**Supplementary Table S1. The dataset used by SitePredict (100 chains).**

|  |
| --- |
| 2Z4N\_A, 3HOG\_A, 4C2M\_A, 3AV4\_A, 3VOC\_A, 1EJ6\_A, 4A0C\_A, 2HPI\_A, 3S5K\_A, 2QF7\_A, 2B5L\_A, 4DDT\_A, 4OGC\_A, 4ANJ\_A, 1PS3\_A, 4KOE\_A, 3F2B\_A, 2WK3\_A, 4L3T\_A, 3ZQJ\_A, 3SE6\_A, 2W3K\_A, 1Q2L\_A, 1PD1\_A, 2WYH\_A, 1FFY\_A, 4K6M\_A, 2ATQ\_A, 2OAJ\_A, 4A7K\_A, 4K5L\_A, 2B3X\_A, 3KZ4\_A, 3ZGZ\_A, 3BJC\_A, 3W5K\_A, 3WAJ\_A, 3UJZ\_A, 1GAX\_A, 2XRG\_A, 3IHP\_A, 1TAQ\_A, 4H3S\_A, 3SEV\_A, 2X2L\_A, 2RHS\_A, 3AYF\_A, 4FWE\_A, 3PPC\_A, 2Y3U\_A, 4BS9\_A, 2FGZ\_A, 1BG3\_A, 2EAB\_A, 1Q55\_A, 1G8K\_A, 1V7V\_A, 1PU4\_A, 1D6U\_A, 1LCF\_A , 1HC1\_A, 1MWH\_A, 3BG5\_A, 1SDD\_A, 3T51\_A, 3PGB\_A, 2YEV\_A, 1I50\_A, 2ZXQ\_A, 4CMQ\_A, 3PIF\_A, 3Q23\_A, 4OGC\_A, 1A9X\_A, 3LDS\_A, 3UFH\_A, 1FGQ\_A, 3CF4\_A, 1KMP\_A, 2IAH\_A, 3UUS\_A, 3VTH\_A, 4AIQ\_A, 1BY5\_A, 1LFG\_A, 3S9L\_A, 1A73\_A, 1AF6\_A, 1AMU\_A, 1B70\_A, 1C1H\_A, 1CS4\_A, 1D9Z\_A, 1F6B\_A, 1FXU\_A, 1GQI\_A, 1H6P\_A,4II3\_A, 4NAB\_A, 4G1E\_A |

Note: PDB chains are described by their PDB IDs followed by chain IDs.

**Supplementary Table S2. The zinc-binding sites predicted by SitePredict and their filtering by mFASD.**

|  |  |  |  |
| --- | --- | --- | --- |
| **PDB chain ID** | **Predicted zinc-binding sites****(amino acid IDs)** | **Experimental fact** | **mFASD prediction** |
| 1BG3\_A | 217,220,221,224 | non-zinc-binding | non-zinc-binding |
| 1Q55\_A | 450,532,533,534 | non-zinc-binding | non-zinc-binding |
| 1G8K\_A | 195,165,166,423 | non-zinc-binding | zinc-binding |
| 1V7V\_A | 385,424,491,493 | non-zinc-binding | non-zinc-binding |
| 1PU4\_A | 521,522,684 | non-zinc-binding | zinc-binding |
| 1D6U\_A | 526,614,689 | non-zinc-binding | zinc-binding |
| 1LCF\_A | 173,499,507,588 | non-zinc-binding | non-zinc-binding |
| 1HC1\_A | 562,606,608,609 | non-zinc-binding | non-zinc-binding |
| 1MWH\_A | 733,790,1078 | non-zinc-binding | non-zinc-binding |
| 1LFG\_A | 157,172,499,588 | non-zinc-binding | non-zinc-binding |
| 1CS4\_A | 430,458,461 | non-zinc-binding | non-zinc-binding |
| 1C1H\_A | 183,222,264 | non-zinc-binding | non-zinc-binding |
| 2FGL\_A | 228,230,259 | non-zinc-binding | non-zinc-binding |
| 2EAB\_A | 605,606,607,609 | non-zinc-binding | non-zinc-binding |
| 2HPI\_A | 20,47,214 | zinc-binding | zinc-binding |
| 2QF7\_A | 713,747,749 | zinc-binding | zinc-binding |
| 2B5L\_A | 313,363,725,726 | zinc-binding | zinc-binding |
| 1PS3\_A | 90,92,204,471 | zinc-binding | zinc-binding |
| 2GAG\_A | 584,585,586 | zinc-binding | zinc-binding |
| 1Q2L\_A | 88,91,92 | zinc-binding | zinc-binding |
| 1PD1\_A | 231,234,253,256 | zinc-binding | zinc-binding |
| 2W3K\_A | 108,112,189 | zinc-binding | zinc-binding |
| 1FFY\_A | 886,889,906,909 | zinc-binding | zinc-binding |
| 2ATQ\_A | 41,45,668,672 | zinc-binding | non-zinc-binding |
| 2OAJ\_A | 835,851 | zinc-binding | zinc-binding |
| 2B3X\_A | 125,126,207,503 | zinc-binding | zinc-binding |
| 3BJC\_A | 613,683,685 | zinc-binding | zinc-binding |
| 1GAX\_A | 420,440,441,442 | zinc-binding | zinc-binding |
| 1TAQ\_A | 564,576,580 | zinc-binding | zinc-binding |
| 2RHS\_A | 203,204,208 | zinc-binding | zinc-binding |

**Supplementary Table S3. The dataset used by CHED (90 chains).**

|  |
| --- |
| 1Q2L\_A, 1PD1\_A, 1FFY\_A, 1NMP\_A, 1ZWJ\_A, 1XV2\_A, 1VDW\_A, 1RW0\_A, 1XTM\_A, 1T8H\_A, 1M86\_A, 1D6U\_A, 1SDD\_A, 1LCF\_A, 1HC1, 1I50\_A, 1MWH\_A, 1FGQ\_A, 1KMP\_A, 1BY5\_A, 1LFG\_A, 1AF6\_A, 1AMU\_A, 1CS4\_A, 1F6B\_A, 1O4T\_A, 1ZTC\_A, 1PS3\_A, 2IFB\_A, 2HPI\_A, 2QF7\_A, 2QO2\_A, 2W3K\_A, 2OAJ\_A, 2XRG\_A, 2QGS\_A, 2DW6\_A, 2PEB\_A, 2PLM\_A, 2P6Y\_A, 2OIK\_A, 2OC5\_A, 2IMR\_A, 2I9W\_A, 2H6I\_A, 2GWG\_A, 2GVI\_A, 2GLZ\_A, 2FQP\_A, 2J5W\_A, 2E1Q\_A, 2DJZ\_A, 2XT6\_A, 2YEV\_A, 2WQ8\_A, 2ZXQ\_A, 2ITB\_A, 3SE6\_A, 3S5K\_A, 3F2B\_A, 3ZQJ\_A, 3UJ2\_A, 3JYG\_A, 3JU2\_A, 3IR9\_A, 3IMI\_A, 3E49\_A, 3E38\_A, 3H0N\_A, 3DI4\_A, 3D00\_A, 3CHV\_A, 3BB6\_A, 3BWW\_A, 3ECQ\_A, 3K6S\_A, 3T51\_A, 3N9H\_A, 3BG5\_A, 3Q23\_A, 3F2C\_A, 3LDS\_A, 3UFH\_A, 3CF4\_A, 3VTH\_A, 4DDT\_A, 4A7K\_A, 4K5L\_A, 4CMQ\_A, 4OGC\_A, 4AIQ\_A |

Note: PDB chains are described by their PDB IDs followed by chain IDs.

**Supplementary Table S4: The metal-binding sites predicted by CHED were assigned to be zinc-binding sites by investigating PDB structure support and filtered by mFASD.**

|  |  |  |  |
| --- | --- | --- | --- |
| **PDB chain ID** | **Predicted metal-binding sites****(amino acid IDs)** | **Experimental fact** | **mFASD prediction** |
| 2HPI\_A | 20,47,214 | zinc-binding | zinc-binding |
| 3SE6\_A | 370,374,393 | zinc-binding | zinc-binding |
| 2QF7\_A | 549,747,749 | zinc-binding | zinc-binding |
| 3S5K\_A | 129,133,243 | zinc-binding | zinc-binding |
| 4DDT\_A | 621,624,635,638 | zinc-binding | zinc-binding |
| 1PS3\_A | 90,92,204,471 | zinc-binding | zinc-binding |
| 3F2B\_A | 919,922,944,947 | zinc-binding | zinc-binding |
| 2W3K\_A | 108,112,189 | zinc-binding | zinc-binding |
| 4L3T\_A | 104,108,205 | zinc-binding | zinc-binding |
| 3ZQJ\_A | 753,756,776,779 | zinc-binding | zinc-binding |
| 1Q2L\_A | 88,92,169 | zinc-binding | zinc-binding |
| 1PD1\_A | 231,234,253,256 | zinc-binding | zinc-binding |
| 1FFY\_A | 886,889,906,909 | zinc-binding | zinc-binding |
| 2OAJ\_A | 835,851 | zinc-binding | zinc-binding |
| 4A7K\_A | 215,295,337 | zinc-binding | zinc-binding |
| 4K5L\_A | 496,500,519 | zinc-binding | zinc-binding |
| 3UJZ\_A | 446,450,456 | zinc-binding | zinc-binding |
| 2XRG\_A | 311,315,474 | zinc-binding | zinc-binding |
| 3JYG\_A | 15,38,40 | zinc-binding | zinc-binding |
| 3JU2\_A | 141,203,247 | zinc-binding | non-zinc-binding |
| 3IR9\_A | 330,333,335,358 | zinc-binding | zinc-binding |
| 3IMI\_A | 147,152,168,172 | zinc-binding | zinc-binding |
| 3E49\_A | 258,49,51 | zinc-binding | zinc-binding |
| 3E38\_A | 113,44,46 | zinc-binding | zinc-binding |
|  | 216,51,76 | zinc-binding | zinc-binding |
| 2PLM\_A | 55,57,200,279 | zinc-binding | zinc-binding |
| 3DI4\_A | 150,167,237 | zinc-binding | zinc-binding |
| 3D00\_A | 165,168,170,180,183 | zinc-binding | zinc-binding |
| 3CHV\_A | 51,53,145,147,233 | zinc-binding | zinc-binding |
| 3BB6\_A | 30,32,83 | zinc-binding | zinc-binding |
| 2QGS\_A | 29,59,123 | zinc-binding | zinc-binding |
| 2PW6\_A | 22,57,234 | zinc-binding | zinc-binding |
| 2PEB\_A | 12,14,84 | zinc-binding | zinc-binding |
| 2P6Y\_A | 75,77,91 | zinc-binding | zinc-binding |
| 2OIK\_A | 11,14,49,95 | zinc-binding | zinc-binding |
| 2IMR\_A | 97,99,238 | zinc-binding | zinc-binding |
| 2I9W\_A | 8,10,28,29 | zinc-binding | zinc-binding |
|  | 167,169,178,179 | zinc-binding | zinc-binding |
| 2H6L\_A | 89,91,104 | zinc-binding | zinc-binding |
| 2GWG\_A | 6,8,178 | zinc-binding | zinc-binding |
| 2GVI\_A | 16,18,20,61 | zinc-binding | zinc-binding |
|  | 174,177,195,198 | zinc-binding | zinc-binding |
| 2GLZ\_A | 15,17,19,55 | zinc-binding | zinc-binding |
| 2FQP\_A | 33,35,76 | zinc-binding | zinc-binding |
| 1ZWJ\_A | 63,66,133,184 | zinc-binding | zinc-binding |
|  | 216,219,255,310 | zinc-binding | zinc-binding |
| 1XV2\_A | 173,175,186 | zinc-binding | zinc-binding |
| 1XTM\_A | 104,112,121,124 | zinc-binding | zinc-binding |
| 1T8H\_A | 182,183,242,245 | zinc-binding | zinc-binding |
| 1M86\_A | 73,101,181 | zinc-binding | zinc-binding |
|  | 15,40,194 | zinc-binding | zinc-binding |
|  |  |  |  |
| 3ECQ\_A | 657,658,661,694,764 | non-zinc-binding | zinc-binding |
|  | 655,703,728,1258 | non-zinc-binding | non-zinc-binding |
| 2J5W\_A | 272,940,973,975,1021,1025 | non-zinc-binding | non-zinc-binding |
|  | 274,276,319,324 | non-zinc-binding | non-zinc-binding |
| 2E1Q\_A | 21,23,232,677,678 | non-zinc-binding | zinc-binding |
| 2DJZ\_A | 24,46,118 | non-zinc-binding | non-zinc-binding |
| 2XT6\_A | 1011,1013,1169,1170 | non-zinc-binding | non-zinc-binding |
|  | 610,643,673 | non-zinc-binding | non-zinc-binding |
| 3K6S\_A | 447,449,451,455 | non-zinc-binding | non-zinc-binding |
| 1SDD\_A | 96,102,111,112 | non-zinc-binding | non-zinc-binding |
| 3T51\_A | 44,98,99,468 | non-zinc-binding | non-zinc-binding |
|  | 277,283.593 | non-zinc-binding | non-zinc-binding |
| 2YEV\_A | 229,250,300 | non-zinc-binding | non-zinc-binding |
|  | 515,518,544 | non-zinc-binding | non-zinc-binding |
| 1D6U\_A | 533,535,539,678 | non-zinc-binding | non-zinc-binding |
| 3N9H\_A | 23,26,267 | non-zinc-binding | zinc-binding |
|  | 456,458,624,637 | non-zinc-binding | zinc-binding |
| 1LCF\_A | 493,504,507,517,523 | non-zinc-binding | non-zinc-binding |
| 2WQ8\_A | 228,496,581 | non-zinc-binding | zinc-binding |
| 1HC1\_A | 194,198,224,344,348,384 | non-zinc-binding | zinc-binding |
| 1I50\_A | 67,70,77,80 | non-zinc-binding | non-zinc-binding |
|  | 107,109,110,148,167 | non-zinc-binding | non-zinc-binding |
| 2ZXQ\_A | 681,682,685,718,789 | non-zinc-binding | zinc-binding |
| 4CMQ\_A | 762,766,982,983,986 | non-zinc-binding | non-zinc-binding |
| 1MWH\_A | 1195,1196,1239 | non-zinc-binding | zinc-binding |
| 3BG5\_A | 246,265,276,332 | non-zinc-binding | non-zinc-binding |
| 3Q23\_A | 277,388,389 | non-zinc-binding | non-zinc-binding |
|  | 376,695,699 | non-zinc-binding | non-zinc-binding |
|  | 557,559,951 | non-zinc-binding | non-zinc-binding |
| 4OGC\_A | 735,736,739,1045 | non-zinc-binding | zinc-binding |
| 3F2C\_A | 346,348,405,670,698,700 | non-zinc-binding | zinc-binding |
| 3LDS\_A | 40,51,57,81 | non-zinc-binding | non-zinc-binding |
|  | 219,272,275 | non-zinc-binding | non-zinc-binding |
|  | 411,684,686,716 | non-zinc-binding | non-zinc-binding |
| 3UFH\_A | 255,656,746 | non-zinc-binding | non-zinc-binding |
| 1FGQ\_A | 499,504,690 | non-zinc-binding | zinc-binding |
| 3CF4\_A | 250,277,278,323 | non-zinc-binding | non-zinc-binding |
| 1KMP\_A | 445,447,470,472 | non-zinc-binding | non-zinc-binding |
| 3VTH\_A | 114,116,117,136,139 | non-zinc-binding | non-zinc-binding |
|  | 164,167,186,188,189 | non-zinc-binding | non-zinc-binding |
| 4AIQ\_A | 140,373,275 | non-zinc-binding | non-zinc-binding |
| 1BY5\_A | 457,459,472 | non-zinc-binding | non-zinc-binding |
| 1LFG\_A | 157,173,181 | non-zinc-binding | zinc-binding |
|  | 493,507,517 | non-zinc-binding | zinc-binding |
| 1A73\_A | 125,132,134,138 | non-zinc-binding | non-zinc-binding |
| 1AF6\_A | 110,188,218 | non-zinc-binding | non-zinc-binding |
| 1AMU\_A | 19,21,22 | non-zinc-binding | non-zinc-binding |
|  | 441,443,444 | non-zinc-binding | non-zinc-binding |
| 1CS4\_A | 396,441,518 | non-zinc-binding | non-zinc-binding |
|  | 431,454,458,461 | non-zinc-binding | non-zinc-binding |
| 1F6B\_A | 43,58,62 | non-zinc-binding | zinc-binding |
|  | 110,113,114 | non-zinc-binding | non-zinc-binding |
| 1O4T\_A | 61,63,102 | non-zinc-binding | non-zinc-binding |
| 1ZTC\_A | 69,71,140 | non-zinc-binding | non-zinc-binding |
|  | 73,74,162 | non-zinc-binding | non-zinc-binding |
| 2ITB\_A | 69,122,154 | non-zinc-binding | non-zinc-binding |
|  | 38,72,151 | non-zinc-binding | non-zinc-binding |
| 2OC5\_A | 73,128,160 | non-zinc-binding | non-zinc-binding |
| 3BWW\_A | 138,171,203 | non-zinc-binding | non-zinc-binding |
| 1NMP\_A | 63,101,219 | non-zinc-binding | non-zinc-binding |
|  | 64,215,219 | non-zinc-binding | non-zinc-binding |
| 1VDW\_A | 84,87,201 | non-zinc-binding | non-zinc-binding |
| 1RWO\_A | 71,107,124 | non-zinc-binding | non-zinc-binding |
| 1T8H\_A | 80,125,142 | non-zinc-binding | non-zinc-binding |