

Supplementary Materials

Structural basis for the selective inhibition of Cdc2-like kinases by CX-4945

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Running title: Crystal structures of CLK isoforms in complex with CX-4945

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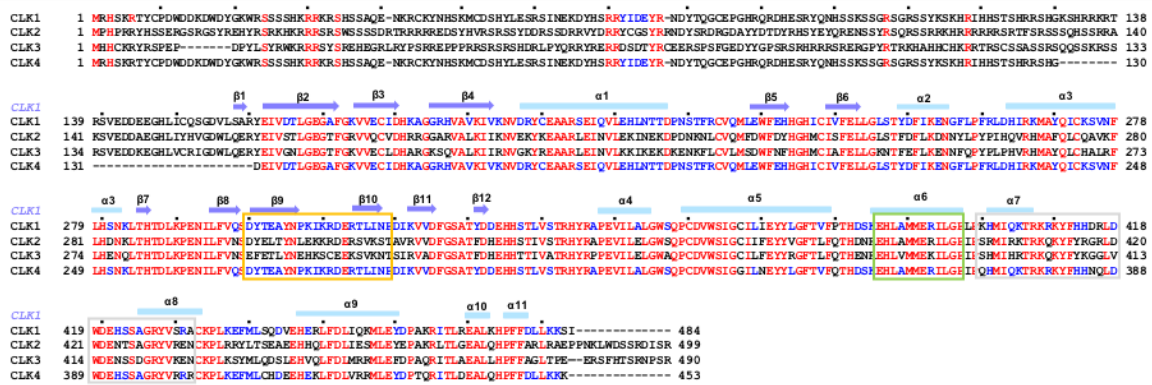
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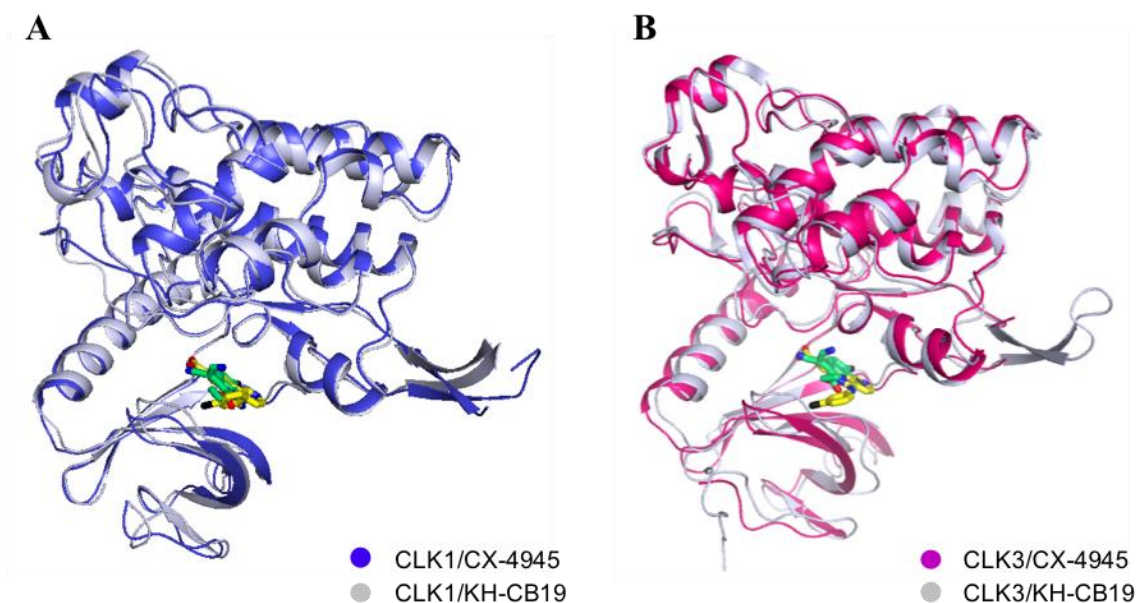
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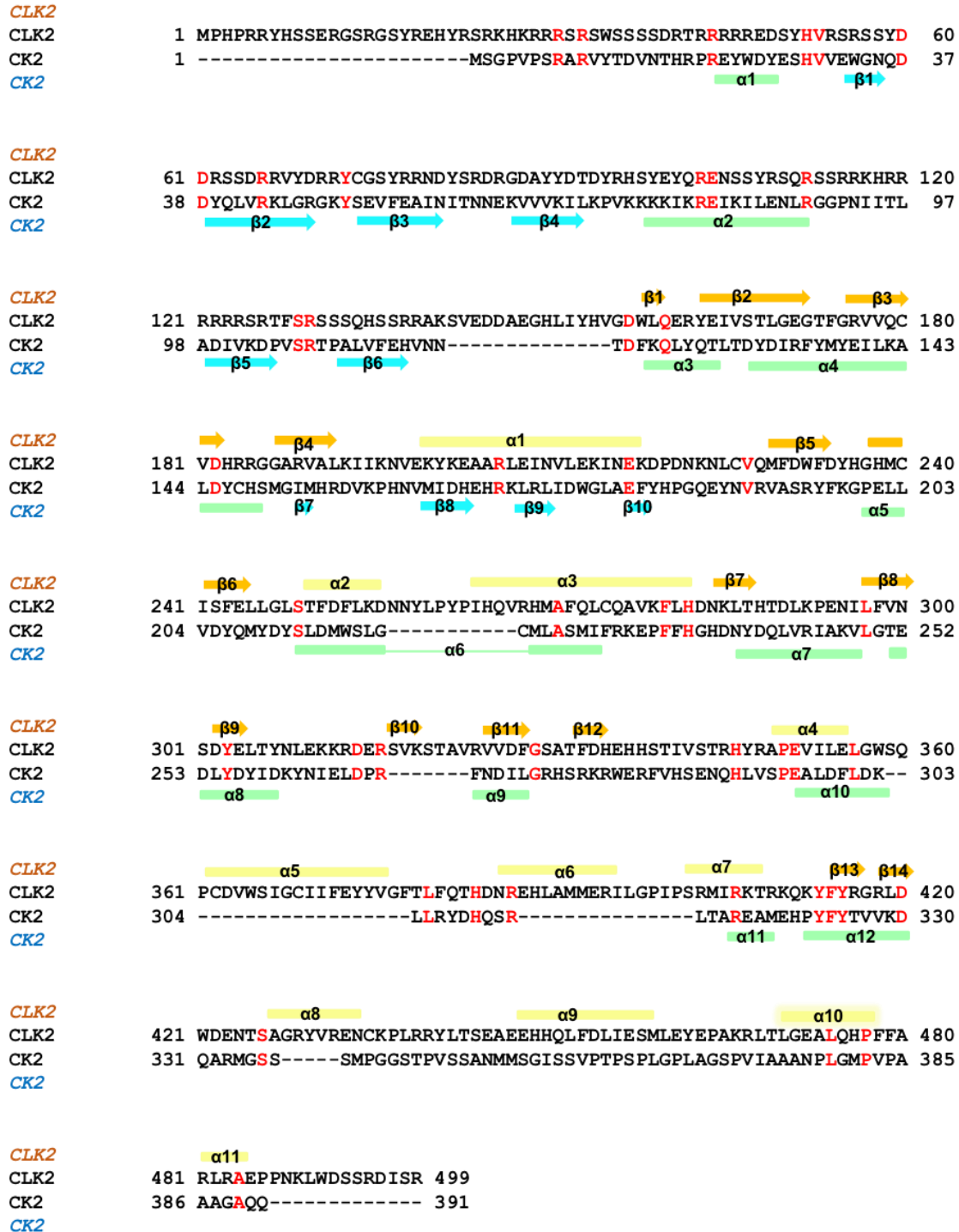
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Supplementary Figure 1. Sequence alignment of the four isoforms of CLKs. Amino acid sequences of the CLK1, CLK2, CLK3, and CLK4 proteins are aligned, and 100% identical residues are colored in red. Identical residues in CLK1 and CLK4 are colored in blue. The α -helix of CLK1 is colored in sky blue, and β -sheet is colored in purple. The common features of CLK are shown in solid line boxes (β -hairpin insertion: yellow; EHLAMMERILG motif: light green; MAPK-like



Supplementary Figure 2. Structural comparison of CLKs with the inhibitors CX-4945 and KH-CB19. (A) Superimposed structures of CLK1/CX-4945 (blue) and CLK1/KH-CB19 (PDB code, 2VAG; gray) structures. The CX-4945 and KH-CB19 molecules are colored in yellow and green, respectively. (B) Superimposed structures of CLK3/CX-4945 (magenta) and CLK3/KH-CB19 (PDB code, 2WUT; gray). The CX-4945 and KH-CB19 molecules are colored in yellow and green, respectively. Nitrogen, oxygen, and chlorine are colored in blue, red, and black, respectively.



Supplementary Figure 3. Structure-based sequence alignment of CLK2 and CK2. Amino acid sequences from CLK2 and CK2 are aligned. Identical amino acids between CLK2 and CK2 are shown in red. The α -helices and β -sheets (secondary structures) of CLK2 are colored in yellow and dark yellow, respectively. The α -helices and β -sheets of CK2 are shown in light green and cyan, respectively.