

Supporting Information

Cell-permeable PROTAC degrader against KEAP1 efficiently suppress hepatic stellate cell activation through antioxidant and anti-inflammatory pathway

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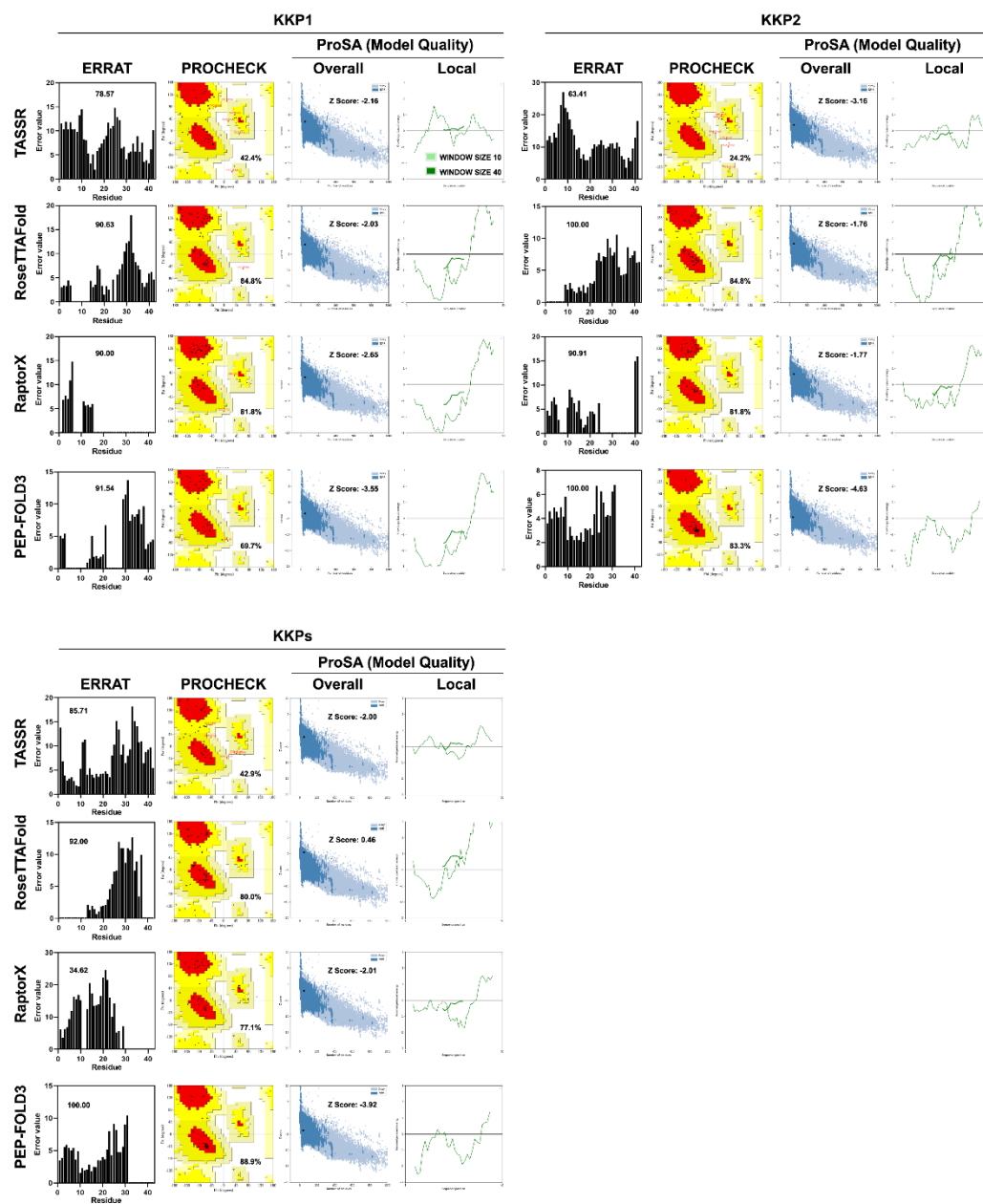


Figure S1 Online server-based validation of structures generated by multiple predictors

Structures of KKP1, KKP2 and KKPs generated using TASSR, RoseTTAFold, RaptorX and PEP-FOLD3 were validated by ERRAT, PROCHECK and ProSA (overall and local) online server, RoseTTAFold generated structures of KKP1, KKP2 and KKPs have highest score among these four predictors.

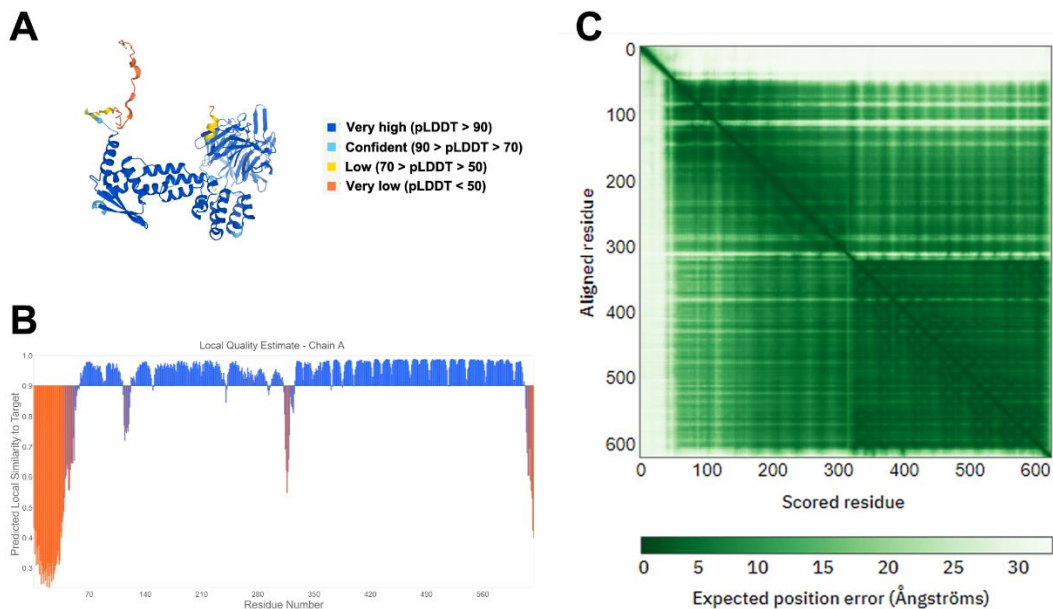


Figure S2 Prediction and quality assay of AlphaFold generated Keap1 structure

A. AlphaFold generated rat Keap1 protein structure.

B. Local quality estimation of predicted rat Keap1 protein structure, blue bar indicated very high, while orange bar indicated low quality in prediction.

C. Heat map of expected position error from aligned residues.

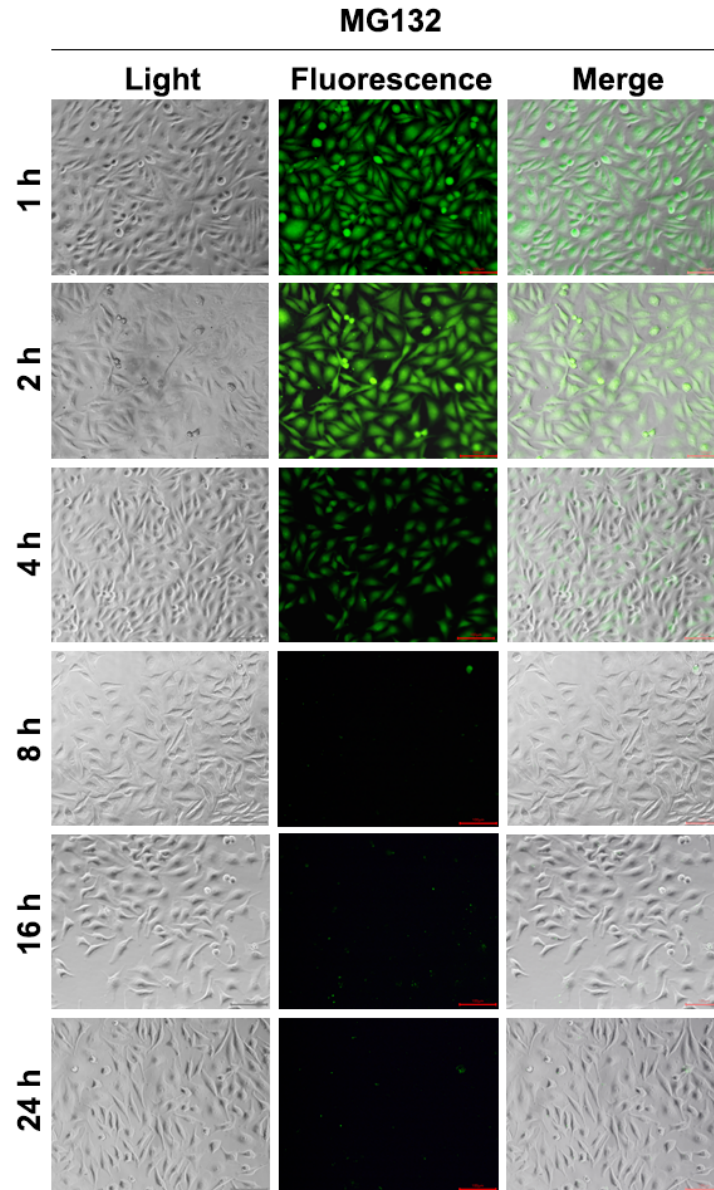


Figure S3 Fluorescence microscopy of FITC-labeled KKP1 at 7.5 μM incubation with different time points under MG132 treatment.

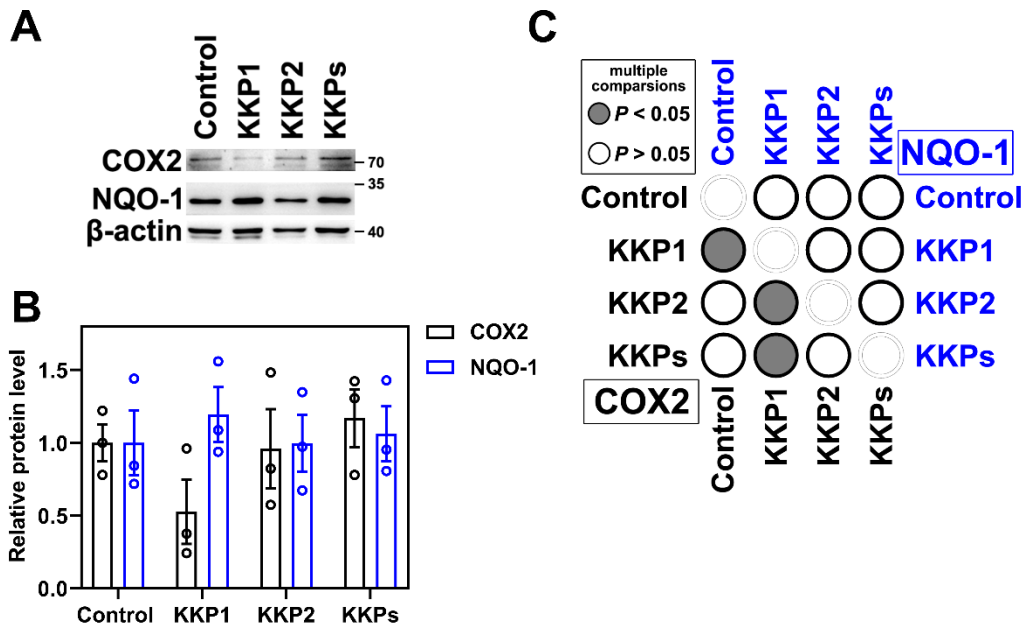


Figure S4 Downstream of Nrf2/ARE pathway involved in KKP1 mediated Keap1 degradation

- A. Western blot analysis of COX 2 and NQO-1 protein level in HSC-T6 treated with KKP1, KKP2 and KKPs for 8 hours.
- B. Densitometric quantification of COX 2 and NQO-1 protein in the blots shown in Figure S4A, data in the graph are means \pm SEM of three independent measurements.
- C. The corresponding p -value plot between data pairs presenting in Figure S4B.