Supplemental Materials and Methods

Molecular modeling

Computer modeling of curcumin with CDKs was performed using the Schrödinger Suite 2013 software programs [1]. First the CDK1/2/4 crystal structures were obtained from the RCSB (The Research Collaboratory for Structural Bioinformatics) Protein Data Bank [2]. These structures were prepared under standard procedures of Protein Preparation Wizard in Schrödinger Suite 2013. Hydrogen atoms were added consistent with a pH of 7 and all water molecules were removed. Finally, an ATP binding site based receptor grid was generated for the docking study. Curcumin was prepared using the LigPrep program of Schrödinger for docking using default parameters. Then curcumin-protein docking was accomplished using the program Glide and default parameters under the extra precision (XP) mode. Using these methods, we obtain the best-docked representative structure.

Results

Supplementary Figure 1. Curcumin inhibits CDK2 kinase activity *ex vivo.* After immunoprecipitation of the CDK2 proteins from HCT116 cell lysates using a specific CDK2 antibody, the effect of curcumin on CDK2 kinase activity was measured. Data are represented as means ± S.D. as determined from 3 independent experiments and the asterisk (*) indicates a significant ($p < 0.001$) difference compared to untreated cell lysate group.

Supplementary Figure 2. *In silico* model of curcumin binding with CDKs at the ATP binding site. To better understand how curcumin interacts with CDK1/4, we performed a computational docking model using the Glide docking program from Schrödinger Suite 2013.

The binding affinity between curcumin and CDK1 and 4 was predicted by a score of −8.94 and −7.63 kcal/mol, respectively. In the docked models, curcumin can bind at the ATP binding pocket of CDK1 or 4 and form some hydrogen bonds and other interactions. (Some images were generated with the UCSF Chimera program [3]). A) Binding of curcumin at the ATP binding pocket of CDK1 or 4. B) Ligand Interaction Diagram (LID) for curcumin binding with CDKs. C) LID legend.

1. Schrödinger, *Schrödinger Suite 2013.* Schrödinger, LLC, New York, NY, 2013, 2013.
2. Berman, H.M., et al., *The Protein Data Bank.* Nucleic Acids Res, 2000. 28(1): p. 235-42.
3. Pettersen, E.F., et al., *UCSF Chimera--a visualization system for exploratory research and analysis.* J Comput Chem, 2004. 25(13): p. 1605-12.