

Supplementary Table S1. The distribution of the mutation in *gyrA* among hpAsia2 and hpEurope

| Mutations | Resistant | | | Susceptible | | | Grand Total |
|-----------|-----------|----------|-------|-------------|----------|-------|-------------|
| | hpAsia2 | hpEurope | Total | hpAsia2 | hpEurope | Total | |
| N87K | 5 | 8 | 13 | 0 | 0 | 0 | 13 |
| N87Y | 1 | | 1 | 0 | 0 | 0 | 1 |
| D91G | 3 | 2 | 5 | 0 | 0 | 0 | 5 |
| D91N | 3 | 10 | 13 | 0 | 0 | 0 | 13 |
| D91Y | 1 | | 1 | 0 | 0 | 0 | 1 |
| Total | 13 | 20 | 33 | 0 | 0 | 0 | |

Supplementary Table S2. Frameshift mutations occurred in the *rdxA*, *mdaB*, *ribF* and *frxA*

| Framehift locus | Resistant | | Susceptible | | Grand Total |
|--------------------|-----------|---------|-------------|---------|-------------|
| | Absent | Present | Absent | Present | |
| <i>rdxA.H97fs</i> | 46 | 7 | 3 | | 56 |
| <i>rdxA.I160fs</i> | 52 | 1 | 3 | | 56 |
| <i>rdxA.K64fs</i> | 52 | 1 | 3 | | 56 |
| <i>rdxA.K78fs</i> | 52 | 1 | 3 | | 56 |
| <i>rdxA.K8fs</i> | 52 | 1 | 3 | | 56 |
| <i>rdxA.M84fs</i> | 51 | 2 | 3 | | 56 |
| <i>rdxA.P96fs</i> | 20 | 33 | 2 | 1 | 56 |
| <i>rdxA.R41fs</i> | 52 | 1 | 3 | | 56 |
| <i>mdaB.A51fs</i> | 36 | 17 | 2 | 1 | 56 |
| <i>mdaB.E55fs</i> | 38 | 15 | 3 | | 56 |
| <i>mdaB.G159fs</i> | 52 | 1 | 3 | | 56 |
| <i>mdaB.H50fs</i> | 15 | 38 | 1 | 2 | 56 |
| <i>mdaB.P68fs</i> | 53 | | 2 | 1 | 56 |
| <i>mdaB.S87fs</i> | 47 | 6 | 3 | | 56 |
| <i>mdaB.V171fs</i> | 52 | 1 | 3 | | 56 |
| <i>mdaB.V44fs</i> | 52 | 1 | 3 | | 56 |
| <i>mdaB.V57fs</i> | 39 | 14 | 3 | | 56 |
| <i>ribF.R256fs</i> | 52 | 1 | 3 | | 56 |
| <i>ribF.S258fs</i> | 52 | 1 | 3 | | 56 |
| <i>frxA.A16fs</i> | 51 | 2 | 3 | | 56 |
| <i>frxA.D109fs</i> | 52 | 1 | 3 | | 56 |
| <i>frxA.D136fs</i> | 52 | 1 | 3 | | 56 |
| <i>frxA.D94fs</i> | 51 | 2 | 3 | | 56 |
| <i>frxA.G69fs</i> | 51 | 2 | 3 | | 56 |
| <i>frxA.K105fs</i> | 52 | 1 | 3 | | 56 |
| <i>frxA.K18fs</i> | 45 | 8 | 2 | 1 | 56 |
| <i>frxA.K204fs</i> | 52 | 1 | 3 | | 56 |
| <i>frxA.K97fs</i> | 52 | 1 | 3 | | 56 |
| <i>frxA.M66fs</i> | 52 | 1 | 3 | | 56 |
| <i>frxA.Q10fs</i> | 52 | 1 | 3 | | 56 |
| <i>frxA.S189fs</i> | 53 | | 2 | 1 | 56 |
| <i>frxA.V36fs</i> | 52 | 1 | 3 | | 56 |
| <i>frxA.W68fs</i> | 51 | 2 | 3 | | 56 |
| Grand Total | 1583 | 166 | 92 | 7 | 1848 |

Supplementary Table S3. Physical and chemical parameters of the fur and ribF protein

| Protein | Theoretical pI | Estimated half-life (mammalian reticulocytes, in vitro; yeast, in vivo; Escherichia coli, in vivo) | Instability index | Aliphatic index | Grand average of hydropathicity (GRAVY) |
|----------------|-----------------------|---|--------------------------|------------------------|--|
| fur_WT | 8.50 | 30hr; >20hr; >10hr | 54.19 | 85.73 | -0.631 |
| fur_N118Q | 8.50 | 30hr; >20hr; >10hr | 55.47 | 85.73 | -0.631 |
| ribF_WT | 9.33 | 5.5h; 3min; 2min | 36.25 | 111.11 | -0.148 |
| ribF_D253E | 9.33 | 5.5h; 3min; 2min | 36.25 | 111.11 | -0.148 |
| ribF_S151L | 9.33 | 5.5h; 3min; 2min | 36.25 | 112.51 | -0.131 |

Analyses **Residue: GLN 118**

Bad
Allowed
Good

Largest pocket
Pocket

JSmol

Take Jmol snapshot Show All analyses Hide All analyses Clear Selection Hover over a residue below to see info. Click to spacefill.

Predicted Secondary structure
SS Confidence
Model Secondary structure
Query Sequence
Modelled Residues
Clashes
Conservation
Disorder
Alignment confidence
Pocket detection
ProQ2 quality assessment
ProteinDB Interface
Ramachandran analysis
Rotamers
Mutational sensitivity

Analyses **Residue: GLU 253**

Bad
Allowed
Good

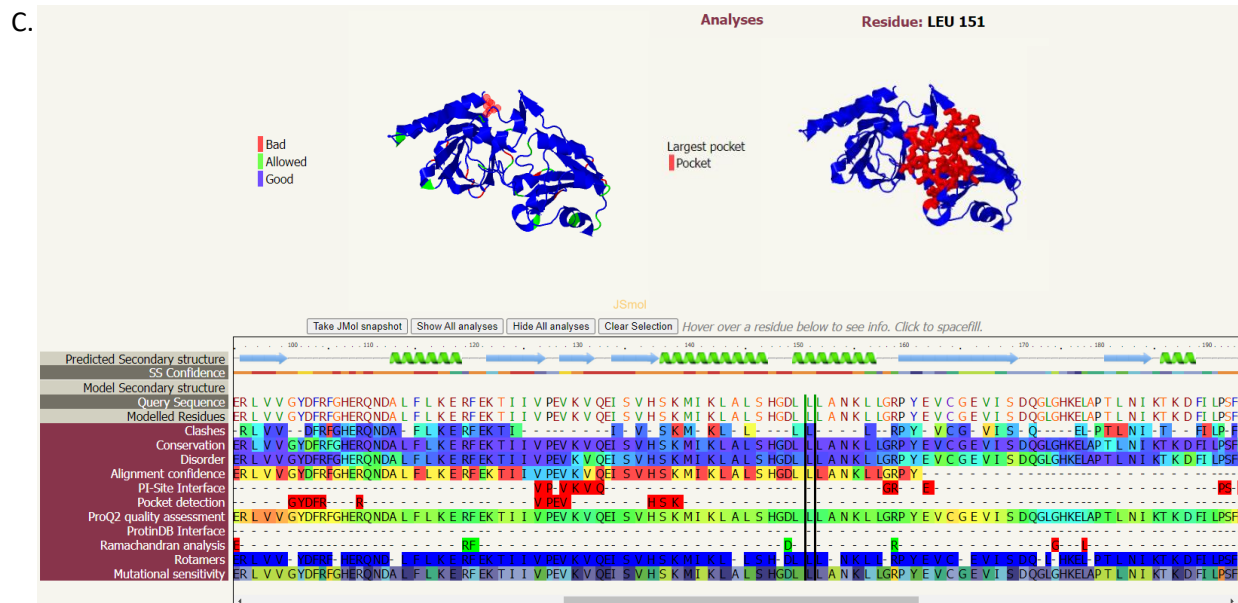
Largest pocket
Pocket

JSmol

Take Jmol snapshot Show All analyses Hide All analyses Clear Selection Hover over a residue below to see info. Click to spacefill.

Predicted Secondary structure
SS Confidence
Model Secondary structure
Query Sequence
Modelled Residues
Clashes
Conservation
Disorder
Alignment confidence
PE-Site Interface
Pocket detection
ProQ2 quality assessment
ProteinDB Interface
Ramachandran analysis
Rotamers
Mutational sensitivity

B.



Supplementary Figure S1. A. In-depth analysis on fur_N118Q amino acid. B. In-depth analysis on ribF_D253E amino acid. C. In-depth analysis on ribF_S151L amino acid. *Red arrow*: represents the location of mutation. *Left structure*: the colour represent the Ramachandran analysis results. *Right structure*: the red mark showed the pocket that possibly become the protein active site. *Bottom table*: informed the secondary structure and other protein analysis results.