**Supplementary Information**

**Discovery of novel and potent InhA inhibitors by an *in silico* screening and pharmacokinetic prediction**

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**Figure S1.** RMSD plots of template molecule (a), **AG-690/13705356** (b), **AG-690/14006355** (c), **AP-845/40876827** (d), **AE-848/34504008** (e), **AP-845/40876825** (f), **AP-845/40876828** (g), **AP-845/40876832** (h) and **AS-871/41615872** (i) complexed with InhA

**Table S1.** The antimycobacterial prediction of hit compounds by antiBac-Pred

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Compound** | ***M. tuberculosis*** | ***M. tuberculosis* H37Rv** | ***M. avium*** | ***M. bovis BCG*** | ***M. kansasii*** | **Resistant *M. avium*** | **Resistant *M. tuberculosis* H37Rv** | ***M. bovis*** |
| AP-124/43238118 (template) | none | 0.1 | none | none | none | none | none | none |
| AE-848/34504008 | 0.1 | 0.2 | none | none | none | none | none | none |
| AG-690/13705356 | none | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | none |
| AG-690/14006355 | none | none | none | none | none | none | none | none |
| AP-845/40876825 | none | 0.1 | none | none | none | none | none | none |
| AP-845/40876827 | none | none | none | none | none | none | none | none |
| AP-845/40876828 | none | none | none | none | none | none | none | none |
| AP-845/40876832 | none | none | 0.1 | none | none | none | none | none |
| AS-871/41615872 | none | none | none | none | none | none | none | 0.1 |

**Table S2.** The antimycobacterial prediction of hit compounds by mycoCSM

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Compound** | ***M. avium*** | ***M. bovis*** | ***M. fortuitum*** | ***M. intracellulare*** | ***M. kansasii*** | ***M. phlei*** | ***M. smegmatis*** | ***M. tuberculosis*** |
| AP-124/43238118 (template) | -4.8 | -6.2 | -4.2 | -4.2 | -4.4 | -4.4 | -4.2 | -4.9 |
| AE-848/34504008 | -3.8 | -6.0 | -4.1 | -4.2 | -4.3 | -4.4 | -4.1 | -5.1 |
| AS-871/41615872 | -4.3 | -5.2 | -4.0 | -4.3 | -4.0 | -4.3 | -4.2 | -4.9 |
| AP-845/40876827 | -4.6 | -6.2 | -4.2 | -4.3 | -4.8 | -4.1 | -4.8 | -4.9 |
| AP-845/40876828 | -4.6 | -6.2 | -4.1 | -4.3 | -4.2 | -4.2 | -4.8 | -4.7 |
| AP-845/40876832 | -5.0 | -5.1 | -4.1 | -4.1 | -4.5 | -4.2 | -4.3 | -4.8 |
| AG-690/13705356 | -4.1 | -6.3 | -4.1 | -4.3 | -3.7 | -3.8 | -4.7 | -5.4 |
| AG-690/14006355 | -4.2 | -3.5 | -4.1 | -4.1 | -4.1 | -4.3 | -4.3 | -4.4 |
| AP-845/40876825 | -4.7 | -5.2 | -4.3 | -4.2 | -4.6 | -4.5 | -4.0 | -4.9 |

**Table S3.** Hydrogen bonding analysis of candidate compounds

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Compound** | **Acceptor** | **DonorH** | **Donor** | **%Occupation**  **(%)** | **Average distance (Å)** | **Average angle (o)** |
| AP-124/43238118 (template) | NAD@O1N | LIG@H20 | LIG@O1 | 79.5 | 2.60 | 167.7 |
| NAD@O2A | LIG@H20 | LIG@O1 | 13.8 | 2.68 | 165.2 |
| AG-690/13705356 | LIG@O13 | Gln214@HE22 | Gln214@NE2 | 24.2 | 2.89 | 160.9 |
| AG-690/14006355 | Gln214@OE1 | LIG@H38 | LIG@O13 | 24.0 | 2.70 | 165.6 |
| AP-845/40876828 | NAD@O1A | LIG@H13 | LIG@O1 | 44.4 | 2.63 | 165.7 |
| AP-845/40876832 | LIG@N7 | Gln214@HE22 | Gln214@NE2 | 5.4 | 2.92 | 162.6 |