Supplementary material

Liposome nanoparticle conjugation and cell penetrating peptide sequences (CPPs) enhance the cellular delivery of the Tau aggregation inhibitor RI-AG03

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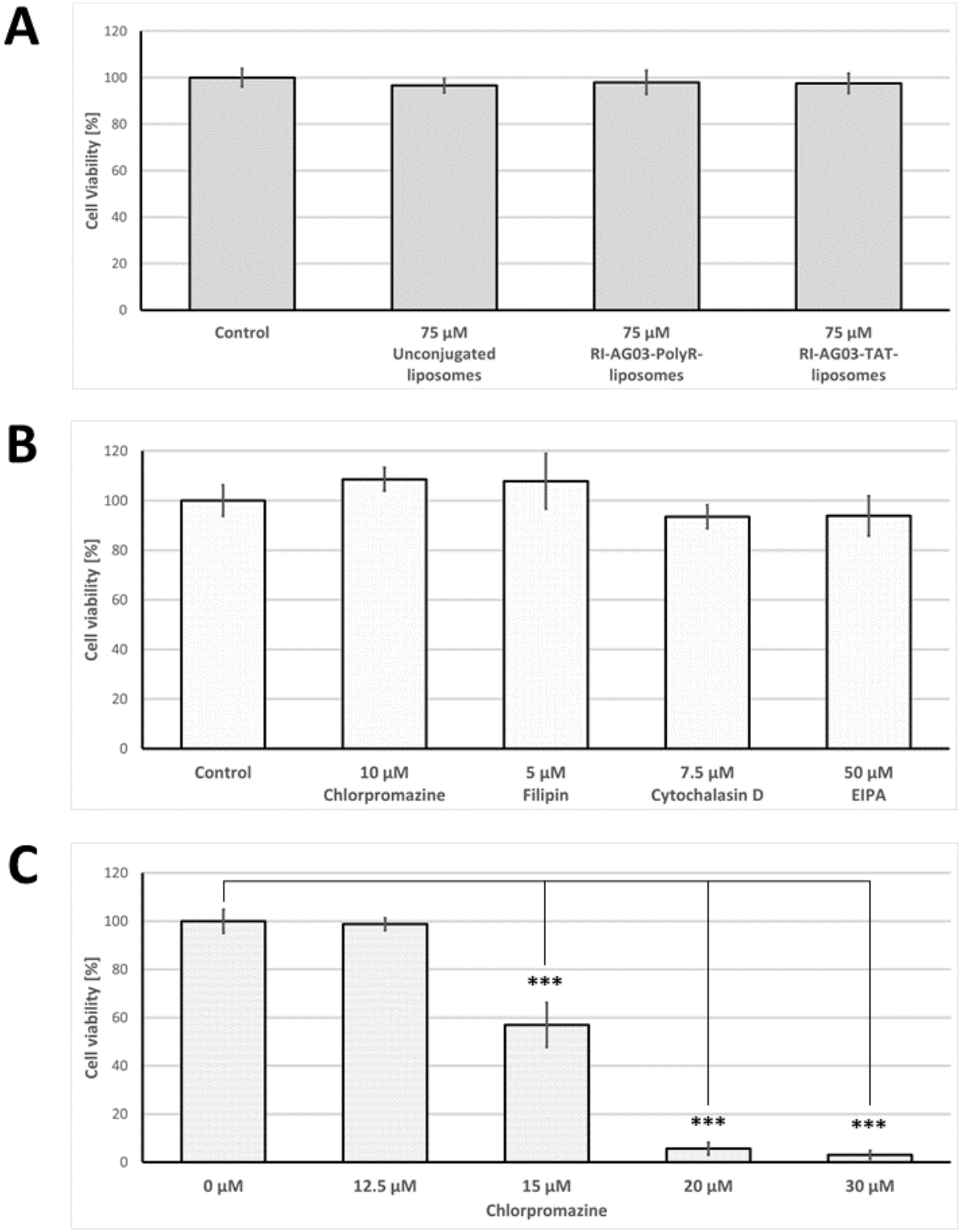

Figure S1: Toxicity analysis of liposomes, peptide-liposomes and endocytosis inhibitors.

SH-SY5Y cells were treated with the indicated final concentrations of (**A**) unconjugated, RI-AG03-polyR-conjugated or RI-AG03-TAT-conjugated liposomes and (**B**) endocytosis

inhibitors for 4.5 h. (**C**) The effects of increasing chlorpromazine concentrations on cell viability. Data show average cell viability in comparison to vehicle-treated controls (n = 6; Mean ± S.E.M), as assessed by the conversion of water-soluble tetrazolium salt-8 (WST-8). *** $p < 0.01$ significant difference from vehicle-treated control (*post-hoc* Tukey's HSD).

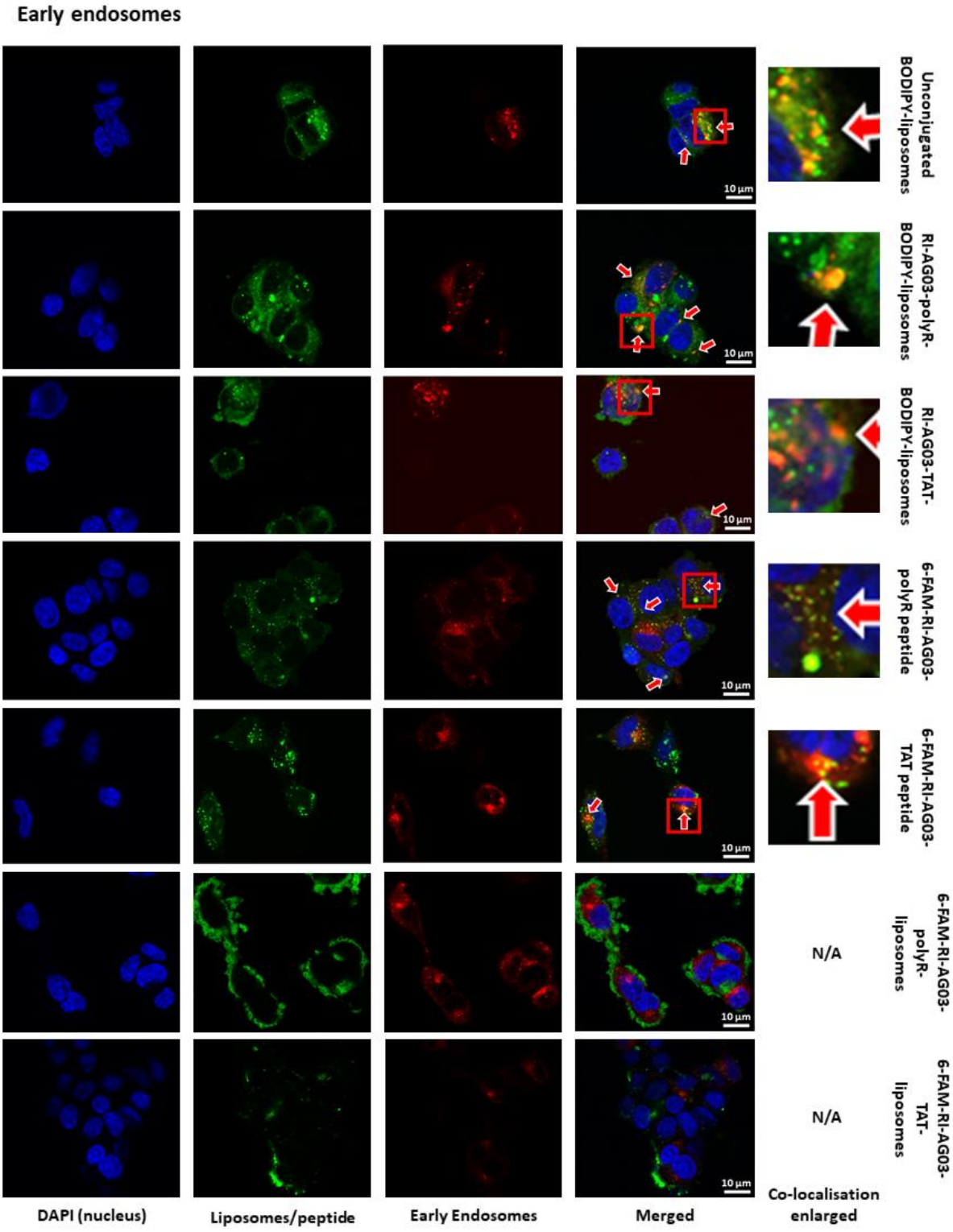

Figure S2: Co-visualisation of RI-AG03, unconjugated liposomes and RI-AG03-conjugated liposomes with early endosomes. SH-SY5Y cells were co-treated with the indicated constructs (either with a free or conjugated fluorescent 6-FAM peptide or fluorescent

BODIPY cholesterol in liposomes; in green) and Rab5a-RFP (CellLight™ Early Endosomes-RFP; in red) for 16 h. The nuclei were stained with DAPI (blue) and arrows indicate co-localisation.

Endoplasmic reticulum

Figure S3: Co-localisation of RI-AG03, unconjugated liposomes and RI-AG03-conjugated liposomes with the endoplasmic reticulum. SH-SY5Y cells were exposed to various constructs, which was either an unconjugated or liposome-conjugated 6-FAM peptide, BODIPY cholesterol in liposomes or peptide-conjugated BODIPY-liposomes (in green), and co-stained with CellLight™ ER-RFP (in red), for 16 h. The nuclei were stained with DAPI (blue).

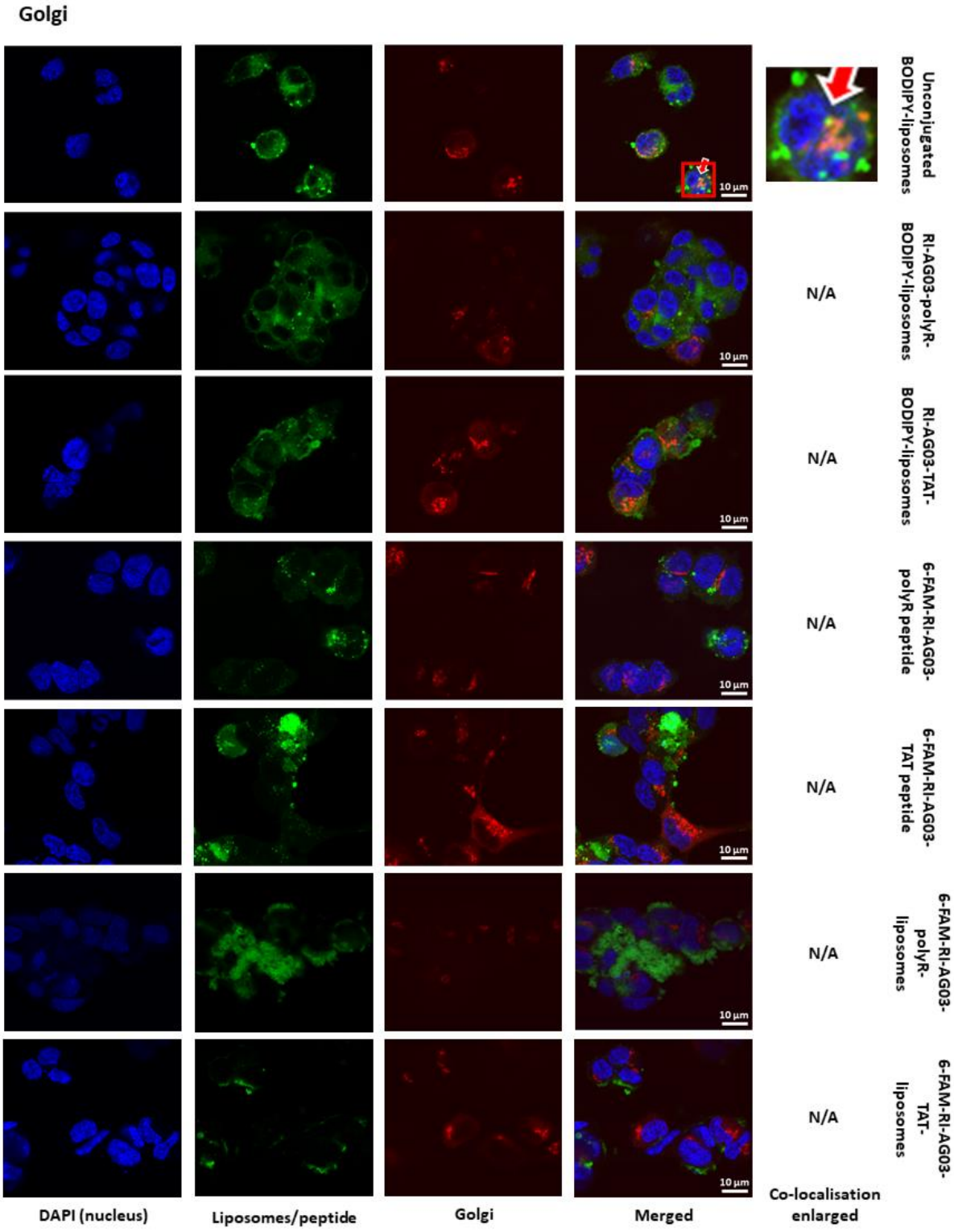

Figure S4: Co-visualisation of RI-AG03, unconjugated liposomes and RI-AG03-conjugated liposomes with the Golgi. SH-SY5Y cells were co-treated with the shown fluorescent 6-FAM-peptide or BODIPY-liposome constructs (in green) and N-acetylgalactosaminyltransferase-

RFP (CellLight™ Golgi-RFP; in red) for 16 h. The nuclei were stained with DAPI (blue) and arrows show co-localisation.