Medicinal Au(I) compounds targeting urease as prospective antimicrobial agents: unveiling the structural basis for enzyme inhibition

SUPPLEMENTARY INFORMATION

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Table 1-SI. Data collection, processing and refinement statistics for the X-ray crystal structures of SPU co-crystallized in the presence of $Au(PEt_3)I$ (**3**, PDB code 7P7N) and $Au(PEt_3)_2Cl$ (**4**, PDB code 7P7O).

Data collection	**7P7N** $Au(PEt_3)I$ (**3**)	**7P7O** $Au(PEt_3)_2Cl$ (**4**)
Wavelength (Å)	0.9762	
Detector	DECTRIS PILATUS 6M	
Crystal-to-Detector distance (mm)	269.4	
Oscillation angle (degrees)	0.100	
Number of images	1800	
Space group	$P6_322$	
Unit cell (*a, b, c,* Å)	131.6 131.6 189.2	131.8, 131.8, 189.4
Resolution range (Å)[a]	114.0–1.80 (1.83–1.80)	114.1–1.87 (1.90–1.87)
Total number of reflections[a]	1180987 (61039)	1400616 (79653)
Unique reflections[a]	89759 (4534)	80498 (4557)
Multiplicity[a]	13.2 (13.5)	17.4 (17.5)
Completeness[a] (%)	100.0 (100.0)	100.0 (100.0)
R_{sym}[a,b] (%)	14.2 (230.0)	15.8 (300.1)
R_{pim}[a,c] (%)	5.8 (93.1)	5.0 (108.0)
Mean I half-set correlation CC(1/2)[a]	0.999 (0.694)	0.999 (0.744)
Mean I/σ(I)[a]	17.0 (1.5)	17.9 (1.5)
Refinement statistics		
Number of monomers in the asymmetric unit	3 (αβγ)	3 (αβγ)
R_{factor}[d] (%)	14.7	16.3
R_{free}[d] (%)	17.7	20.4
Cruickshank's DPI for coordinate error[e] based on R_{factor} (Å) [e]	0.093	0.116
Wilson plot B-factor (Å^2)	25.3	26.9
Average all atom B-factor[f] (Å^2)	31.7	38.9
B-factor[f] for the Ni atoms (Å^2)	31.6; 30.3	36.1; 36.7
RMS (bonds)[d]	0.01	0.01
RMS (angles)[d]	1.69	1.63
Total number of atoms	6937	6879
Total number of water molecules	549	469
Solvent content (%)	53.2	53.6
Matthews Coefficient (Å^3/Da)	2.63	2.65
Ramachandran plot[d]		
Favored regions (%)	95.5	95.6
Additionally allowed regions (%)	3.7	3.7
Disallowed regions (%)	0.8	0.7

[a] Highest resolution bin in parentheses;

[b] $R_{sym} = \sum_{hkl}\sum_{j}|I_j - \langle I\rangle| / \sum_{hkl}\sum_{j} I_j$, where I is the intensity of a reflection, and $\langle I\rangle$ is the mean intensity of all symmetry related reflections j; [c] $R_{p.i.m.} = \sum_{hkl}\left\{[1/(N-1)]^{1/2}\sum_{j}|I_j - \langle I\rangle|\right\} / \sum_{hkl}\sum_{j} I_j$, where I is the intensity of a reflection, and $\langle I\rangle$ is the mean intensity of all symmetry related reflections j, and N is the multiplicity[13];

[d] Taken from REFMAC; R_{free} is calculated using 5% of the total reflections that were randomly selected and excluded from refinement;

[e] $DPI = R_{factor} \cdot D_{max} \cdot compl^{-1/3} \sqrt{\frac{N_{atoms}}{(N_{refl} - N_{params})}}$, where N_{atoms} is the number of the atoms included in the refinement, N_{refl} is the number of the reflections included in the refinement, D_{max} is the maximum resolution of reflections included in the refinement, *compl* is the completeness of the observed data, and for isotropic refinement, $N_{params} \approx 4N_{atoms}$;

[f] Taken from BAVERAGE.

Table 2-SI. Selected distances (Å) and angles (°) around the Ni(II) ions in the crystal structures of SPU co-crystallized in the presence of $Au(PEt_3)I$ (**3**, PDB code 7P7N) and $Au(PEt_3)_2Cl$ (**4**, PDB code 7P7O). The same parameters reported for the structures of native (PBD 4CEU) and Au(I)-bound SPU (PDB code 6I9Y) are reported for comparison.

	7P7N $Au(PEt_3)I$ (**3**)	**7P7O** $Au(PEt_3)_2Cl$ (**4**)	**4CEU** Native	**6I9Y** Au(I)-SPU
Ni - L Distances (Å)				
Ni(1) - αLys220* Oθ1	2.0	2.0	1.9	2.0
Ni(1) - O_B[a]	2.1	2.1	2.1	1.9
Ni(1) - O_1	2.2	2.1	2.2	2.2
Ni(1) - αHis249 Nδ	2.0	2.1	2.0	2.1
Ni(1) - αHis275 Nε	2.1	2.0	2.0	2.2
Ni(2) - αLys220* Oθ2	2.0	2.1	2.1	2.1
Ni(2) - O_B	2.1	2.2	2.1	2.2
Ni(2) - O_2	2.3	2.3	2.1	2.6
Ni(2) - αHis137 Nε	2.1	2.1	2.1	2.1
Ni(2) - αHis139 Nε	2.1	2.1	2.1	2.2
Ni(2) - αAsp363 Oδ1	2.1	2.1	2.1	2.2
Ni(1) ••• Ni(2)	3.6	3.7	3.7	3.6
O_1 ••• O_2	2.1	2.0	2.4	2.2
L - Ni - L Angles (°)				
αLys220* Oθ1 - Ni(1) - αHis249 Nδ	108.3	103.7	100.4	103.2
αLys220* Oθ1 - Ni(1) - αHis275 Nε	102.5	103.2	107.2	104.0
αLys220* Oθ1 - Ni(1) - O_B	93.8	96.4	96.6	91.2
αLys220* Oθ1 - Ni(1) - O_1	107.0	101.6	108.2	110.8
αHis249 Nδ - Ni(1) - αHis275 Nε	97.1	98.5	98.6	91.9
αHis275 Nε - Ni(1) - O_B	95.1	96.1	94.6	93.2
O_B - Ni(1) - O_1	63.0	61.2	67.0	80.2
O_1 - Ni(1) - αHis249 Nδ	93.2	94.9	89.3	86.4
αHis249 Nδ - Ni(1) - O_B	151.9	151.6	154.2	163.1
αHis275 Nε - Ni(1) - O_1	143.8	148.1	141.6	144.7
αLys220* Oθ2 - Ni(2) - αHis137 Nε	95.1	93.5	90.8	90.9
αLys220* Oθ2 - Ni(2) - αHis139 Nε	93.4	92.3	91.7	91.2
αLys220* Oθ2 - Ni(2) - O_2	91.2	88.6	92.9	93.5
αLys220* Oθ2 - Ni(2) - O_B	95.8	95.1	95.6	91.7
αAsp363 Oδ1 - Ni(2) - αHis137 Nε	84.4	83.5	82.8	83.6
αAsp363 Oδ1 - Ni(2) - αHis139 Nε	81.7	85.0	86.4	87.2
αAsp363 Oδ1 - Ni(2) - O_2	91.6	94.8	94.5	93.1
αAsp363 Oδ1 - Ni(2) - O_B	90.0	90.2	89.1	92.3
O_2 - Ni(2) – O_B	61.3	61.3	67.7	68.8
O_B - Ni(2) - αHis137 Nε	94.8	95.8	95.0	90.1
αHis137 Nε- Ni(2) - αHis139 Nε	114.4	113.4	108.5	112.8
αHis139 Nε- Ni(2) - O_2	88.5	89.3	88.4	88.0
αLys220* Oθ2 - Ni(2) - αAsp363 Oδ1	174.3	174.5	172.4	173.1
O_B - Ni(2) - αHis139 Nε	148.5	149.3	155.3	156.8
O_2- Ni(2) - αHis137 Nε	155.8	157.1	162.6	158.6
Ni(1) - O_B - Ni(2)	119.0	117.8	122.1	125.8

Figure 1-SI. *Per* residue Cα RMSD calculated between the α, β and γ subunits (coloured red, magenta and blue, respectively) of SPU co-crystallized in the presence of $Au(PEt_3)I$ (**3**, PDB code P7PN) (upper panel) and $Au(PEt_3)_2Cl$ (**4**, PDB code P7PO) (bottom panel) with respect to native SPU (PDB code 4CEU).

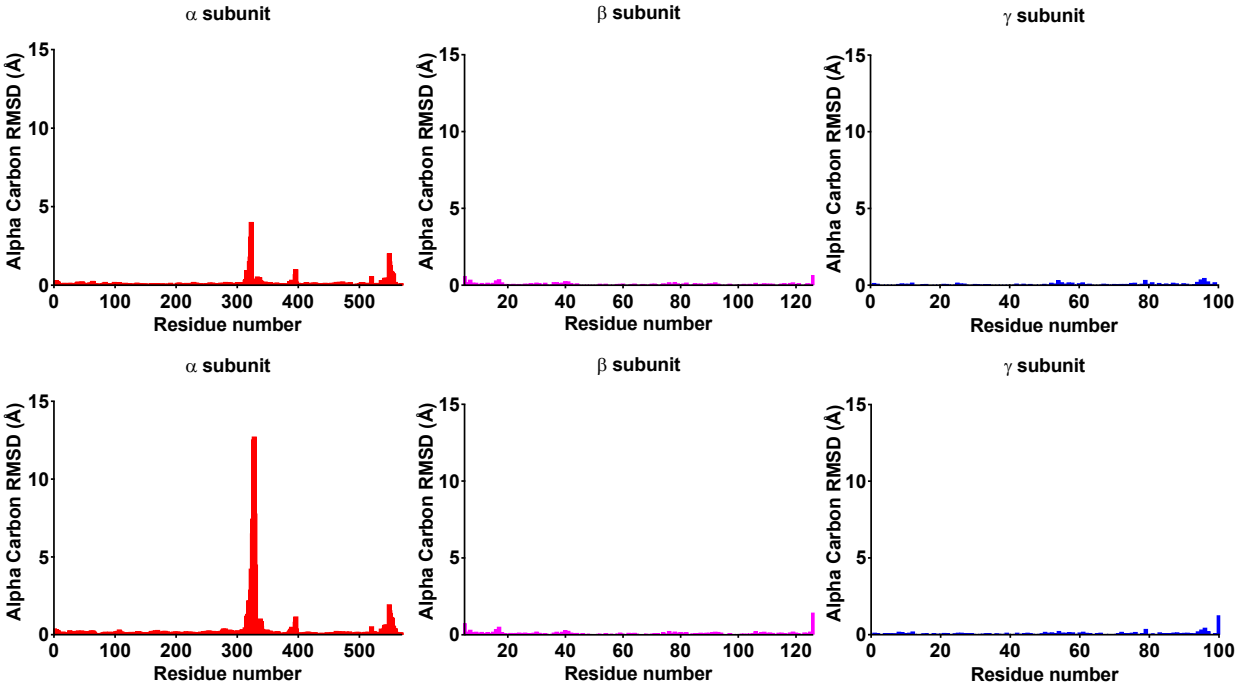

Figure 2-SI. *Per* residue Cα RMSD calculated between the α, β and γ subunits (coloured black, dark grey and grey, respectively) of SPU co-crystallized in the presence of $Au(PEt_3)I$ (**3**, PDB code 7P7N) (upper panel) and $Au(PEt_3)_2Cl$ (**4**, PDB code 7P7O) (bottom panel) with respect to Au(I)-inhibited SPU (PDB code 6I9Y).