

Electronic Supplementary Material

National Epidemiology and Evolutionary History of Four Hand, Foot and Mouth Disease-related Enteroviruses in China from 2008 to 2016

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Supplementary Table S1. Cohorts of enteroviruses associated HFMD cases in China from 2008 to 2016 used in the molecular epidemiological analyses.

| Region | Province (City) | serotype | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | References |
|-----------------|----------------------------|---------------------|------|------|------|------|------|------|------|------|------|--|
| Northeast China | Heilongjiang (Harbin) | EV-A71 | 59 | 146 | 152 | 386 | 52 | 52 | 305 | NA | NA | Liang, <i>et al.</i> 2012; Feng, <i>et al.</i> 2016 |
| | | CV-A16 | 4 | 82 | 14 | 48 | 470 | 29 | 249 | NA | NA | |
| | | Other enteroviruses | 63 | 232 | 21 | 70 | 94 | 104 | 60 | NA | NA | |
| | Jilin | EV-A71 | 67 | 237 | 516 | 661 | 255 | 230 | 964 | 64 | 147 | Shan, <i>et al.</i> 2017; Li, <i>et al.</i> 2018; Huang, <i>et al.</i> 2017 |
| | | CV-A16 | 19 | 205 | 508 | 307 | 595 | 107 | 417 | 212 | 326 | |
| | | Other enteroviruses | 33 | 118 | 333 | 231 | 324 | 435 | 340 | 436 | 529 | |
| | Liaoning (Shenyang) | EV-A71 | NA | 33 | 112 | 87 | 141 | 227 | 126 | 48 | 24 | Liu, <i>et al.</i> 2014; Qi, <i>et al.</i> 2018b |
| | | CV-A16 | NA | 2 | 88 | 14 | 305 | 131 | 123 | 28 | 167 | |
| | | Other enteroviruses | NA | 43 | 29 | 28 | 76 | 201 | 86 | 392 | 125 | |
| Northwest China | Shaanxi | EV-A71 | 18 | 219 | 516 | 550 | 1073 | 601 | 1885 | 664 | NA | Yu, <i>et al.</i> 2012; Zheng, <i>et al.</i> 2016; Zheng, <i>et al.</i> 2015 |
| | | CV-A16 | 22 | 21 | 409 | 105 | 345 | 366 | 855 | 620 | NA | |
| | | Other enteroviruses | 2 | 26 | 203 | 197 | 455 | 1517 | 965 | 1712 | NA | |
| | Gansu | EV-A71 | 166 | 301 | 174 | 560 | 359 | 321 | 333 | 203 | 296 | Chen, <i>et al.</i> 2017; Yu, <i>et al.</i> 2014 |
| | | CV-A16 | 198 | 120 | 475 | 96 | 492 | 276 | 625 | 197 | 354 | |
| | | Other enteroviruses | 11 | 12 | 91 | 122 | 145 | 347 | 225 | 531 | 606 | |
| | Ningxia | EV-A71 | 93 | 60 | 211 | 164 | 163 | 104 | 415 | 140 | NA | Ma, <i>et al.</i> 2012; Ma, <i>et al.</i> 2016 |
| | | CV-A16 | 59 | 18 | 264 | 72 | 301 | 407 | 439 | 720 | NA | |
| | | Other enteroviruses | 23 | 61 | 89 | 71 | 128 | 277 | 183 | 530 | NA | |
| | Qinghai | EV-A71 | 50 | 56 | NA | 27 | 149 | 226 | NA | NA | NA | Liu, <i>et al.</i> 2009; Xu, <i>et al.</i> 2014; Yang, <i>et al.</i> 2015; Zhang <i>et al</i> 2013 |
| | | CV-A16 | 13 | 41 | NA | 8 | 10 | 47 | NA | NA | NA | |
| | | Other enteroviruses | 0 | 0 | NA | 0 | 0 | 41 | NA | NA | NA | |
| | Xinjiang | EV-A71 | 46 | 25 | 251 | 401 | 225 | 380 | 401 | 288 | NA | Deng, <i>et al.</i> 2016; Liu, <i>et al.</i> 2018 |
| | | CV-A16 | 48 | 16 | 261 | 395 | 744 | 93 | 797 | 498 | NA | |
| | | Other enteroviruses | 10 | 26 | 83 | 73 | 83 | 366 | 134 | 279 | NA | |
| North China | Beijing | EV-A71 | 347 | 420 | 950 | 608 | 738 | 458 | 616 | 111 | NA | Li, <i>et al.</i> 2016; Wang, <i>et al.</i> 2014 |
| | | CV-A16 | 76 | 634 | 716 | 666 | 1191 | 519 | 729 | 246 | NA | |
| | | Other enteroviruses | 150 | 150 | 602 | 223 | 233 | 1498 | 362 | 810 | NA | |
| | Tianjin | EV-A71 | 142 | 128 | 564 | 646 | 623 | 277 | 242 | NA | NA | Chen, <i>et al.</i> 2015; Tan, <i>et al.</i> 2015 |
| | | CV-A16 | 16 | 88 | 535 | 285 | 565 | 200 | 567 | NA | NA | |
| | | Other enteroviruses | 8 | 52 | 191 | 373 | 351 | 883 | 135 | NA | NA | |
| | Hebei | EV-A71 | NA | 703 | 2230 | 1865 | 3687 | 1503 | 2873 | NA | NA | Liu, <i>et al.</i> 2012; Liu, <i>et al.</i> 2016 |
| | | CV-A16 | NA | 436 | 696 | 886 | 1781 | 272 | 1561 | NA | NA | |
| | | Other enteroviruses | NA | 167 | 863 | 610 | 1133 | 1446 | 1044 | NA | NA | |
| | Shanxi (Taiyuan) | EV-A71 | NA | NA | NA | 151 | 291 | 272 | 215 | NA | NA | Duan, 2015; Guo, 2016 |
| | | CV-A16 | NA | NA | NA | 171 | 183 | 116 | 223 | NA | NA | |
| | | Other enteroviruses | NA | NA | NA | 42 | 48 | 49 | 54 | NA | NA | |
| | Inner Mongolia | EV-A71 | 8 | 21 | 130 | 412 | 174 | 582 | 875 | 359 | NA | Qian, <i>et al.</i> 2017 |
| | | CV-A16 | 0 | 4 | 128 | 306 | 427 | 413 | 486 | 313 | NA | |
| | | Other enteroviruses | 0 | 9 | 297 | 529 | 589 | 572 | 696 | 697 | NA | |
| Central China | Henan | EV-A71 | 190 | 3601 | 5081 | 2417 | 3298 | 1843 | NA | NA | NA | He, <i>et al.</i> 2015 |
| | | CV-A16 | 27 | 825 | 402 | 899 | 867 | 894 | NA | NA | NA | |
| | | Other enteroviruses | 46 | 1921 | 1794 | 816 | 1213 | 1498 | NA | NA | NA | |

| | | | | | | | | | | | | |
|-----------------|------------------------------|---------------------|-----|-----|------|------|-------|------|------|------|------|---|
| East China | Hubei | EV-A71 | 141 | 195 | 889 | 1442 | 38974 | NA | NA | 603 | NA | Dai, et al. 2017; Wang, et al. 2013; Zou, et al. 2017 |
| | | CV-A16 | 26 | 87 | 494 | 787 | 4094 | NA | NA | 595 | NA | |
| | | Other enteroviruses | 59 | 63 | 421 | 507 | 4895 | NA | NA | 1676 | NA | |
| | Hunan | EV-A71 | 239 | 152 | 2520 | 1006 | 4510 | 1565 | 2675 | 2037 | NA | Wu, et al. 2017b; Zeng, et al. 2013 |
| | | CV-A16 | 39 | 140 | 655 | 1019 | 685 | 630 | 1595 | 537 | NA | |
| | | Other enteroviruses | 28 | 112 | 1186 | 911 | 1689 | 2177 | 1811 | 2965 | NA | |
| | Shandong (Jinan) | EV-A71 | NA | 119 | 177 | 329 | 182 | 277 | 208 | 208 | NA | Geng, et al. 2016 |
| | | CV-A16 | NA | 21 | 263 | 156 | 359 | 149 | 365 | 82 | NA | |
| | | Other enteroviruses | NA | 109 | 123 | 145 | 103 | 236 | 170 | 337 | NA | |
| | Jiangsu (Nanjing) | EV-A71 | 1 | 76 | 299 | 313 | 188 | 123 | 137 | 167 | NA | Feng, et al. 2015; Zhang, et al. 2017; Zhang, et al. 2015 |
| | | CV-A16 | 0 | 19 | 185 | 153 | 330 | 48 | 203 | 154 | NA | |
| | | Other enteroviruses | 2 | 3 | 79 | 115 | 135 | 282 | 186 | 289 | NA | |
| | Anhui (Hefei& Fuyang) | EV-A71 | 884 | 195 | 220 | 902 | 115 | 160 | 165 | NA | NA | Hu, et al. 2014; Wu, et al. 2017a; Hu, 2015; Zhang, et al. 2012 |
| | | CV-A16 | 248 | 55 | 27 | 452 | 61 | 9 | 49 | NA | NA | |
| | | Other enteroviruses | 63 | 49 | 53 | 504 | 87 | 130 | 85 | NA | NA | |
| | Shanghai (Fengxian& Hongkou) | EV-A71 | NA | 38 | 54 | 221 | 88 | 29 | 45 | 44 | NA | Wang, 2017b; Yu, et al. 2018; Yang, et al. 2012 |
| | | CV-A16 | NA | 38 | 49 | 85 | 94 | 28 | 85 | 34 | NA | |
| | | Other enteroviruses | NA | 11 | 44 | 86 | 27 | 155 | 56 | 76 | NA | |
| | Zhejiang | EV-A71 | 804 | 461 | 2379 | 2085 | 1735 | 975 | 2171 | 691 | NA | Wu, et al. 2016 |
| | | CV-A16 | 63 | 433 | 1320 | 747 | 1336 | 397 | 1493 | 812 | NA | |
| | | Other enteroviruses | 588 | 191 | 650 | 882 | 1313 | 3022 | 2950 | 2753 | NA | |
| | Jiangxi (Nanchang) | EV-A71 | NA | 45 | 63 | 167 | 401 | NA | 148 | NA | NA | He, et al. 2013; Li, 2011; Liu, et al. 2011; Zhang, et al. 2015 |
| | | CV-A16 | NA | 25 | 19 | 82 | 105 | NA | 66 | NA | NA | |
| | | Other enteroviruses | NA | 4 | 70 | 75 | 125 | NA | 22 | NA | NA | |
| | Fujian | EV-A71 | 780 | 746 | 2546 | 324 | 1977 | 811 | 953 | 1278 | NA | Ye, et al. 2018 |
| | | CV-A16 | 124 | 172 | 715 | 177 | 685 | 364 | 1147 | 207 | NA | |
| | | Other enteroviruses | 28 | 7 | 99 | 133 | 1273 | 2245 | 1507 | 2165 | NA | |
| South China | Guangdong (Guangzhou) | EV-A71 | 205 | 195 | 1005 | 520 | 1127 | 411 | 637 | 232 | NA | Chen, et al. 2014a; Liu, et al. 2017 |
| | | CV-A16 | 166 | 747 | 536 | 928 | 1200 | 276 | 1109 | 152 | NA | |
| | | CA-V6 | 101 | 673 | 660 | 1204 | 1832 | 4129 | 498 | 1614 | NA | |
| | Guangxi | EV-A71 | 178 | 101 | 2178 | 933 | 4092 | 468 | 3475 | 854 | NA | He, et al. 2017 |
| | | CV-A16 | 34 | 205 | 194 | 1927 | 561 | 1579 | 1580 | 528 | NA | |
| | | Other enteroviruses | 210 | 45 | 828 | 1223 | 2443 | 3091 | 2727 | 4523 | NA | |
| | Hainan | EV-A71 | 84 | 220 | 214 | 280 | 295 | NA | NA | NA | NA | Chen, et al. 2014b; Jin, et al. 2009 |
| | | CV-A16 | 0 | 17 | 224 | 276 | 197 | NA | NA | NA | NA | |
| | | Other enteroviruses | 44 | 81 | 193 | 47 | 298 | NA | NA | NA | NA | |
| Southwest China | Sichuan (Mianyang) | EV-A71 | NA | 86 | 9 | 128 | 27 | 179 | 45 | NA | NA | Wang, et al. 2016; Zhou, et al. 2012 |
| | | CV-A16 | NA | 2 | 96 | 4 | 125 | 10 | 37 | NA | NA | |
| | | Other enteroviruses | NA | 2 | 5 | 6 | 103 | 164 | 6 | NA | NA | |
| | Guizhou | EV-A71 | 5 | 101 | 294 | 836 | 1484 | 826 | 921 | 537 | NA | Wang, et al. 2017a |
| | | CV-A16 | 0 | 2 | 291 | 387 | 1194 | 378 | 968 | 312 | NA | |
| | | Other enteroviruses | 4 | 76 | 142 | 507 | 1347 | 2045 | 1393 | 1927 | NA | |
| | Yunnan | EV-A71 | 28 | 341 | 1337 | 3024 | 2198 | 2691 | 3401 | 3750 | 3303 | Yang. |

| | | | | | | | | | | | |
|-----------|---------------------|----|-----|------|-----|------|------|------|------|------|----------------------------------|
| | CV-A16 | 7 | 25 | 2215 | 808 | 4004 | 612 | 3769 | 1857 | 3286 | 2017; Cun, <i>et al.</i> 2015 |
| | Other enteroviruses | 1 | 14 | 30 | 88 | 119 | 923 | 1438 | 2904 | 4487 | |
| Chongqing | EV-A71 | NA | 159 | 268 | 750 | 414 | 514 | 710 | 621 | 500 | Qi, <i>et al.</i> 2018a |
| | CV-A16 | NA | 35 | 558 | 620 | 546 | 222 | 1087 | 565 | 628 | |
| | Other enteroviruses | NA | 3 | 97 | 412 | 638 | 1119 | 1330 | 916 | 1024 | |
| Tibet | EV-A71 | NA | 17 | 163 | 28 | 8 | 11 | NA | NA | NA | Da, <i>et al.</i> 2014 |
| | CV-A16 | NA | 23 | 58 | 11 | 15 | 0 | NA | NA | NA | |
| | Other enteroviruses | NA | 4 | 2 | 2 | 1 | 0 | NA | NA | NA | |

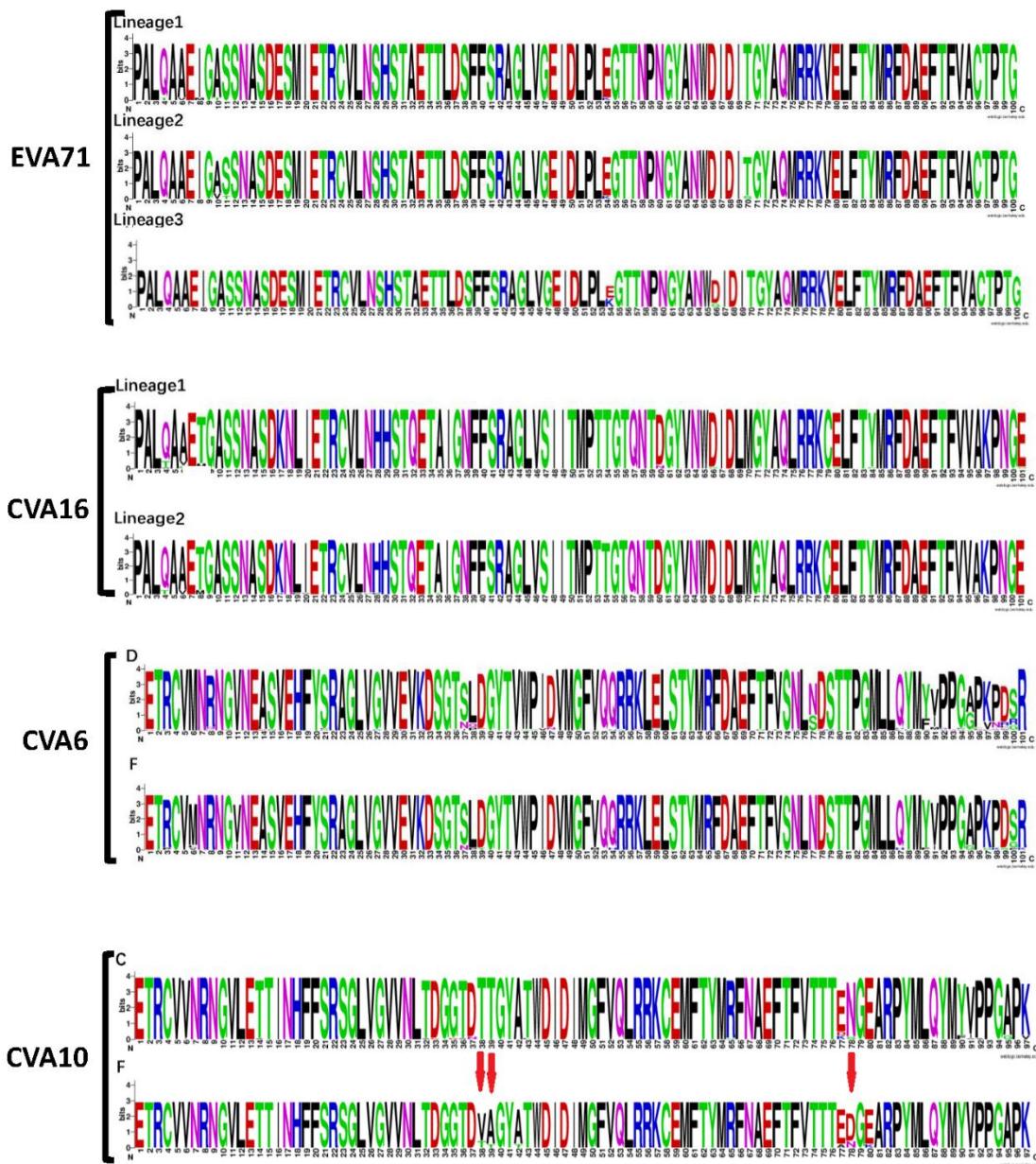


Fig. S1. Amino acid sequence features of the partial VP1 genes of different lineages of the targeted enteroviruses. The character and size of each logo represent the proportion of an amino acid at the specific site. The three different amino acids between CVA10 genotypes C and D are highlighted by red arrows.

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