

**Cobaltabis(dicarbollide) ([o-COSAN]-) loaded apoferritin:
an innovative high-capacity boron delivery system to target tumour
cells for BNCT applications.**

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Supporting Information

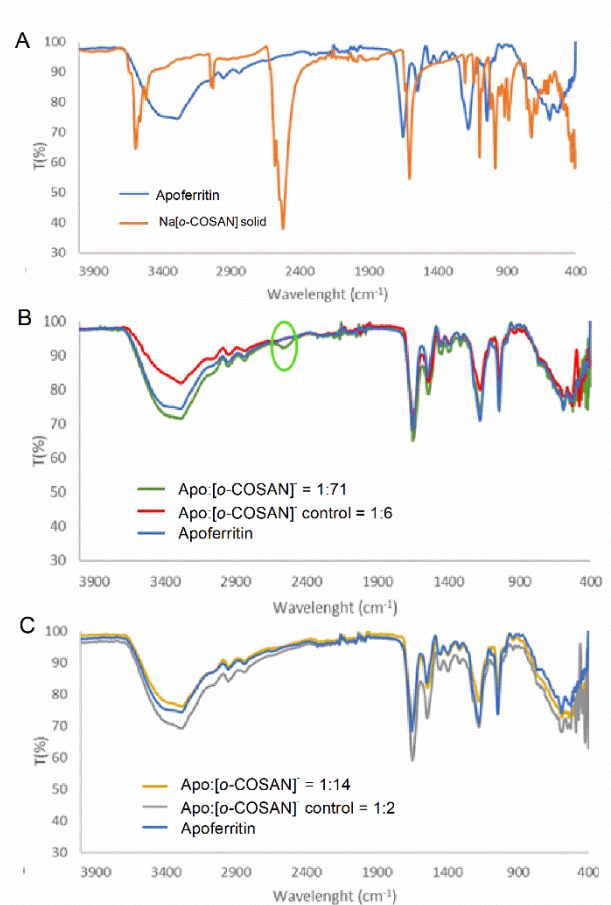


Figure S1. A) IR spectra of apoferritin and the Na[o-COSAN] in solid state as references. B) FT-IR spectra of Apoferritin as a reference (in blue), the nanohybrid Apo:[o-COSAN]⁻ prepared via the dissociation method at acidic pH=2 at ratio 1:71 (in green), and the control nanohybrid Apo:[o-COSAN]⁻ at ratio 1:6 (in red), both incubated at a ratio 1:88. C) FT-IR spectra of apoferritin as a reference (in blue), the nanohybrid Apo:[o-COSAN]⁻ prepared via the dissociation method at acidic pH=2 at ratio 1:14 (in orange), and the control nanohybrid Apo:[o-COSAN]⁻ at ratio 1:2 (in grey), both prepared at 1:18 ratio.

Table S1: Student *t*-test statistical analysis based on AB22 uptake results shown in Figure 6A. In red, not significant (ns) *p* > 0.05.

AB22 uptake 16h	Apo:[o-COSAN] ⁻ / 10μM	Apo:[o-COSAN] ⁻ / 20μM	Apo:[o-COSAN] ⁻ / 50μM
[o-COSAN] ⁻ / 10μM	0.5422		
[o-COSAN] ⁻ / 20μM		0.4050	
[o-COSAN] ⁻ / 50μM			0.7168

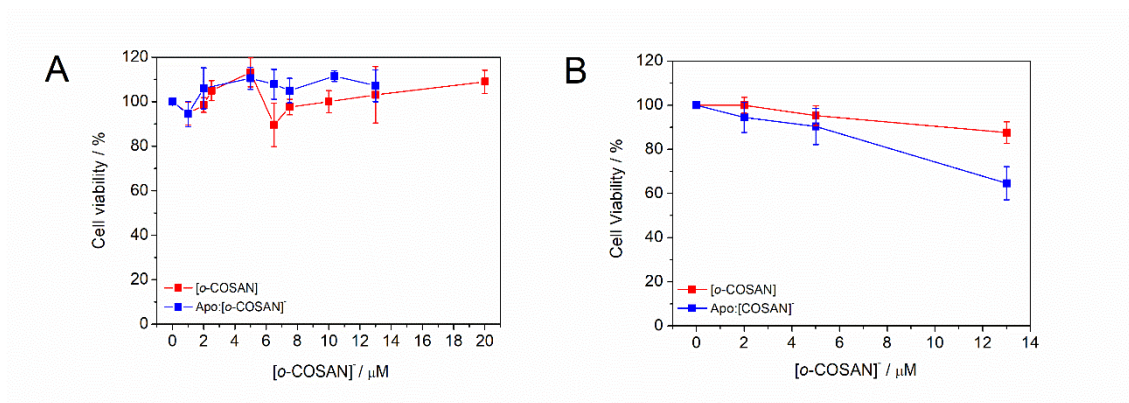


Figure S2: Percentage of viable cells measured by Bradford assay after incubation of MCF7 cells for 6h (A) or 16h (B) with increasing concentration of Apo:[o-COSAN]⁻ nanohybrid (blue) or free [o-COSAN]⁻ molecules (red).

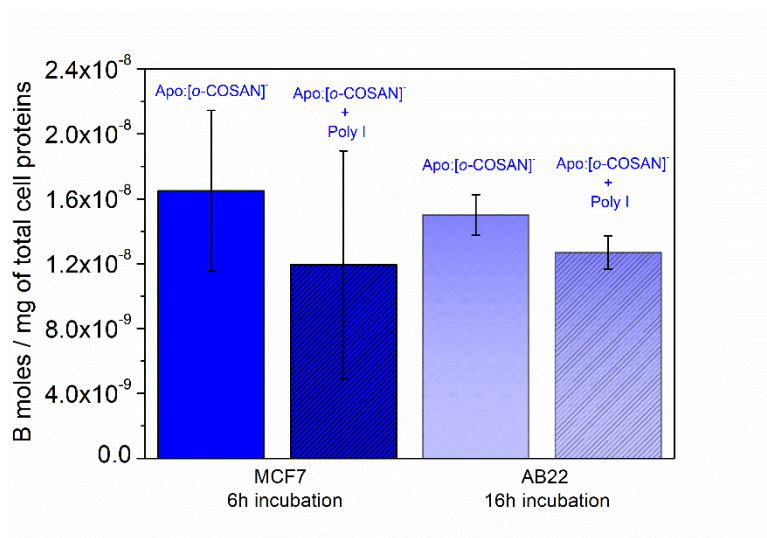


Figure S3: competition studies: boron uptake by MCF7 cells after 6 h incubation and AB22 cells after 16h incubation in the presence of 20 μM Apo:[o-COSAN]⁻ nanohybrid without and with the addition of 0.1 mg/mL of polyinosinic acid.

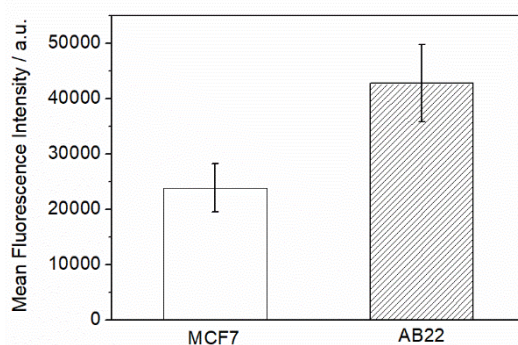


Figure S4: Quantification of SCARA5 expression by ImageJ software on acquired images by Leica STELLARIS 8 confocal microscope.

Table S2: Student *t*-test statistical analysis based on results shown in Figure 7A and B. In red, not significant

Cell viability 24h after Neutron Irradiation	[o-COSAN] ⁻	Apo:[o-COSAN] ⁻	CTRL IRR	[o-COSAN] ⁻ IRR	Apo:[o-COSAN] ⁻ IRR
CTRL	0.7970	0.0547	0.1734	0.3838	0.0611
[o-COSAN] ⁻		0.0014	0.0168	0.0481	0.0026
Apo:[o-COSAN] ⁻			0.0025	0.0032	0.3276
CTRL IRR				0.0103	0.0030
[o-COSAN] ⁻ IRR					0.0055
Clonogenic assay	[o-COSAN] ⁻	Apo:[o-COSAN] ⁻	CTRL IRR	[o-COSAN] ⁻ IRR	Apo:[o-COSAN] ⁻ IRR
CTRL	0.4741	0.7395	0.0021	0.0002	0.0004
[o-COSAN] ⁻		0.2682	0.0014	<0.0001	0.0002
Apo:[o-COSAN] ⁻			0.0014	<0.0001	0.0003
CTRL IRR				0.1631	0.0076
[o-COSAN] ⁻ IRR					0.0076

(ns) $p > 0.05$, in yellow $*p \leq 0.05$, in orange $**p \leq 0.01$ and in green $***p \leq 0.001$.

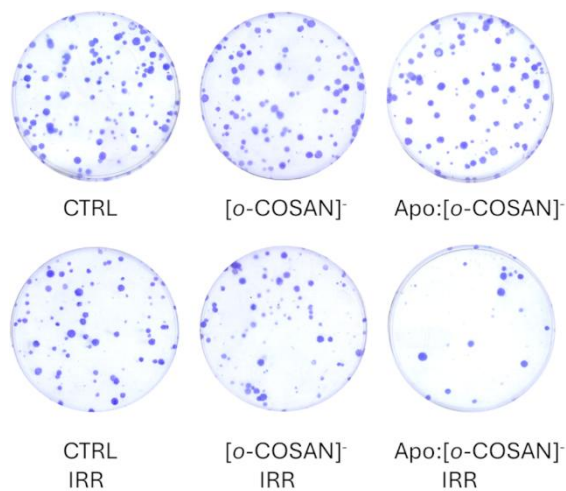


Figure S5: Representative images of clonogenic assay performed at day 10 after Neutron Irradiation.