Supporting Information

Intracellular reduction/activation of a disulfide switch in thiosemicarbazone iron chelators

Eman A. Akam, Tsuhen M. Chang, Andrei V. Astashkin and Elisa Tomat*

Contents

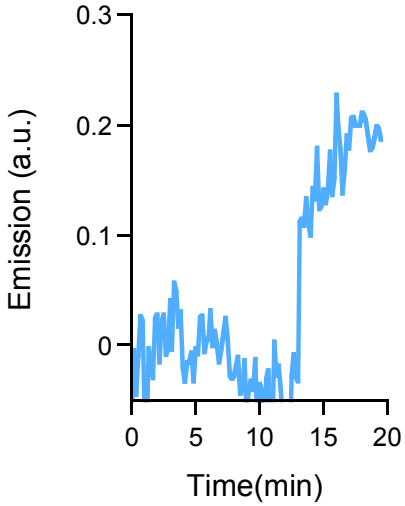

Fig. S1. Calcein fluorescence emission upon addition of DMSO at 5 min and then SIH (50 uM) at 13 min in suspended Jurkat cell cultures. Fluorescence intensity at 517 nm (excitation, 488 nm) is plotted as the difference from the initial values before any addition.

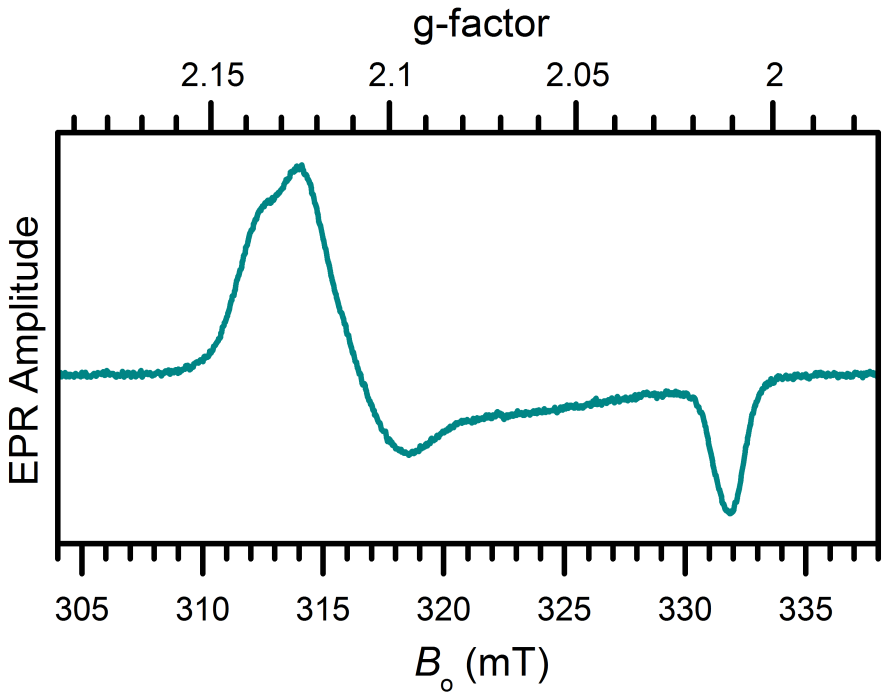

Fig. S2. EPR spectrum of the synthetic complex $[(TC1\text{-}S)_2Fe^{III}][BF_4]$ in DMSO. Experimental conditions: microwave frequency, 9.339 GHz; microwave power, 20 μW; magnetic field modulation amplitude, 0.2 mT; temperature, 6 K.

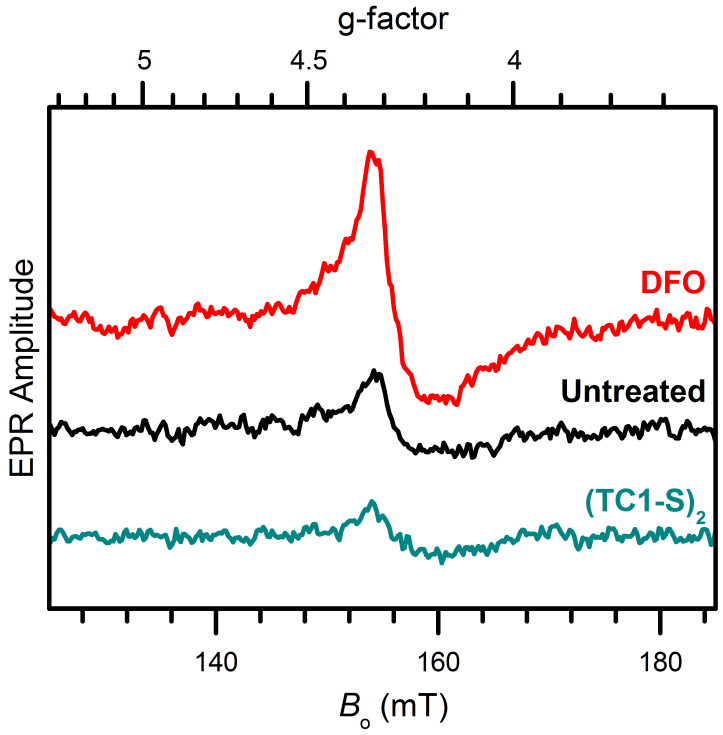

Fig. S3. $g \sim 4$ region of the EPR spectra of intact Jurkat cells. Black, untreated cells; red, after treatment with 50 μM DFO for 3 hours; green, after treatment with 50 μM $(TC1\text{-}S)_2$ for 1 hour. Experimental conditions: microwave frequency, 9.338 GHz; microwave power, 20 mW; magnetic field modulation amplitude, 0.5 mT; temperature, 10 K.

Compound	IC_{50} (μM), 48 h	
	SK-N-MC	**MDA-MB-231**
$(TC1\text{-}S)_2$[a]	6.81 ± 0.17	4.59 ± 0.06
TC1-SH[a]	5.19 ± 0.17	15.01 ± 0.05
$[(TC1\text{-}S)_2Fe]^+$	42.07 ± 0.14	30.63 ± 0.05

Table S1. Antiproliferative activity of iron complex $[(TC1\text{-}S)_2Fe]^+$ compared to the free prochelator and chelator systems in SK-N-MC (neuroepithelioma) and MDA-MB-231 (breast adenocarcinoma) cell cultures. IC_{50} values were determined from MTT assays after exposure to tested compounds for 48 h; (a) data from: T. M. Chang and E. Tomat, *Dalton Trans.*, 2013, **42**, 7846-7849.