Electronic Supplementary Material (ESI) for Inorganic Chemistry Frontiers.
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Figure S1

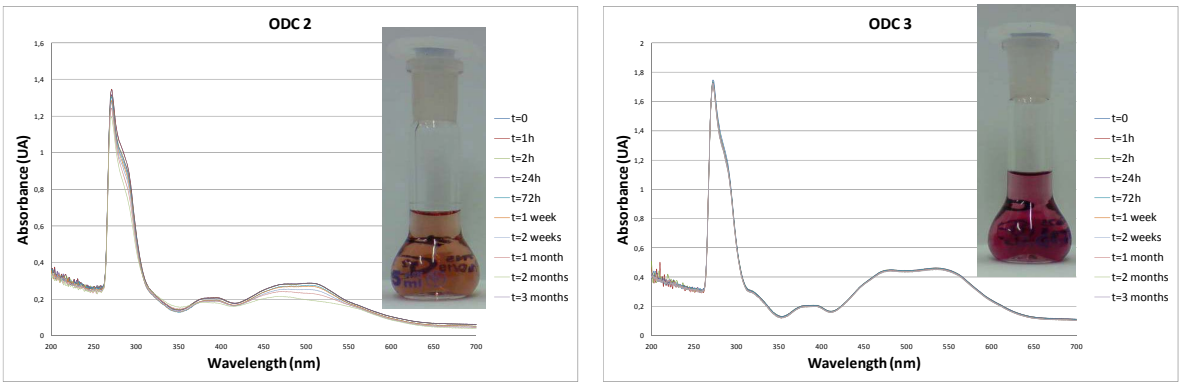

Figure S1: Stability data of ODC2 and ODC3. Evolution of ODC2 and ODC3 stability over the time as measured by spectrometry (UA for arbitrary unit).

Figure S2

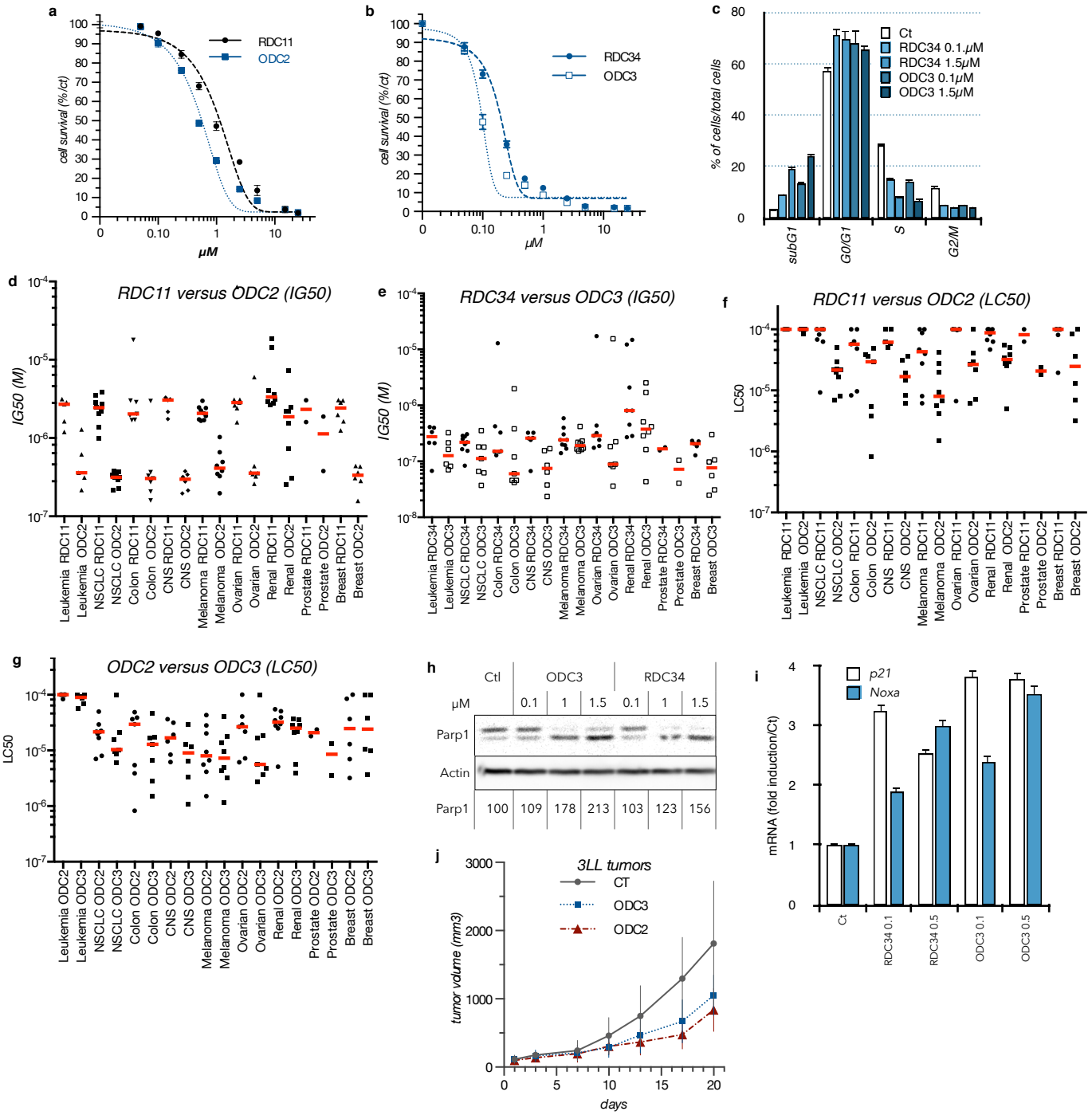

Figure S2: Cell growth and cytotoxicity of ODC2 and ODC3 compared to RDC11 and RDC34, on the 60 cancer cell lines of the National Cancer Institute

a., MTT test on HCT116 cells treated for 48h.

b, Survival of HCT116 treated with RDC11 and ODC2 for 48 hours and measured by MTT assay.

c, Identification of the cell cycle and sub-G1 populations by Flow Cytometry Analysis (FACS) in HCT116 cells treated by RDC34 and ODC3 (F).

d, **e**, Diagrams representing the concentration for 50% of cell growth inhibition (IG_{50}). NCI cancer cell lines (60) were grouped by cancer origins. Each point indicate a cell line. Red line indicate the median.

f, g, Diagrams representing the concentration for 50% of cell lethality (LC_{50}). NCI cancer cell lines were grouped by cancer origins. Each point indicate a cell line. Red line indicate the median.

h, Cleaved PARP1 visualized by western blot in extracts of HCT116 cells treated with the indicated drugs. Actin serves as internal control for protein concentration and loading.

i. mRNA levels of two known p53 target genes (*p21, noxa*) in the HCT116 cells treated with RDC34 or ODC3 at the indicated concentrations (μM). mRNA levels were assessed by RT-qPCR. Graphs are means and standard deviations relative to the control (Ct, DMSO 1%)

j. 3LL tumor growth folowing treatment with OD2 or ODC3. C57BL/6 mice (8-weeks old) were injected subcutaneously with 5 x e^{-5} 3LL cells. Injections of RDC (RDC34 and ODC3 at 4 mmol/kg; RDC11 and ODC2 at 13.3 mmol/kg) started when tumors were palpable (100 mm3) and were performed twice a week. Solutions were prepared in PBS/5% Cremophore. Data are representative of two independent experiments (n = 7). Drugs effect were statistically different ($p < 0.01$) compared to control, as calculated by a one-way ANOVA test followed by a Tukey test.

Figure S3

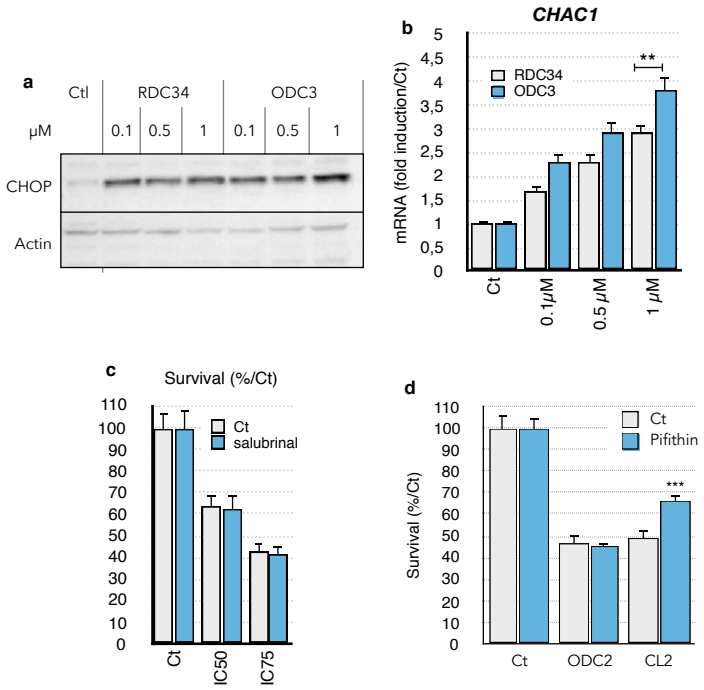

Figure S3: Expression and inactivation of ER stress effectors.

a, CHOP expression detected by western blot in extract of HCT116 cells treated with the indicated drugs. Actin serves as internal control for protein concentration and loading.
b. mRNA levels of the known CHOP target gene CHAC1 in the HCT116 colon cancer cell line treated with RDC34 or ODC3 at the indicated concentrations. mRNA levels were assessed by RT-qPCR.
c. Survival of HCT116 cells treated with ODC2 at the IC50 of IC75 and with salubrinal (10μM). Graph shows mean and standard deviation of % of surviving cells compared to the control condition (Ct)
d. Impact of the p53 inhibitor pifithrin on ODC2 and CL2 cytotoxicity. Pifithrin (10μM) was added 1h prior ODC2 and CL2. IC50 for ODC2 and CL2 were used (see figure 1). Cell survival was assessed using MTT test after 48h of treatment. Graph represents means and standard deviations in % of surviving cells compared to the control (Ct, DMSO 1%).

** indicate statistical differences of 0.01 as determined by ANOVA followed by Tukey post-test using GraphPad Prism software

Figure S4

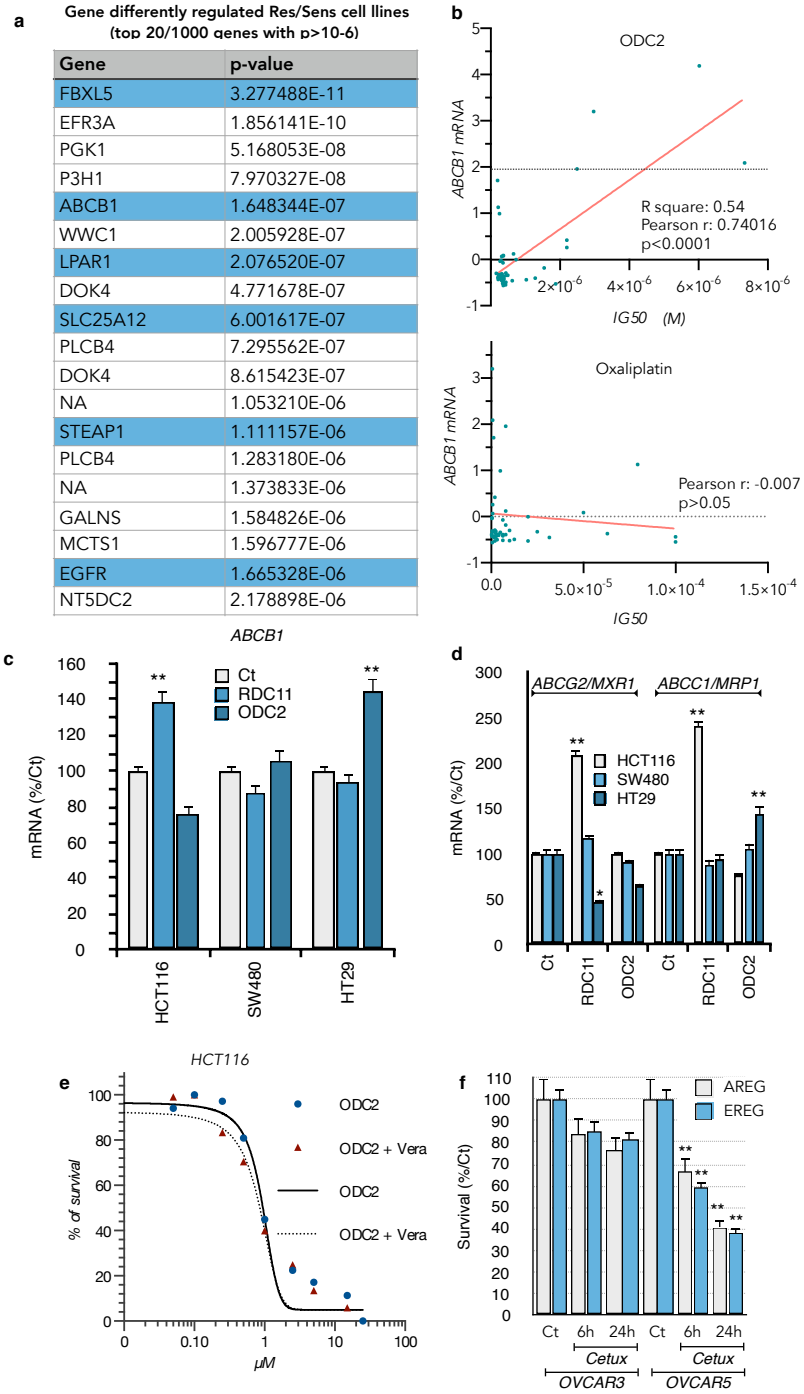

Figure S4:

a, List of the 20 most relevant genes differentially expressed between the two groups of cell lines with low and high sensibility towards RDC11. 4 sensitive cell lines (HOP92, SKMEL5, H522, OVCAR3) and 4 resistant cell lines (NCI AR, CAKI1, HCT15, UO31) for RDC11 were chosen and the genes commonly expressed in each group were identified using the CellExpress website.

b. Correlation of *ABCB1* expression with the IG50 of the 60 different cancer cell lines of the NCI panel**.** mRNA are indicated as z score.

c, mRNA level of *ABCB1* in response to RDC11 and ODC2. mRNA level are shown as % relative to the Ct.

d. Gene expression of export proteins (*ABCG2*, *ABCC1*). mRNA levels of two known drug export proteins (*ABCG2* and *ABCC1*) in the indicated colon cancer cell lines treated with ODC2 or RDC11 at their IC_{50}. mRNA levels were assessed by RT-qPCR.

e, MTT assay in HCT116 cells treated with ODC2, or ODC2 and verapamil (50µM). Cells were treated for 1h with ODC2 and MTT was performed 48h later. Verapamil was left during the whole experiment.

f. Gene expression of EGFR regulated genes (*AREG*, *EREG*) in OVCAR3 and OVCAR5 cells treated with Cetuximab (cetux, 0.5µM. mRNA levels were assessed by RT-qPCR.

** indicate statistical differences of 0.01 as determined by anova followed by Tukey post-test using GraphPad Prism software

Supplementary materials

P21	**Hs01121172_m1 (Taqman GEA, Applied)**	
NOXA	**Hs00560402_m1 (Taqman GEA, Applied)**	
ABCB1	**Hs00184500_m1 (Taqman GEA, Applied)**	
EREG	**5′-TCCCAGGAGAGTCCAGTGAT-3′**	**5′-GTGTTCACATCGGACACCAG-3′**
AREG	**5′-CCACAGTGCTGATGGATTTG-3′**	**5′-GCCAGGTATTTGTGGTTCGT-3′**
CHAC1	**5′-GCCCTGTGGATTTTCGGGTA-3’**	**5′-ATCTTGTCGCTGCCCCTATG-3’**
ABCG2	**Hs01053790_m1 (Taqman GEA, Applied)**	
ABCC1	**Hs00219905_m1 (Taqman GEA, Applied)**	
TBP	**GCC CATA GTG ATC TTT GCA GT**	**CGC TGG AAC TCG TCT CAC TA**