and Fpocket | 0.87 ± 0.15 score | http://pockdrug.rpbs.univ-paris-diderot.fr/cgi-bin/index.py?page=home/ | FOSS |
| FTMap [66] | Hotspot-based | Web server | Solvent mapping algorithm | S>16 and the presence of at least one additional hotspot within 8 Å of a strong hotspot. | http://ftmap.bu.edu/login.php/ | Free |
| Sitemap [41] | Structured-based | Software | Geometric and energetic criteria on 3D grids | SiteScore>0.8 and Dscore>0.83 | https://www.schrodinger.com/products/sitemap/ | FOSS |
| Fpocket [67] | Structured-based | Software | Radii values between minimal and maximal in a-spheres. | 0.5–0.7(druggable); 0.7–1.0 (highly druggable) | http://www.sourceforge.net/projects/fpocket/ | FOSS |
| DoGSiteScorer [68] | Structured-based | Web server | 3D image enhancement techniques | A pocket volume of 1466 Å ³ , a depth of 19.27 Å as well as a polar amino acid ratio of 0.5 | https://www.biosolveit.de/DoGSiteScorer/ | FOSS |

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