SUPPLEMENTAL MATERIAL

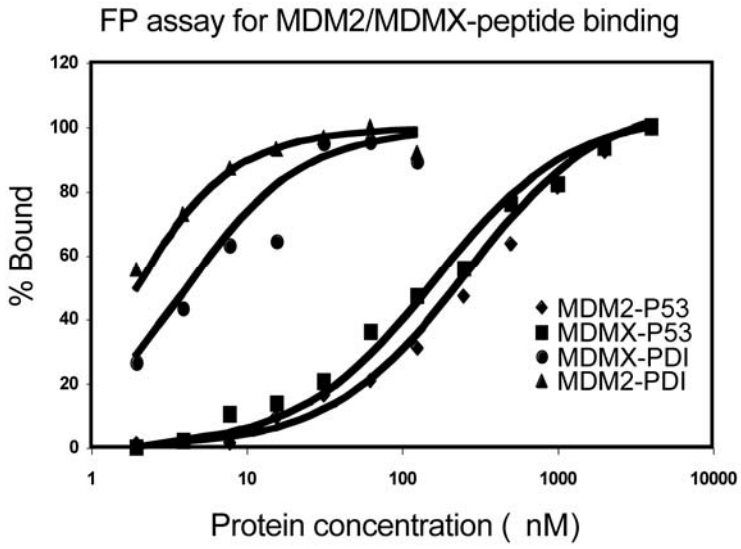

FIGURE S1: **Determination of the dissociation constants for peptide binding to MDM2 and MDMX.**
The binding of N terminal FITC-conjugated peptides was detected by fluorescence polarization for the indicated peptide protein interactions.

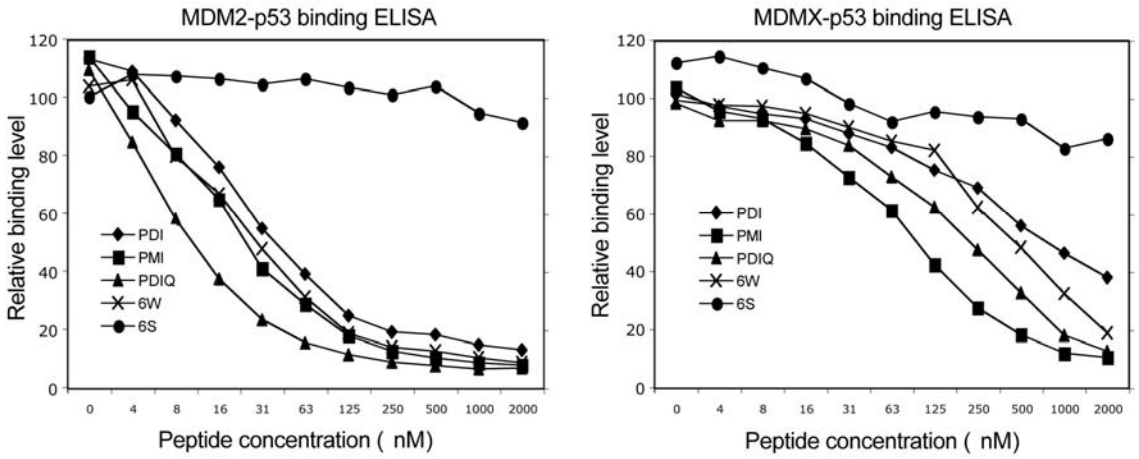

FIGURE S2: **Determination of the inhibitory activity of peptides against MDM2 and MDMX.** The potency of peptides to disrupt His6-p53 binding to GST-MDM2 and GST-MDMX N terminal domains was determined using ELISA assay to yield the IC50 values of Table 1. Displayed are representative dose-response curves.

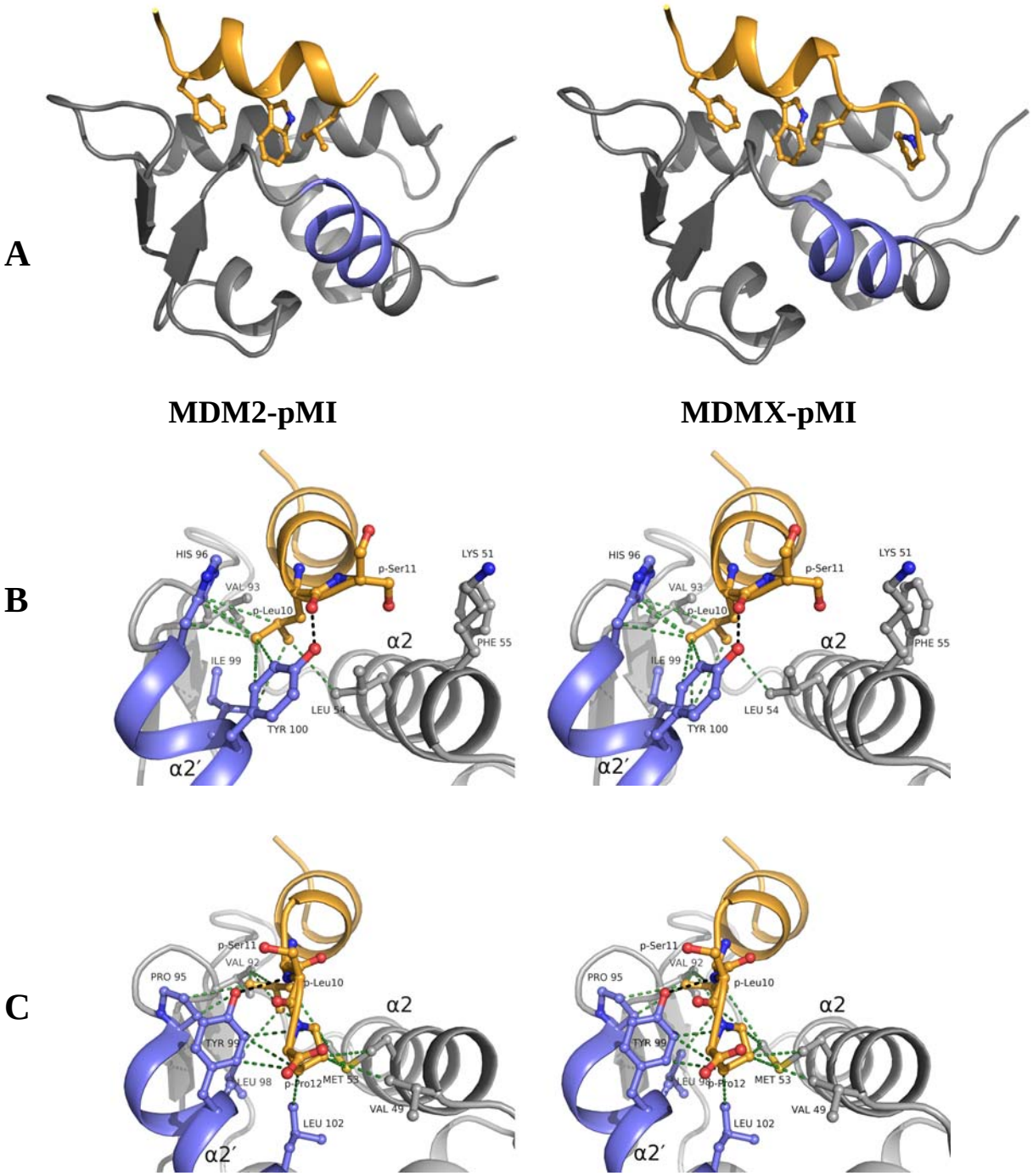

FIGURE S3: **Molecular basis for the high-affinity binding of the pMI peptide.**
(A) Overall structures of MDM2 and MDMX liganded with the pMI peptide. Note the structural changes in the C-terminal part of the pMI peptide upon interaction with MDMX.
(B) Stereo view of the interaction pattern between the C-terminal residues of the pMI peptide with MDM2.
(C) Stereo view of the interaction pattern between the C-terminal residues of the pMI peptide with MDMX.
Hydrogen bonding interactions ($d \leq 3.3$ Å) are indicated by black dotted lines, van-der-Waals interactions ($d \leq 4.2$ Å) by green dotted lines. The figures are based on the PDB codes 3EQS and 3EQY (reference 31). Note that the peptide Pro12 residue was excluded from refinement of the MDM2-pMI structure.