Supporting Information

Discovery of potent pyruvate dehydrogenase kinases inhibitors and their anti-lung cancer activity evaluation under hypoxia

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1. ITC Titration

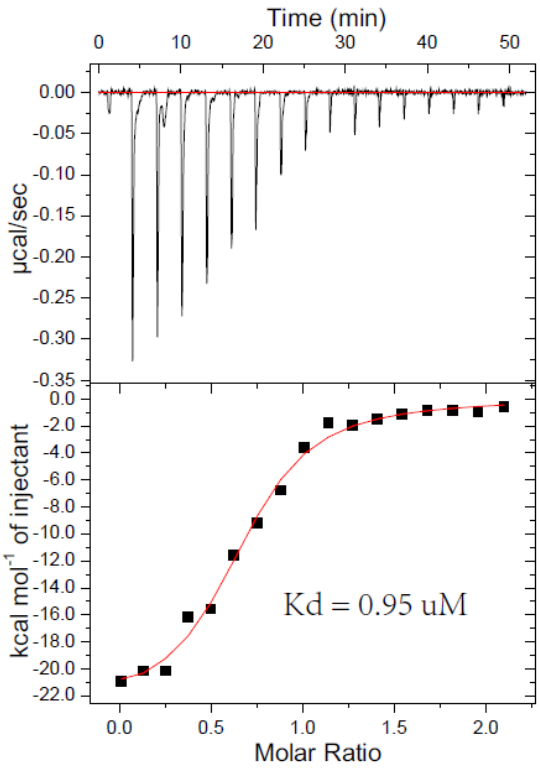

Fig. S1 ITC analysis of the binding affinity for **11** and PDK1, raw data for the titration, in which the power output in microcalories per second is measured as a function of time in minutes, compound **11** (100 µM) titrated into PDK1 buffer solution (10 µM).

2. Molecular docking

The selected 12 candidates were then docked into the ATP binding pocket of PDK1, PDK3, and PDK4. For PDK1, we aligned the PDK1 (PDB: 2Q8F) into PDK2 (PDB: 4V25), then remove PDK amino acid sequences, leaving VER-246608 in PDK1 ATP binding pocket. Then we did a Molecular dynamics simulation of the PDK1-VER-246608 complex. Then 12 candidates were docked into the ATP binding pocket of PDK1. For PDK3 and PDK4, the PDB files 2Q8I and 2E0A were selected.

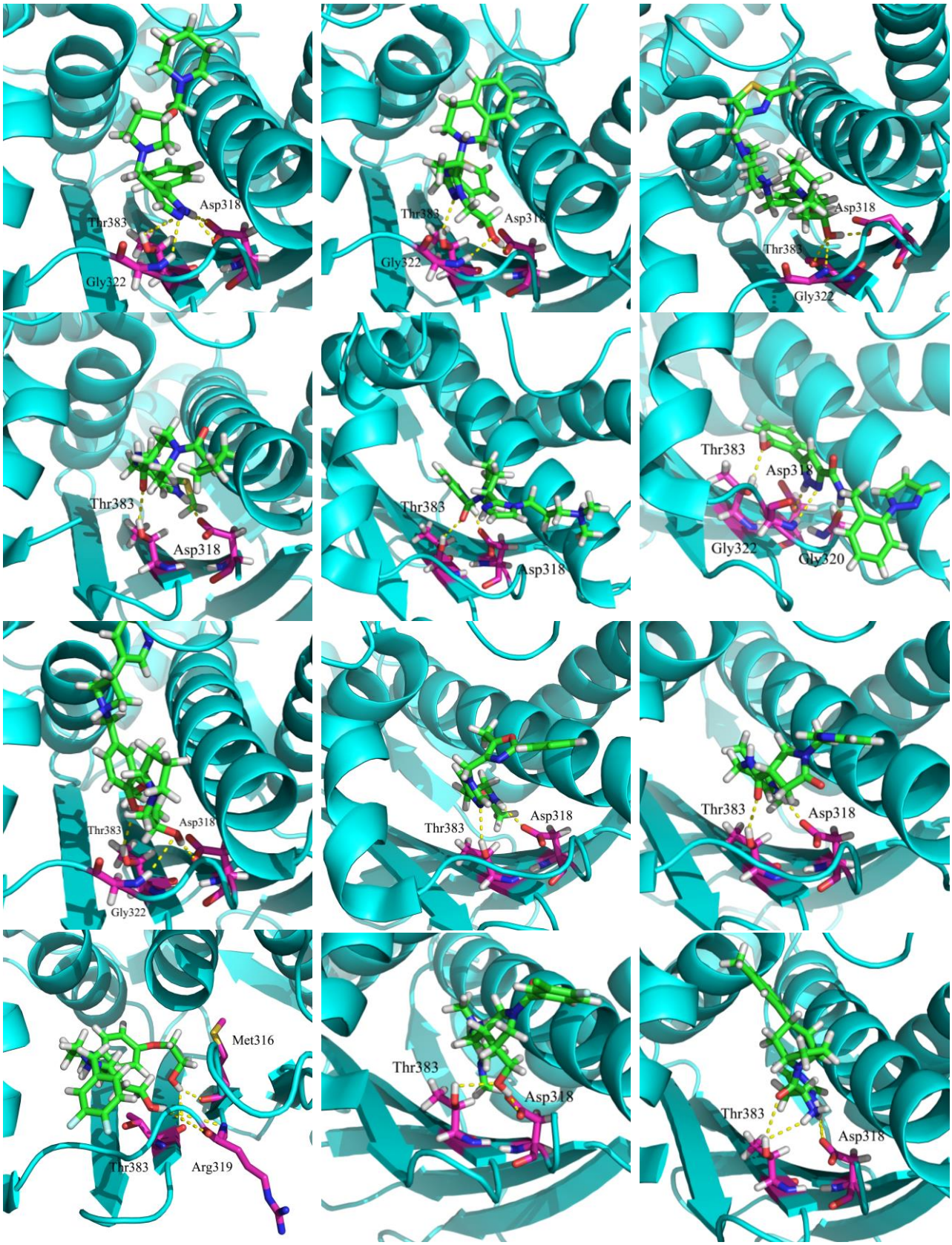

Fig. S2 The 12 candidates were docked into the ATP binding pocket of PDK1. All the amino acid residues involved in the hydrogen bond interactions were shown as stick models, the formed hydrogen bonds were shown as yellow dash lines, the graphics of 3D views were drawn by PyMOL.

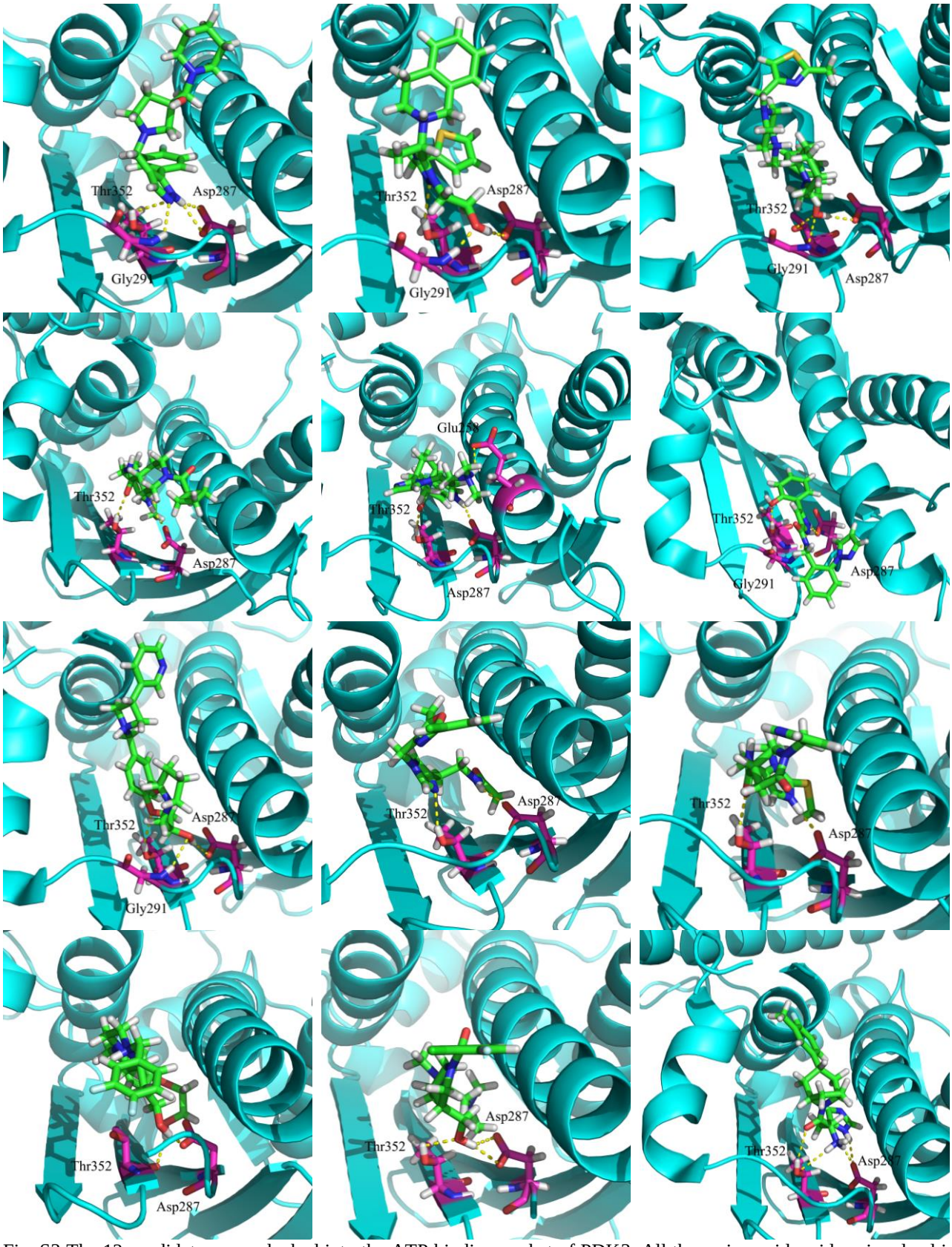

Fig. S3 The 12 candidates were docked into the ATP binding pocket of PDK3. All the amino acid residues involved in the hydrogen bond interactions were shown as stick models, the formed hydrogen bonds were shown as yellow dash lines, the graphics of 3D views were drawn by PyMOL.

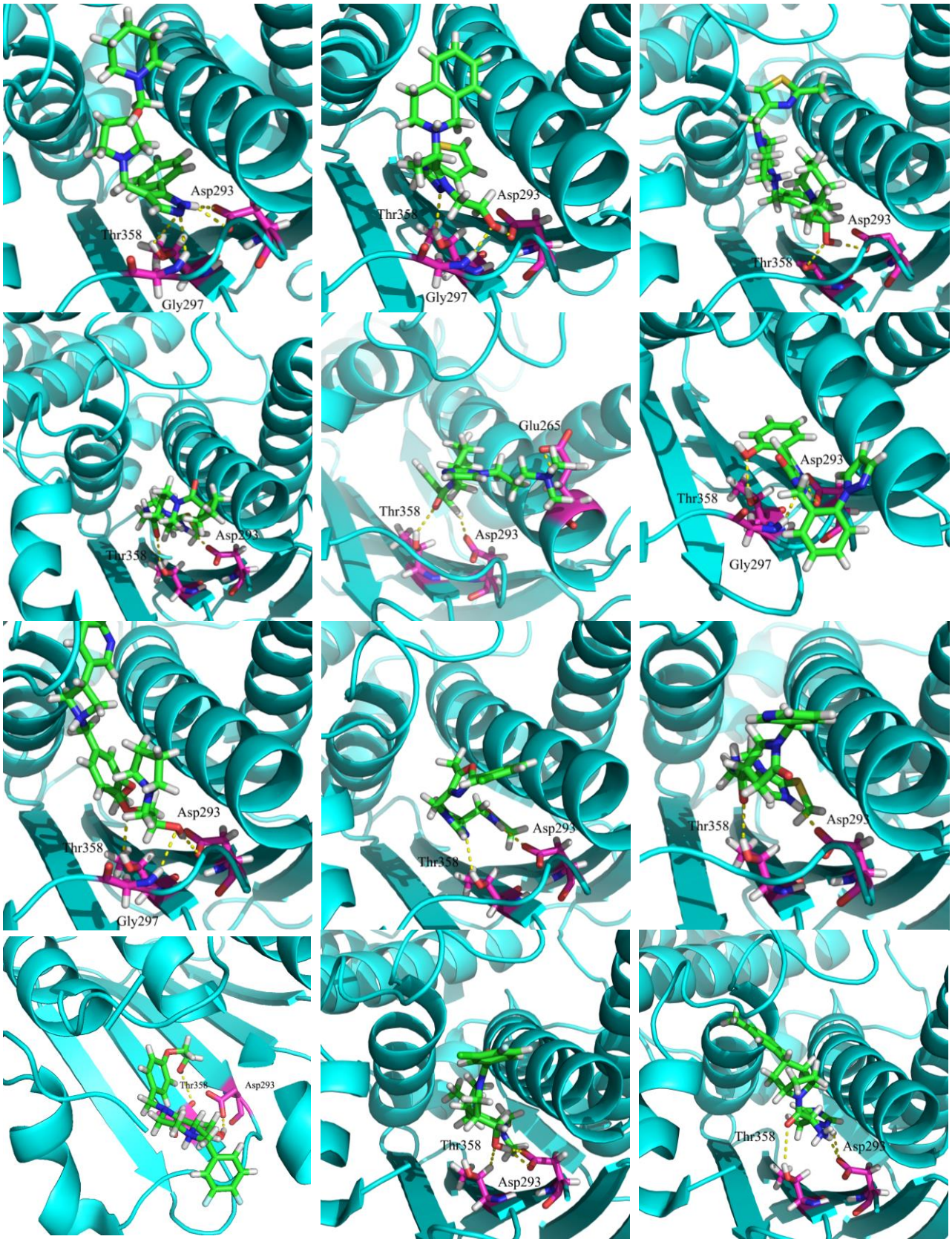

Fig. S4 The 12 candidates were docked into the ATP binding pocket of PDK4. All the amino acid residues involved in the hydrogen bond interactions were shown as stick models, the formed hydrogen bonds were shown as yellow dash lines, the graphics of 3D views were drawn by PyMOL.