

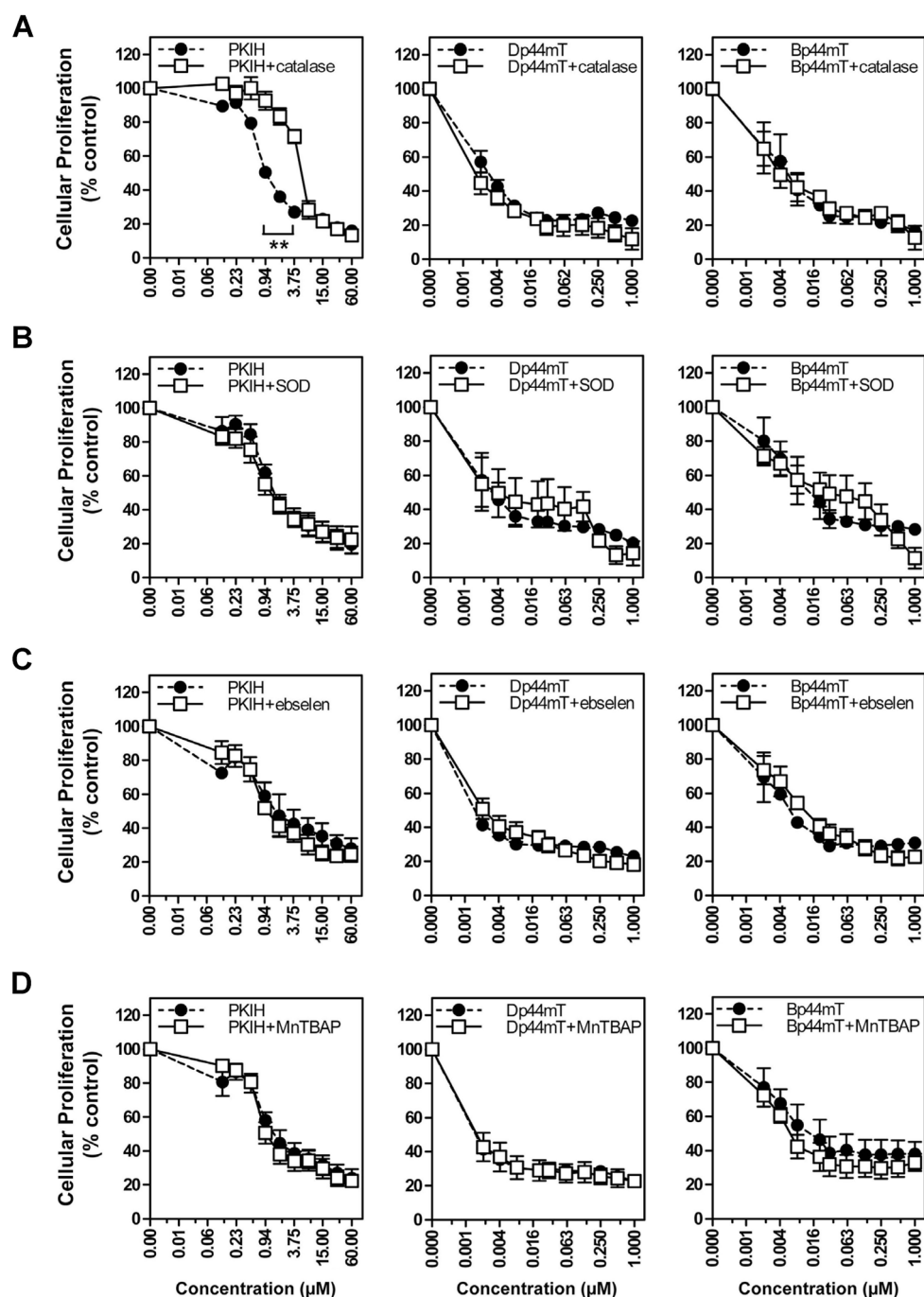
## **SUPPLEMENTAL DATA**

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**The Potent and Novel Thiosemicarbazone Chelators, Dp44mT and Bp44mT, Affect Crucial Thiol Systems Required for Ribonucleotide Reductase Activity.**

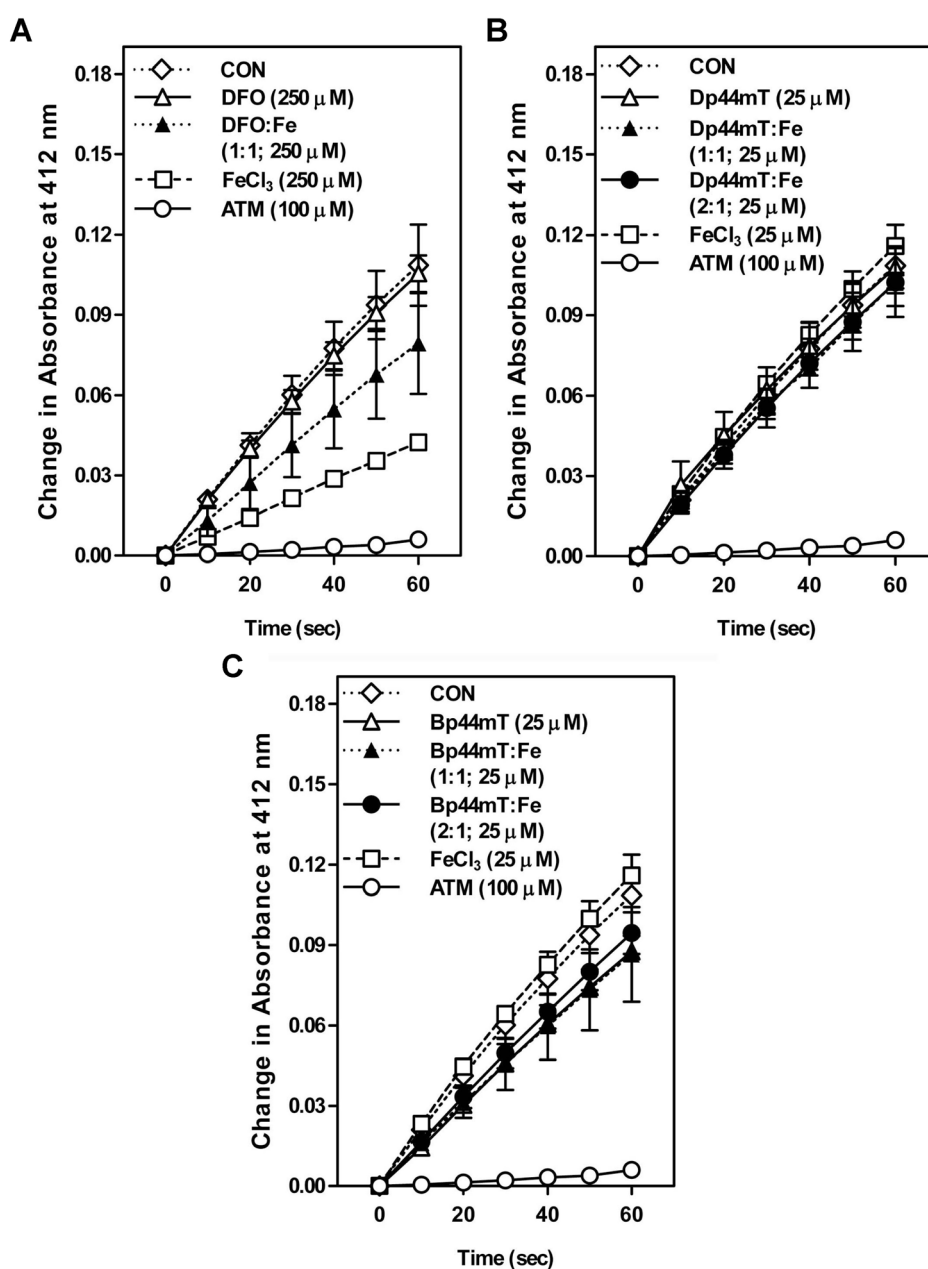
Molecular Pharmacology

## Supplementary Figure S1



**Figure S1.** The effect of anti-oxidants on the anti-proliferative activity of chelators. The effects of the anti-oxidants **(A)** catalase (1000 U/mL); **(B)** superoxide dismutase (SOD) (1000 U/mL); **(C)** ebselen (15  $\mu$ M) and **(D)** MnTBAP (100  $\mu$ M) on the anti-proliferative effect of PKIH and thiosemicarbazone chelators (Dp44mT and Bp44mT) as determined by the MTT proliferation assay using DMS-53 lung cancer cells. The cells were incubated with either chelators alone or in combination with the anti-oxidants for 72 h/37°C. Data are expressed as cell proliferation (% control). Results are mean  $\pm$  SEM (at least 3-5 experiments). \*\* $p$ <0.01

## Supplementary Figure S2



**Figure S2.** The effect of chelators on thioredoxin reductase (TrxR) activity in a cell free system. (A-C) The activity of TrxR in the cell-free system after a 2 h incubation with either DFO (250  $\mu$ M), Dp44mT (25  $\mu$ M), Bp44mT (25  $\mu$ M) or their iron(III) complexes. The hexadentate DFO-iron complex was examined at a 1:1 molar ratio (chelator:iron(III) ratio; 250  $\mu$ M). Tridentate Dp44mT and Bp44mT were assessed at 1:1 molar ratio (chelator:iron(III) ratio; 25  $\mu$ M) or 2:1 molar ratio (chelator:iron(III) ratio; 25  $\mu$ M:12.5  $\mu$ M). The iron(III) complexes were pre-formed using ferric chloride (FeCl<sub>3</sub>) prior to the incubation. FeCl<sub>3</sub> at 25  $\mu$ M or 250  $\mu$ M was included as a relevant control as it is a component of the complexes. ATM (100  $\mu$ M) acted as positive control and demonstrated a significant ( $p < 0.001$ ) reduction of TrxR activity. The TrxR activity was determined spectrophotometrically using the DTNB assay in the presence of NADPH at 412 nm. Results are mean  $\pm$  SEM (4 experiments).