Supporting information

Copper(II) complexes with tridentate halogen-substituted Schiff base ligands: synthesis, crystal structures and investigating the effect of halogenation, leaving group and ligand flexibility on antiproliferative activities

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Table S1 -Relative IC_{50} values (μM) in A2780, HCT116 and MCF7 cancer lines and in human normal primary dermal fibroblasts.

Complexes	IC_{50} A2780 (μM)	IC_{50} HCT116 (μM)	IC_{50} MCF7 (μM)	IC_{50} Fibroblasts (μM)
$Cu(I_2\text{-}L_1)Cl$	19.9±6.07	22.3±7.93	46.0±6.86	42.9±3.22
$Cu(Br_2\text{-}L_1)NO_3$	18.3±8.7	IC_{50}>50	39.2±2.89	34.9±5.20
$Cu(I_2\text{-}L_1)NO_3$	19.9±4.48	23.1±2.24	47.5±8.53	10<IC_{50}<50
$Cu(BrCl\text{-}L_1)NO_3$	20.0±1.87	30.7±4.05	47.7±7.51	43.1±5.69
$Cu(Cl_2\text{-}L_2)Cl$	28.1±4.52	IC_5>50	IC_{50}>50	IC_{50}>50
$Cu(Br_2\text{-}L_2)Cl$	48.0±6.50	33.2±2.70	IC_{50}>50	IC_{50}>50
$Cu(I_2\text{-}L_2)Cl$	42.7±1.89	IC_5>50	IC_5>50	IC_{50}>50
$Cu(BrCl\text{–}L_2)Cl$	IC_{50}>50	IC_{50}>50	IC_{50}>50	IC_{50}>50
$Cu(Cl_2\text{–}L_2)NO_3$	26.5±6.76	48.2±8.05	IC_{50}>50	IC_{50}>50
$Cu(Br_2\text{–}L_2)NO_3$	28.3±0.53	19.7±4.29	IC_{50}>50	IC_{50}>50
$Cu(I_2\text{–}L_2)NO_3$	46.0±7.50	44.2±12.26	IC_{50}>50	IC_{50}>50
$Cu(BrCl\text{–}L_2)NO_3$	46.4±0.92	IC_{50}>50	30.8±9.77	IC_{50}>50

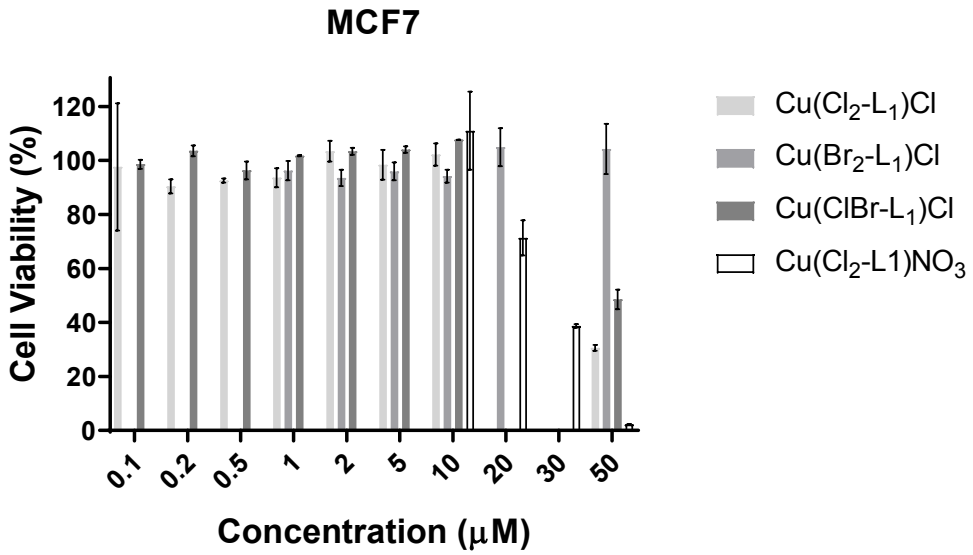

Fig. S1 Antiproliferative effect of complexes **Cu(Cl_2-L_1)Cl** (light grey), **Cu(Br_2-L_1)Cl** (intermediate grey), **Cu(BrCl-L_1)Cl** (dark grey) and **Cu(Cl_2-L_1)NO_3** (white) in MCF7 cancer cell line exposed to increasing concentrations of each complex for 48 h evaluated by the MTS method. The vehicle control condition was DMSO 0.1% (v/v) (negative control). The results shown are expressed as the mean ± SD from three independent assays.

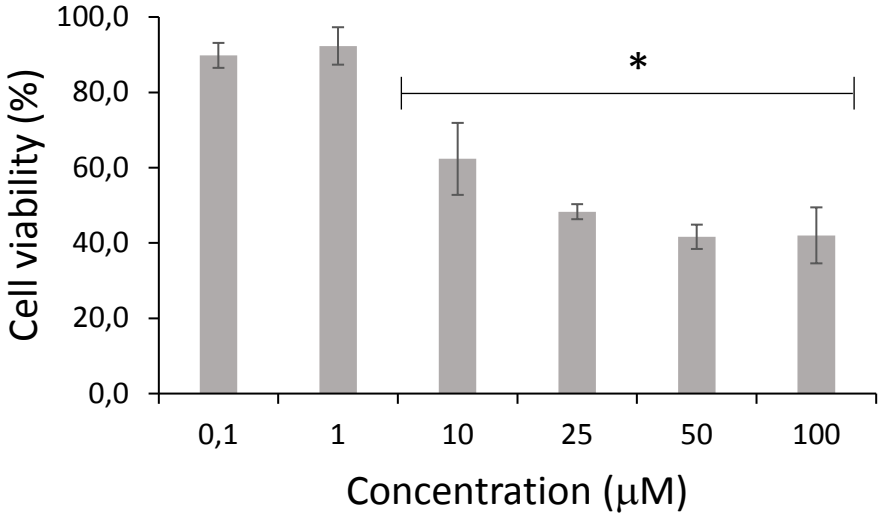

Fig. S2 Cytotoxicity of cisplatin in normal dermal fibroblasts after 48 h of incubation. Cell viability was determined using the MTS assay. Data normalized against the control (0.1% (v/v) DMSO) and expressed as the mean ± SD of three independent assays. The symbol * indicates that p-value < 0.05.

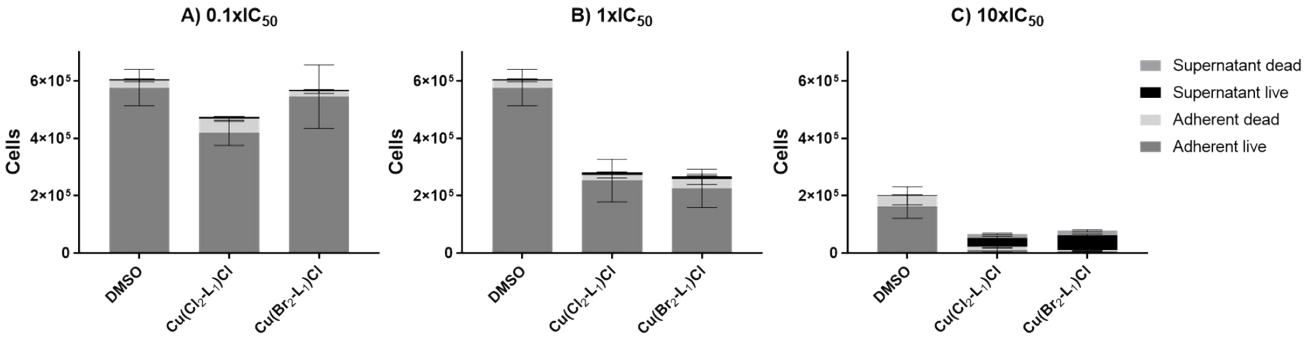

Fig. S3 Evaluation by the trypan blue exclusion method of the number of live and dead cells in the population of adherent and in the culture media supernatant (non-adherent) A2480 cells. Cells were incubated for 48 h with DMSO 0.01% (v/v) (A), DMSO 0.1% (v/v) (B) and DMSO 1% (C) as solvent controls and with $0.1xIC_{50}$ (A), $1xIC_{50}$ (B) and $10xIC_{50}$ (C) concentrations of complexes **Cu(Cl$_2$-L$_1$)Cl** and **Cu(Br$_2$-L$_1$)Cl**. The results shown are expressed as the mean±SD from three independent experiments.