

Design and Synthesis of Novel Dual-Target Agents for HDAC1 and CK2 Inhibition

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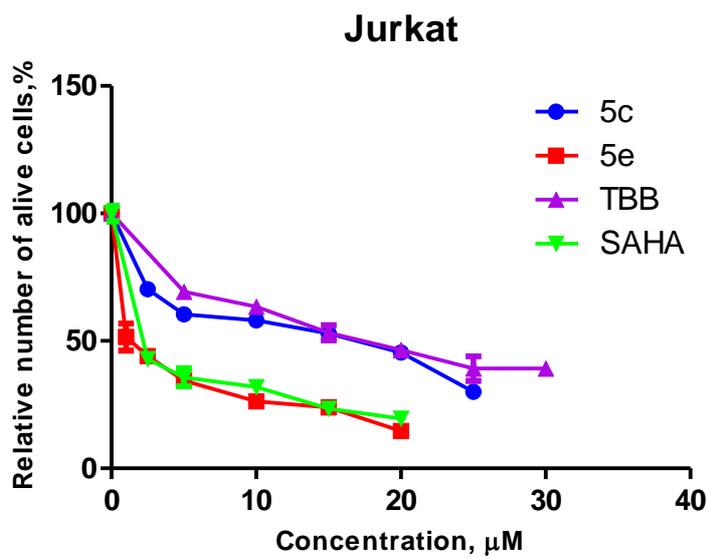
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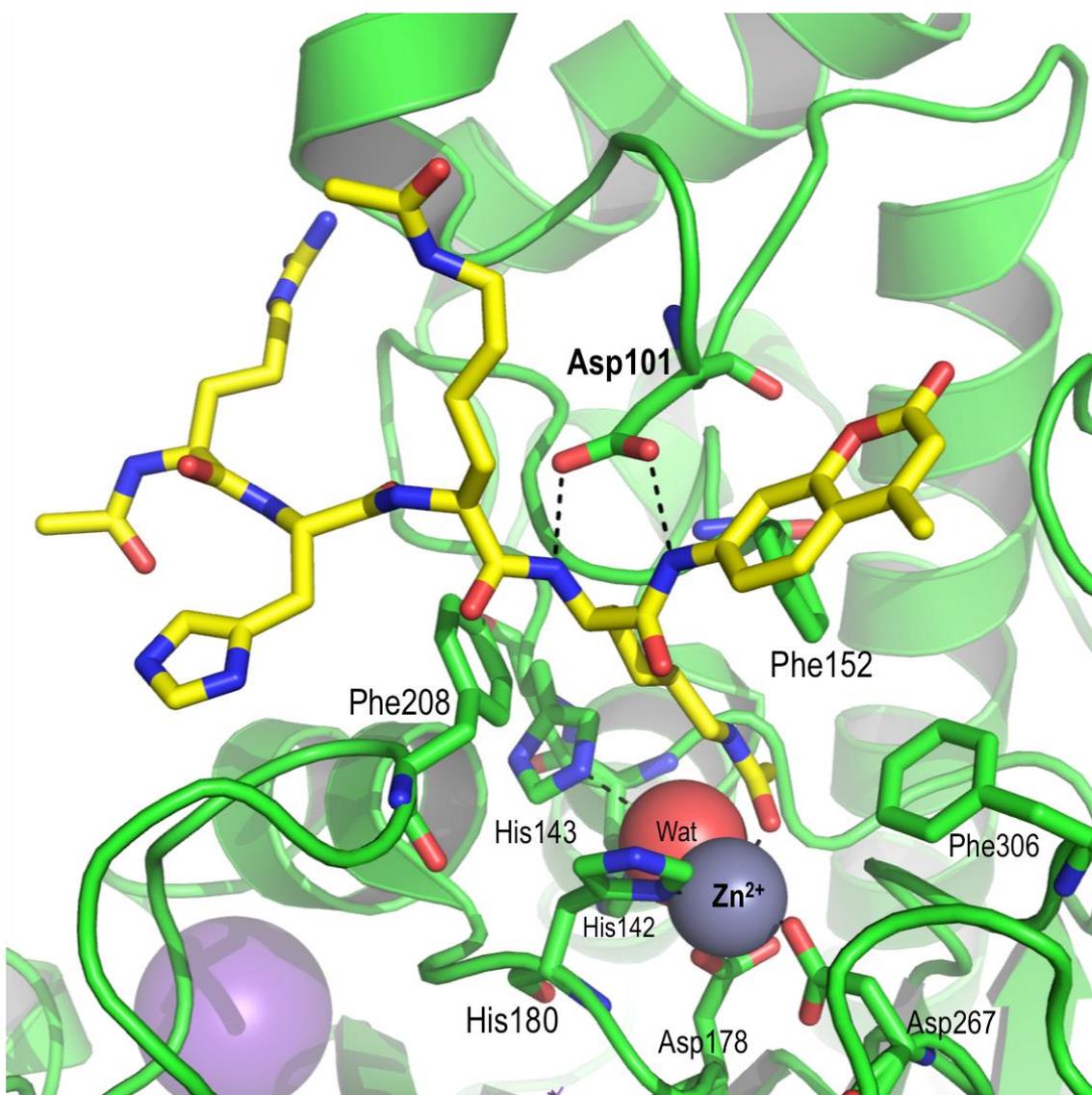
SUPPORTING INFORMATION

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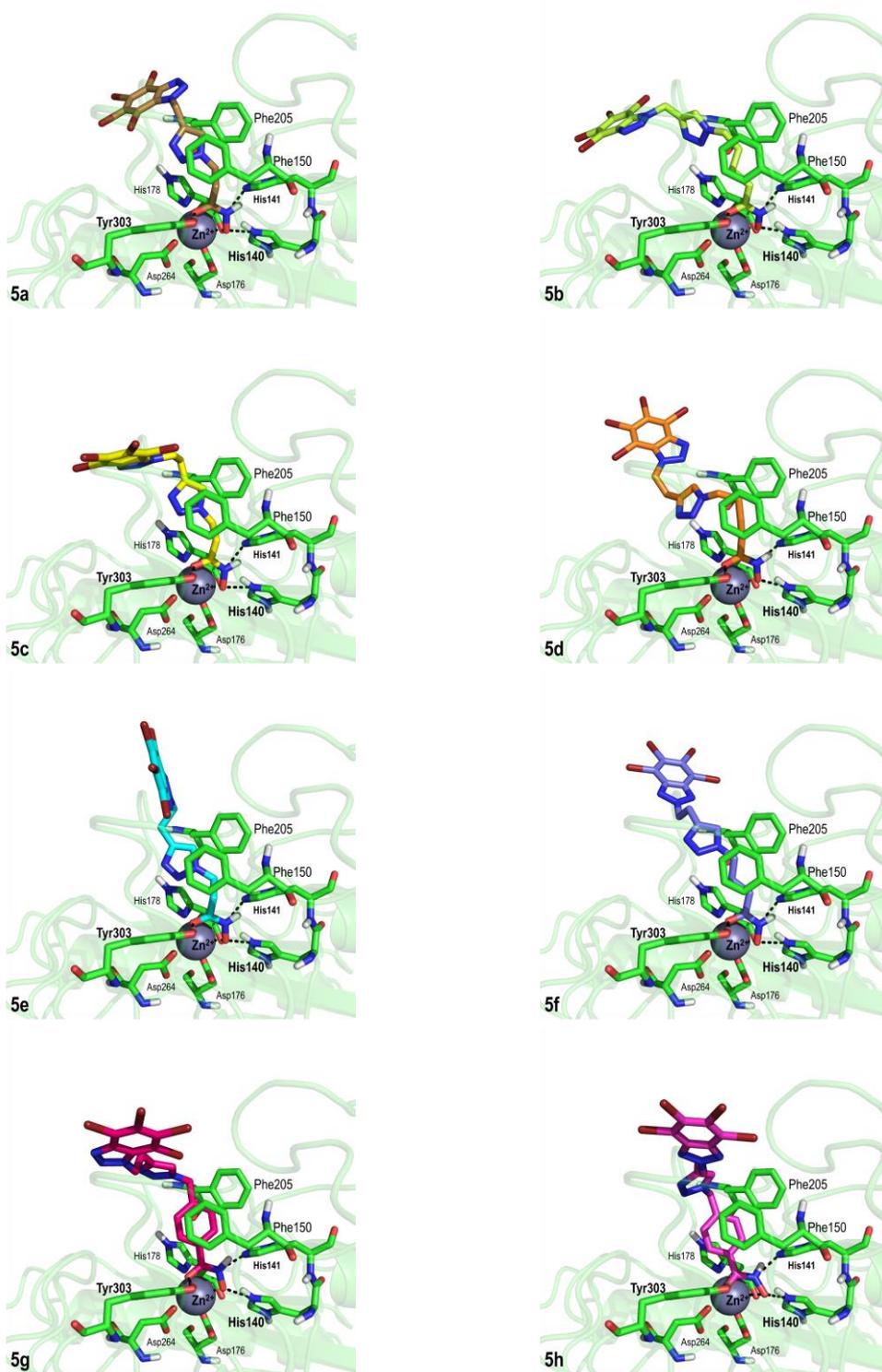
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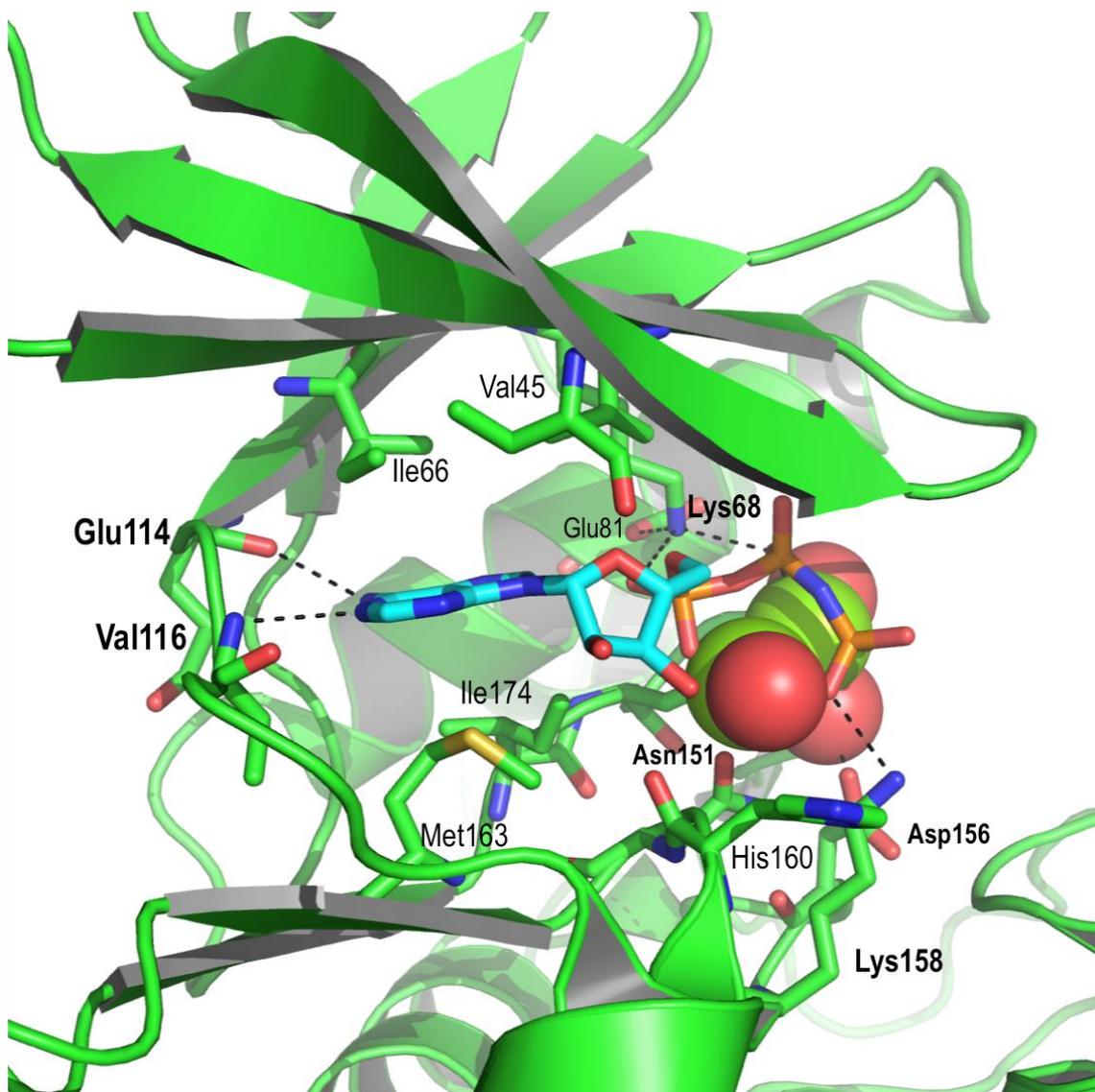
Supplementary Figure S1. Cytotoxic activity of compounds **5c** and **5e** compared to TBB and SAHA towards human T-leukemia cells of Jurkat line .



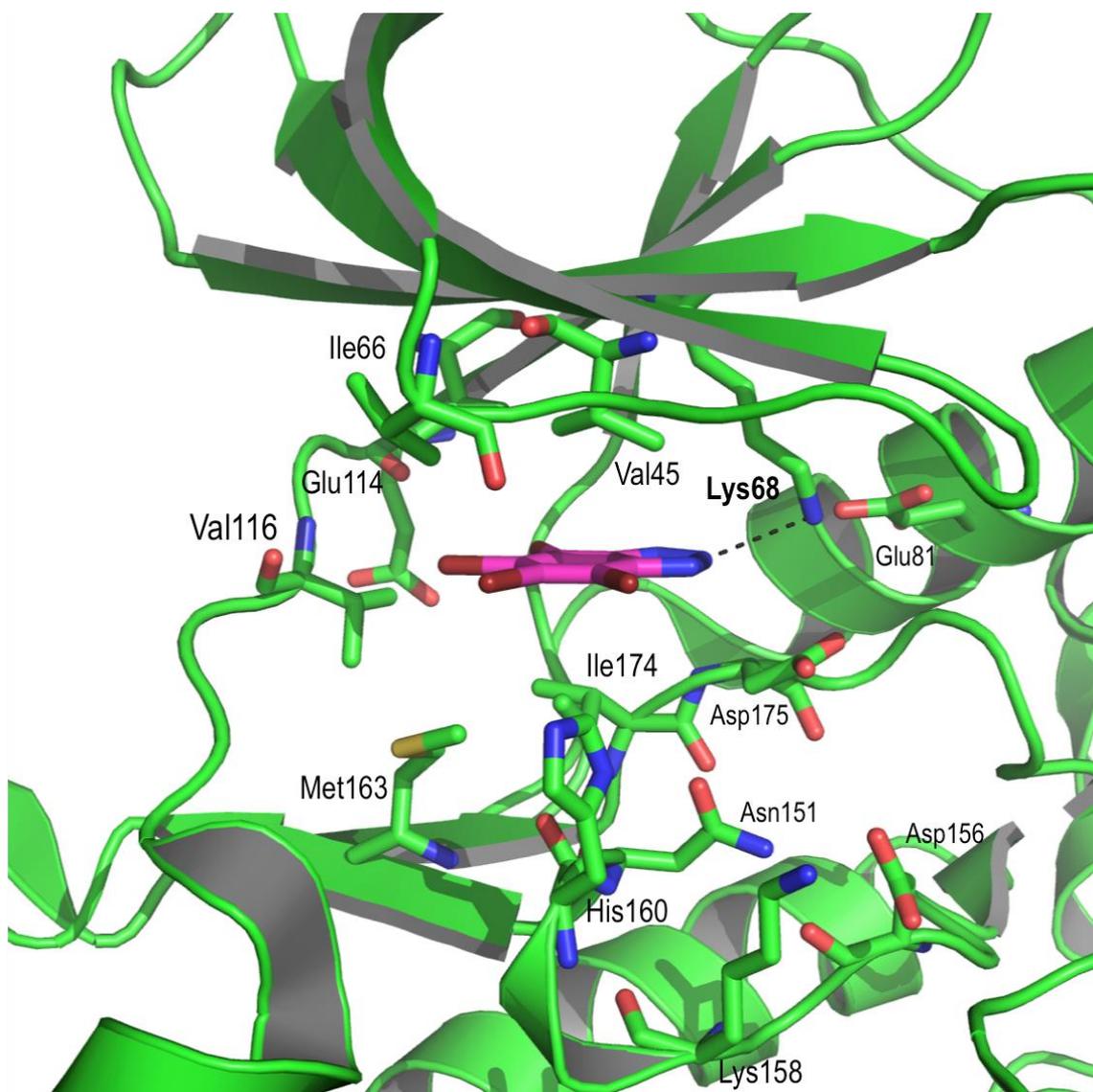
Supplementary Figure S2: PyMOL stick and cartoon representation of the binding of a substrate-like molecule (yellow sticks) to HDAC-8 (green) such as it appears in PDB structure 2V5W. The main amino acids involved in the binding are represented as sticks and the catalytic Zn²⁺ and the water molecule that completes its coordination sphere are represented as a grey and red sphere respectively. Hydrogen bonding and coordinating interactions are shown as dashed lines and the residues involved are labelled in bold.



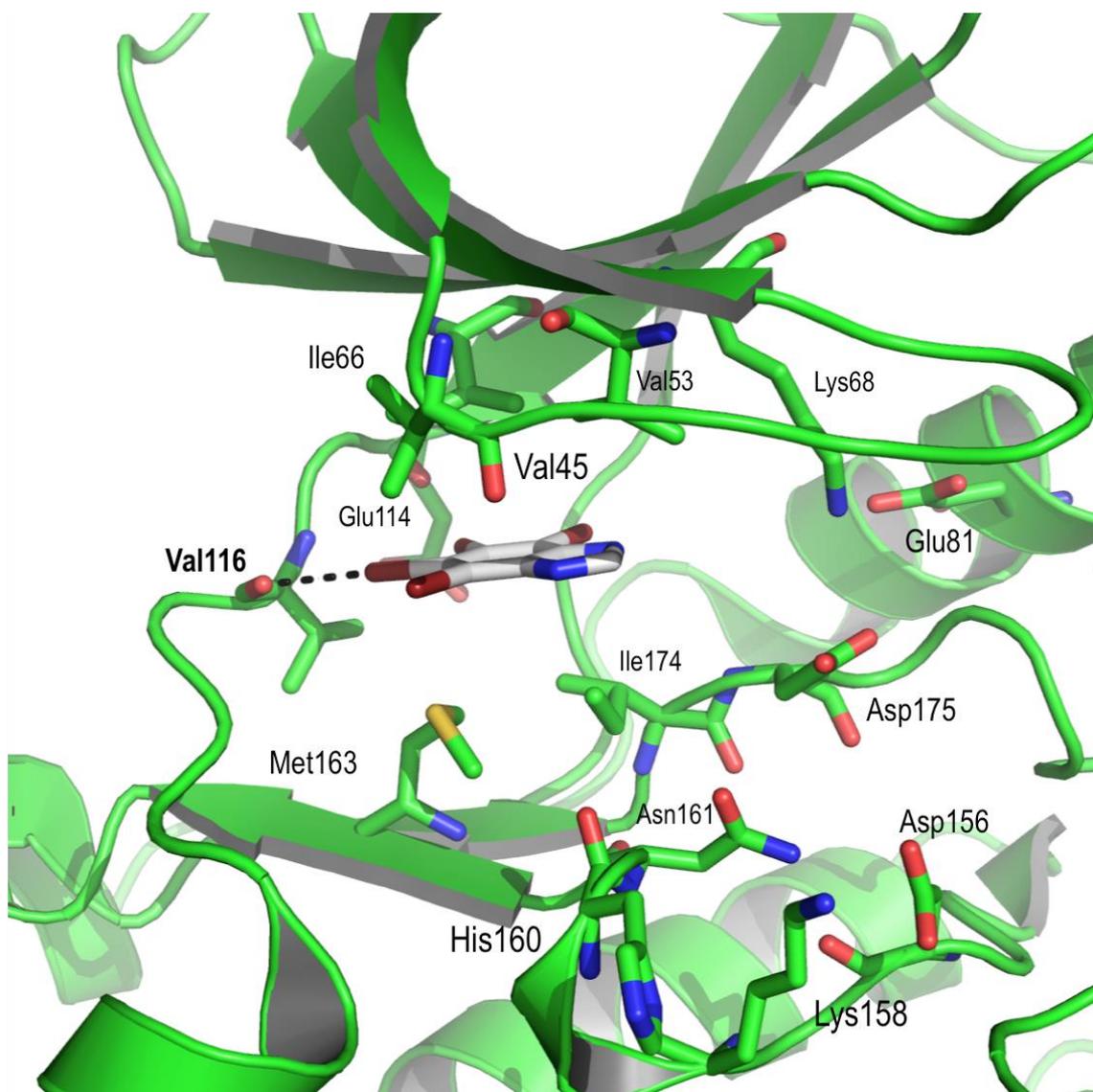
Supplementary Figure S3: PyMOL stick and cartoon representation of the docking poses obtained for the series of new ligands in HDAC1. The main amino acids involved in the binding are represented as sticks and the catalytic Zn²⁺ is represented as a grey sphere. Hydrogen bonding and coordinating interactions are shown as dashed lines and the residues involved are labelled in bold. Compounds **5a** to **5d** are coloured in shades of yellow, **5e** and **5f** are coloured in shades of blue, and **5g** and **5h** are coloured in shades of pink.



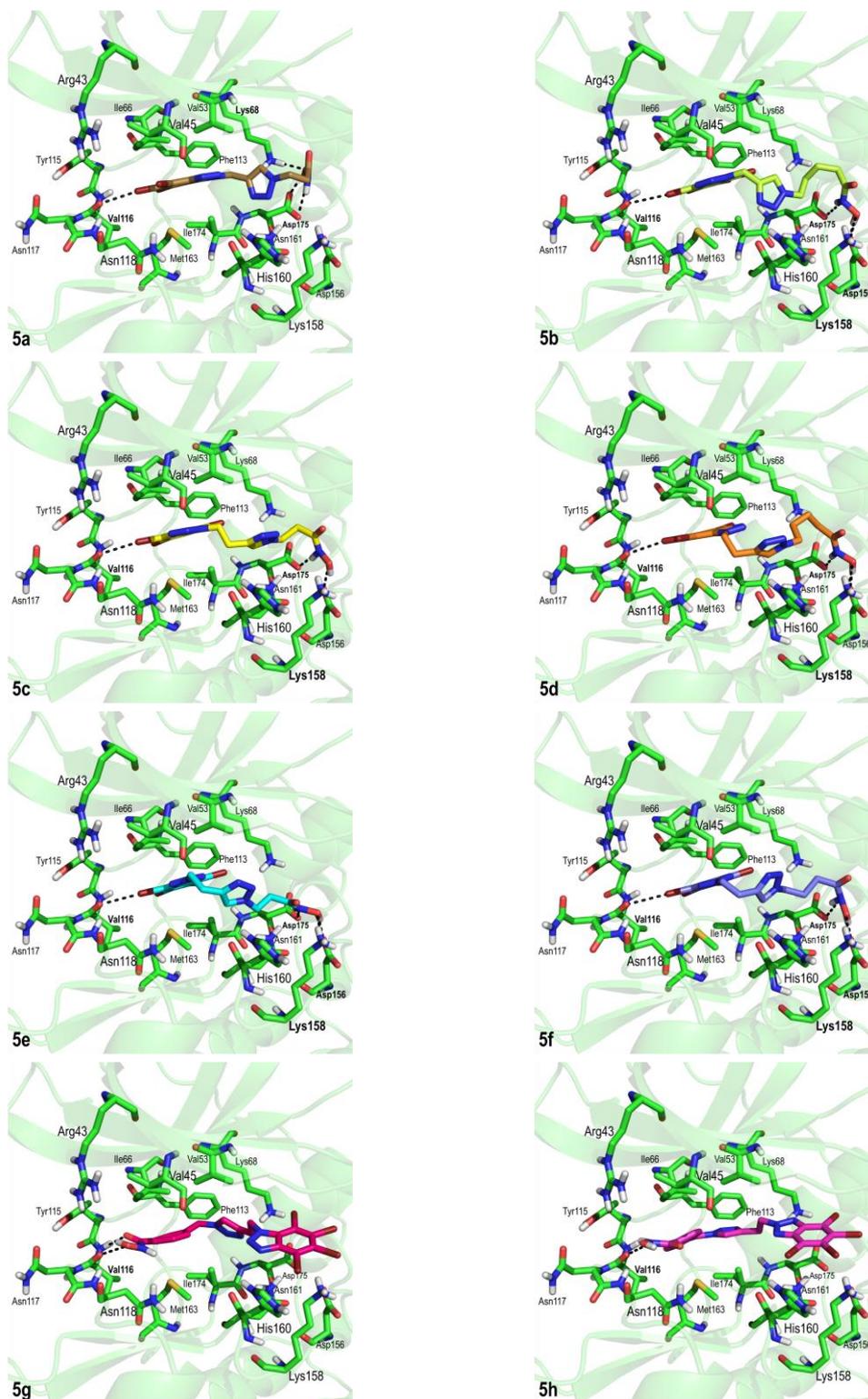
Supplementary Figure S4: PyMOL stick and cartoon representation of the binding of slow-hydrolysis-rate ATP analog ANP (cyan sticks) to the alpha subunit of CK2 such as it appears in PDB structure 1DAW. The main amino acids involved in the binding are represented as sticks, the two Mg^{2+} and the water molecules that complete the coordination spheres are represented as green and red sphere respectively. Hydrogen bonding and coordinating interactions are shown as dashed lines and the residues involved are labelled in bold.



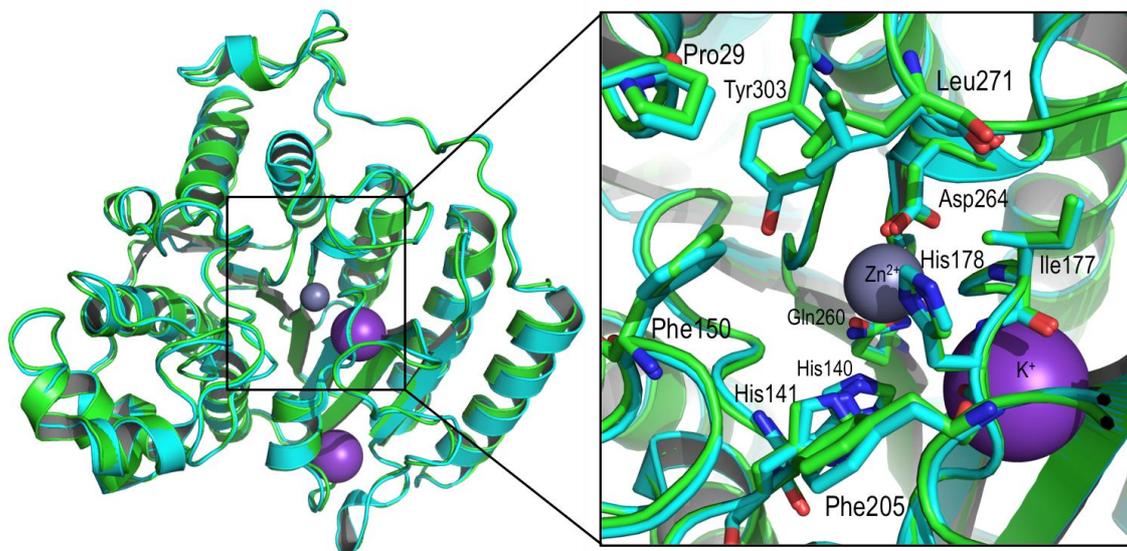
Supplementary Figure S5: PyMOL stick and cartoon representation of the binding of TBB (magenta sticks) to the alpha subunit of CK2 such as it appears in PDB structure 1J91. The main amino acids involved in the binding are represented as sticks, the hydrogen bonding interactions are shown as dashed lines and the residues involved are labelled in bold.



Supplementary Figure S6: PyMOL stick and cartoon representation of the binding of tetrabromobenzoimidazole (white sticks) to the alpha subunit of CK2 such as it appears in PDB structure 2OXY. The main amino acids involved in the binding are represented as sticks, the hydrogen-bonding interactions are shown as dashed lines and the residues involved are labelled in bold.



Supplementary Figure S7: PyMOL stick and cartoon representation of the docking poses obtained for the series of new ligands in CK2. The main amino acids involved in the binding are represented as sticks. Hydrogen bonding and halogen bonding interactions are shown as dashed lines and the residues involved are labelled in bold. Compounds **5a** to **5d** are coloured in shades of yellow, **5e** and **5f** are coloured in shades of blue, and **5g** and **5h** are coloured in shades of pink.



Supplementary Figure S8: PyMOL stick and cartoon representation of the superimposition of the HDAC1 structures from the SWISS MODEL (green) and the HDAC1 crystal structure as it appears in PDB structure 4BKX. The main amino acids of the active site are represented as sticks in the close up (right) where the acetic acid present in 4BKX is not shown for clarity. The catalytic Zn^{2+} and the structural K^+ in 4BKX, which occupy the same positions as the cations in the HDAC1 model, are represented as grey and purple spheres, respectively.

