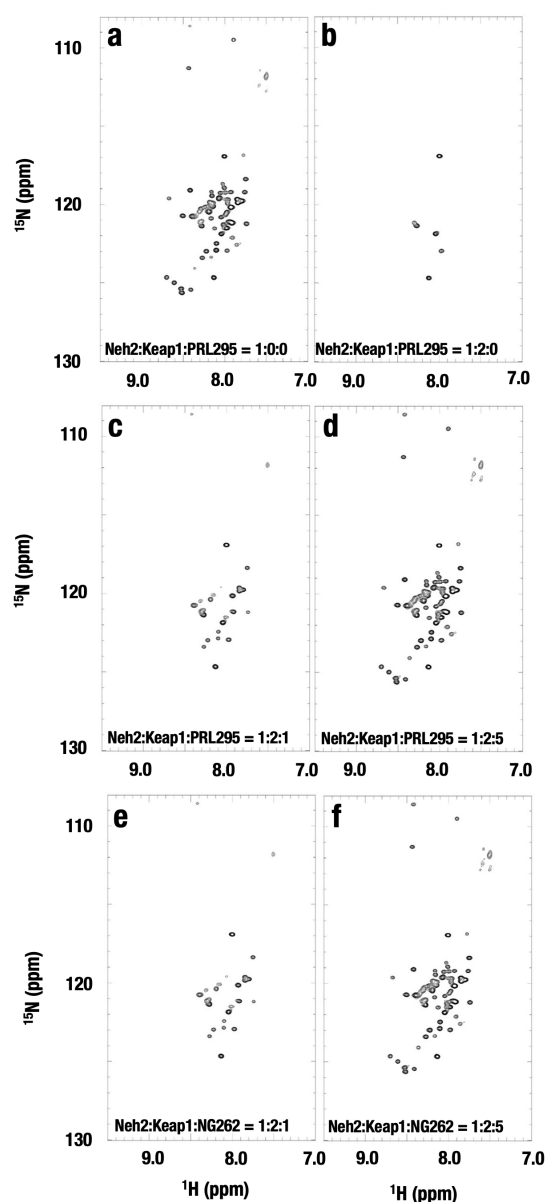
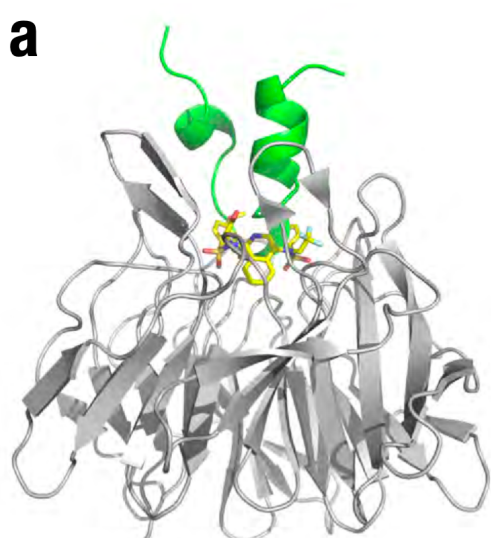




Supplementary Figure 1. Titration of Neh2-Keap1 complex with pharmacological Keap1-Nrf2 PPI inhibitors. 2D TROSY-HSQC spectrum of $^{13}\text{C}/^{15}\text{N}$ -labeled Neh2 in the absence (a) or presence (b) of 2-fold excess of Keap1. 2D TROSY-HSQC spectrum of $^{13}\text{C}/^{15}\text{N}$ -labeled Neh2 in the presence of 2-fold excess of Keap1 after the addition of equal amount (c) or 5-fold excess amount (d) of PRL295. 2D TROSY-HSQC spectrum of $^{13}\text{C}/^{15}\text{N}$ -labeled Neh2 in the presence of 2-fold excess of Keap1 after the addition of equal amount (e) or 5-fold excess amount (f) of NG262.

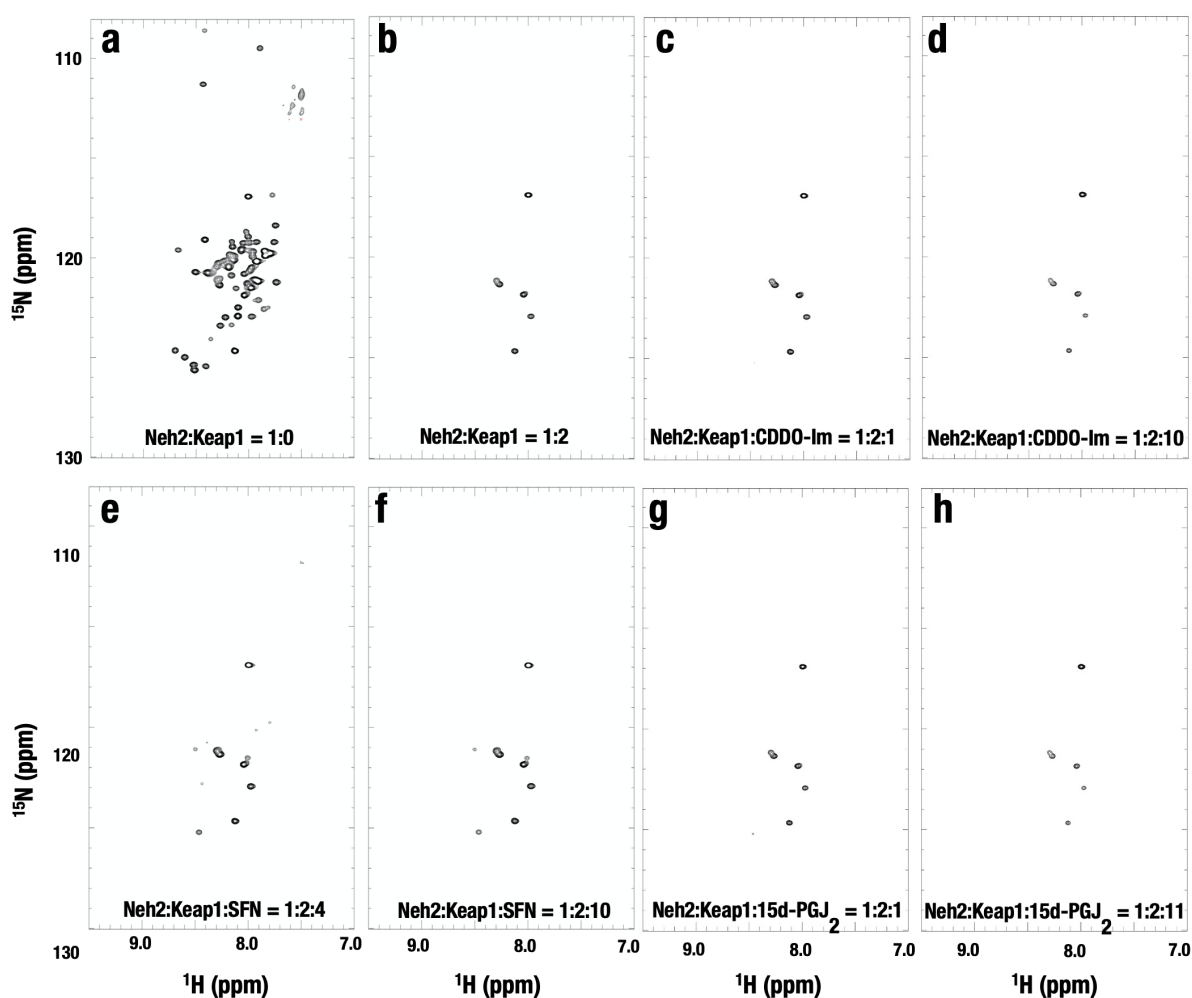


PRL295

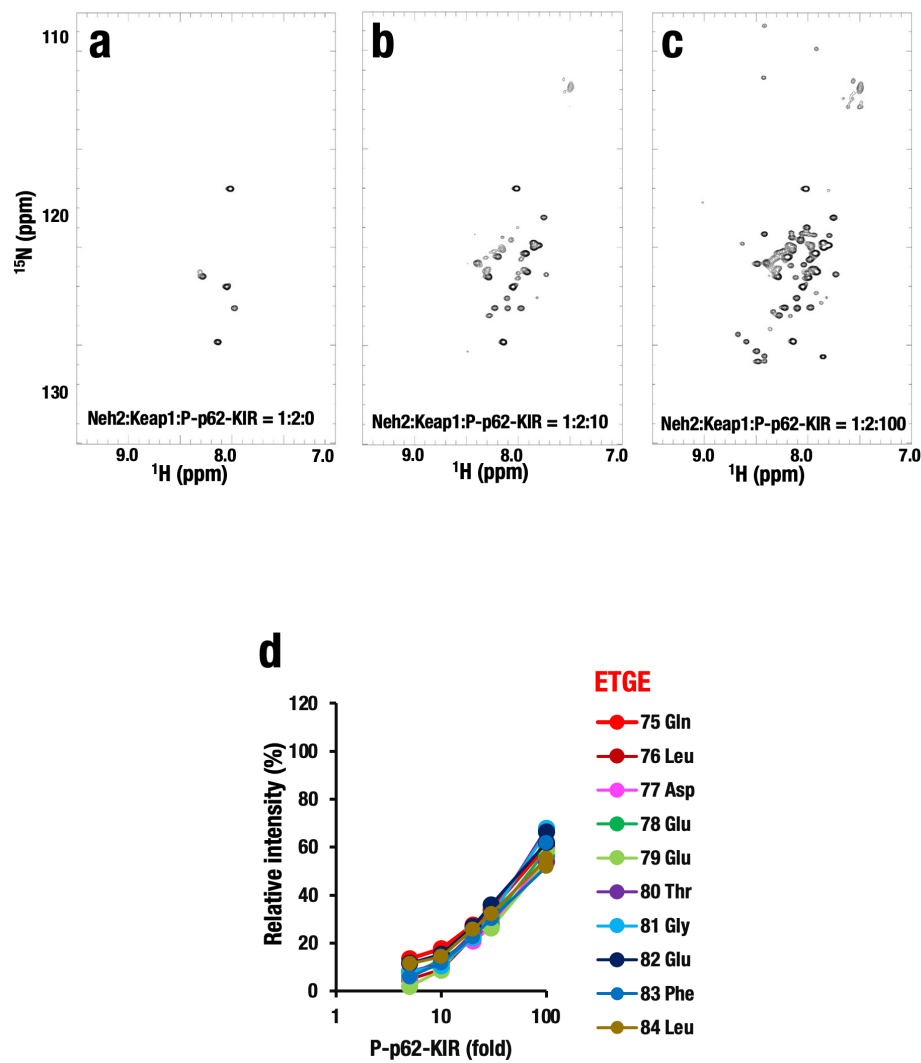


NG262

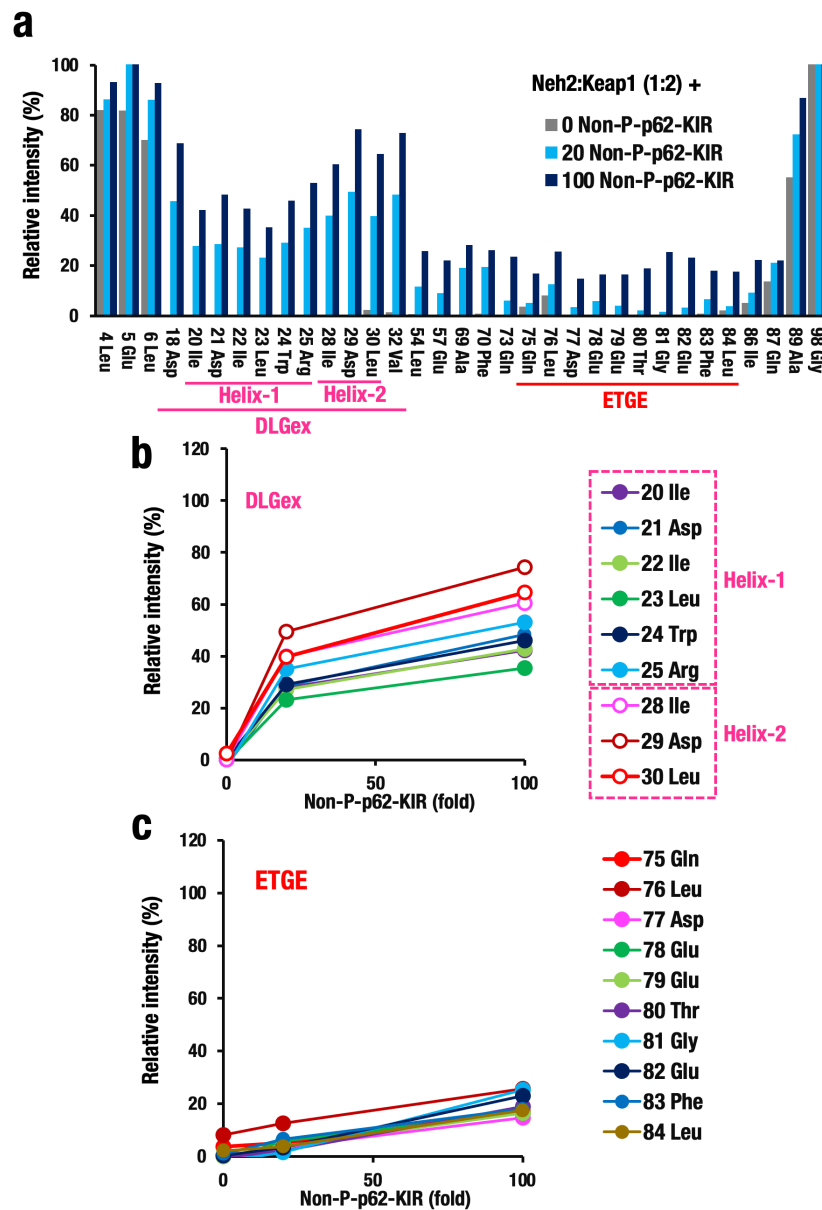
Supplementary Figure 2. Merged images of DLGex with PRL295 (a) or NG262 (b) associating with Keap1 pocket.



Supplementary Figure 3. Titration of Neh2-Keap1 complex with electrophilic Nrf2 inducers. 2D TROSY-HSQC spectrum of $^{13}\text{C}/^{15}\text{N}$ -labeled Neh2 in the absence (a) or presence (b) of 2-fold excess of Keap1. 2D TROSY-HSQC spectrum of $^{13}\text{C}/^{15}\text{N}$ -labeled Neh2 in the presence of 2-fold excess of Keap1 after the addition of equal (c) or 10-fold excess amount (d) of CDDO-Im. 2D TROSY-HSQC spectrum of $^{13}\text{C}/^{15}\text{N}$ -labeled Neh2 in the presence of 2-fold excess of Keap1 after addition of 4-fold excess (e) or 10-fold excess (f) of SFN. 2D TROSY-HSQC spectrum of $^{13}\text{C}/^{15}\text{N}$ -labeled Neh2 in the presence of 2-fold excess of Keap1 after the addition of equal amount (g) or 11-fold excess amount (h) of 15d-PGJ₂.



Supplementary Figure 4. Titration of Neh2-Keap1 complex with P-p62-KIR peptide. (a-c) 2D TROSY-HSQC spectrum of $^{13}\text{C}/^{15}\text{N}$ -labeled Neh2 in the presence of 2-fold excess of Keap1 in the absence of the peptide (a), or in the presence of 10-fold (b) or 100-fold P-p62-KIR peptide (c). (d) Relative peak intensity of ETGE motif by the addition of P-p62-KIR peptide.



Supplementary Figure 5. Titration of Neh2-Keap1 complex with Non-P-p62-KIR peptide.

(a) Relative peak intensity of each amino acid residue of Neh2 in the Neh2-Keap1 complex (1:2) in the titration experiments by the addition of 20- and 100-fold excess of Non-P-p62-KIR peptides. (b) Relative peak intensity of each amino acid residue within the DLGex motif by the addition of Non-P-p62-KIR peptides. Closed and open circles indicate the amino acids corresponding to Helix-1 and Helix-2, respectively. (c) Relative peak intensity of each amino acid residue within the ETGE motif by the addition of Non-P-p62-KIR peptide.