SUPPLEMENTARY MATERIAL

Phosphonic Acid-containing Inhibitors of Tyrosyl-DNA Phosphodiesterase 1

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Table S1. X-ray Data Collection and Refinement Statistics.

|                        | TDP1-4c complex | TDP1-3b complex |
|------------------------|-----------------|-----------------|
| **Data collection Statistics** |                 |                 |
| Diffraction source     | APS, SER-CAT, 22-BM | APS, SER-CAT, 22-BM |
| Wavelength (Å)         | 1.0000          | 1.0000          |
| Temperature (K)        | 100             | 100             |
| Detector               | MX300-HS        | MX300-HS        |
| Space group            | P2₁2₁2₁         | P2₁2₁2₁         |
| Unit cell parameters   |                 |                 |
| a,b,c (Å)              | 49.81, 104.73, 193.15 | 49.89, 104.60, 193.10 |
| α,β,γ (°)              | 90, 90, 90      | 90, 90, 90      |
| Resolution range (Å)   | 50-1.58 (1.62-1.58)* | 50-1.56 (1.59-1.56) |
| Total reflections       | 994965          | 965807          |
| Unique reflections      | 137386 (6750)   | 142916 (6267)   |
| Completeness (%)        | 99.9 (99.6)     | 98.8 (87.6)     |
| Multiplicity            | 7.2 (5.6)       | 6.8 (4.7)       |
| Mean I/σ(I)             | 35.8 (2.0)      | 30.2 (1.8)      |
| Rmerge                  | 0.068 (0.671)   | 0.072 (0.652)   |
| Rp.i.m.                 | 0.027 (0.304)   | 0.030 (0.286)   |
| CC₁/₂                   | 0.996 (0.848)   | 0.997 (0.775)   |
| **Refinement Statistics** |                 |                 |
| Resolution range (Å)    | 49.27-1.58      | 43.83-1.56      |
| Number of reflections   | 137247          | 142797          |
| Number of reflections used in $R_{free}$ | 6803 | 6955 |
| Final $R_{work}$        | 0.166           | 0.171           |
| Final $R_{free}$        | 0.193           | 0.195           |
| Number of non-H atoms   |                 |                 |
| Protein, chain A        | 3647            | 3664            |
| Protein, chain B        | 3646            | 3627            |
| 4c (XZ766)              | 66              |                 |
| 3b (XZ768)              |                 | 74              |
| Water                   | 808             | 777             |
| Ethylene glycol         | 28              | 28              |
| DMSO                    |                 | 4               |
| Average $B$ factors (Å²) |                 |                 |
| Protein, chain A        | 25.5            | 22.1            |
| Protein, chain B        | 32.2            | 33.1            |
| 4c (XZ766)              | 45.8            |                 |
| 3b (XZ768)              |                 | 35.5            |
| Water                   | 42.6            | 38.9            |
| Ethylene glycol         | 35.4            | 28.6            |
| DMSO                    |                 | 55.4            |
| Estimated coordinate error (Å) |             | 0.16            |
| R.m.s. deviations from ideal |  |  |
|----------------------------|---|---|
| Bond lengths (Å)           | 0.01 | 0.01 |
| Bond angles (°)            | 1.1 | 1.0 |
| Ramachandran plot          |  |  |
| Favored (%)                | 98.0 | 97.1 |
| Allowed (%)                | 2.0 | 2.8 |
| Outliers (%)               | 0 | 0.1 |
| **MolProbity Analysis**    |  |  |
| Clashscore, all atoms      | 2.05 (99th percentile) | 2.54 (99th percentile) |
| Protein geometry score     | 0.97 (100th percentile) | 1.20 (98th percentile) |
| PDB deposition code        | 7UFY | 7UFZ |

*Values in parentheses are for the highest resolution shell of data.*