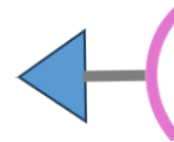
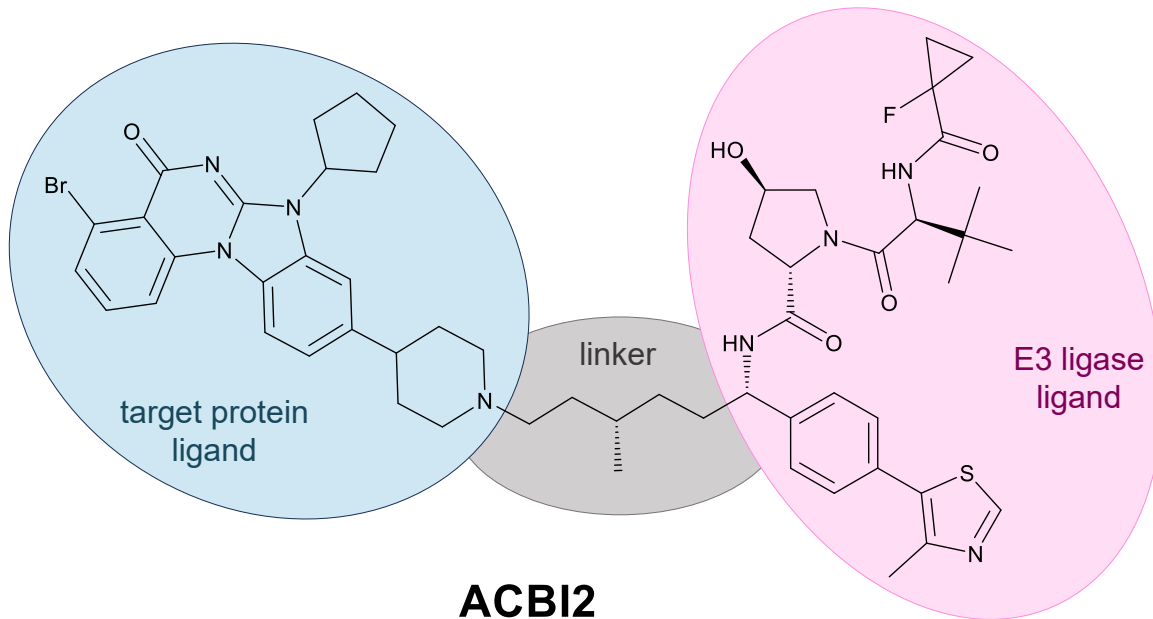


# ***Advancing Parenteral PROTAC Delivery: Liposomal, BSA, and Cyclodextrin- Based Formulations for ACBI2***

Miriam Jaki

# What Are PROTACs\*?



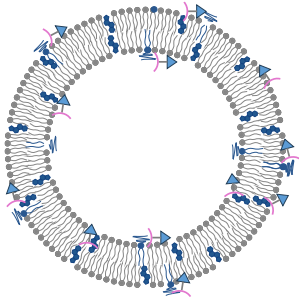
Targeted protein degradation

PROTAC characteristics:

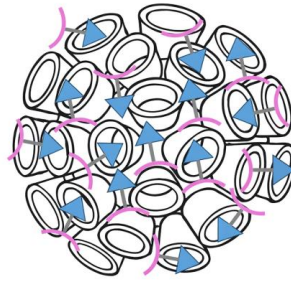
- Large MW (1,064 Da)
  - Low solubility (< 1 µg/mL)
  - Poor membrane permeability
- Low bioavailability

\***PRO**teolysis-**TAR**geting Chimeras

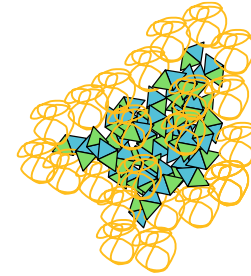
# Nanocarrier



Liposomes

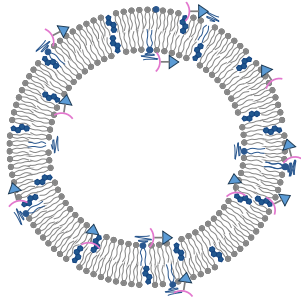


Cyclodextrin-  
Aggregates

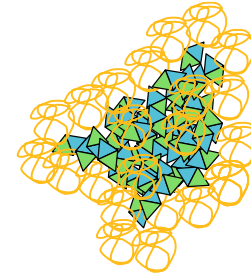


Albumin-based  
Nanoparticles

# Nanocarrier

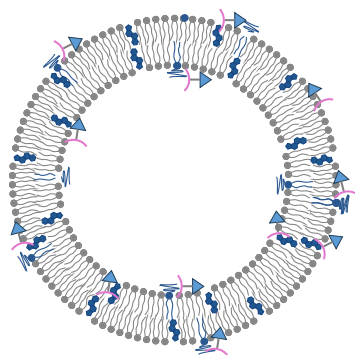


Liposomes



Albumin-based  
Nanoparticles

# Liposomal Formulation Development



## Lipid Composition:

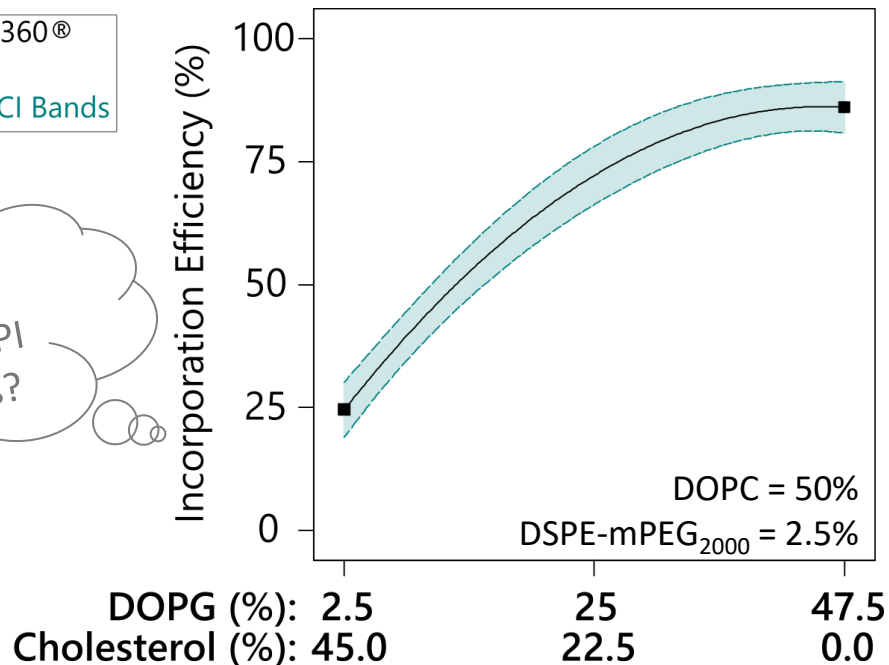
20-100% DOPC  
0-50% DOPG  
0-45% Cholesterol  
0-5% DSPE-mPEG<sub>2000</sub>

D-optimal KCV model

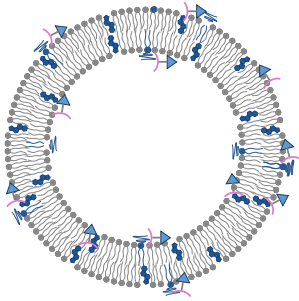
Stat-Ease 360®  
Software

— 90% CI Bands

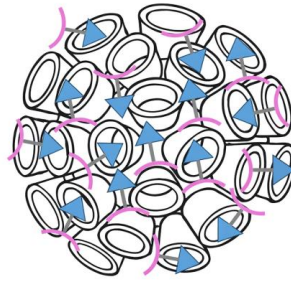
Electrostatic  
Interaction of API  
+ Phospholipids?



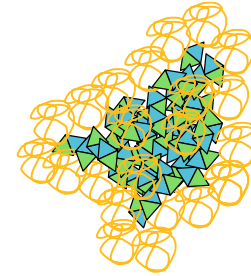
# Nanocarrier



Liposomes

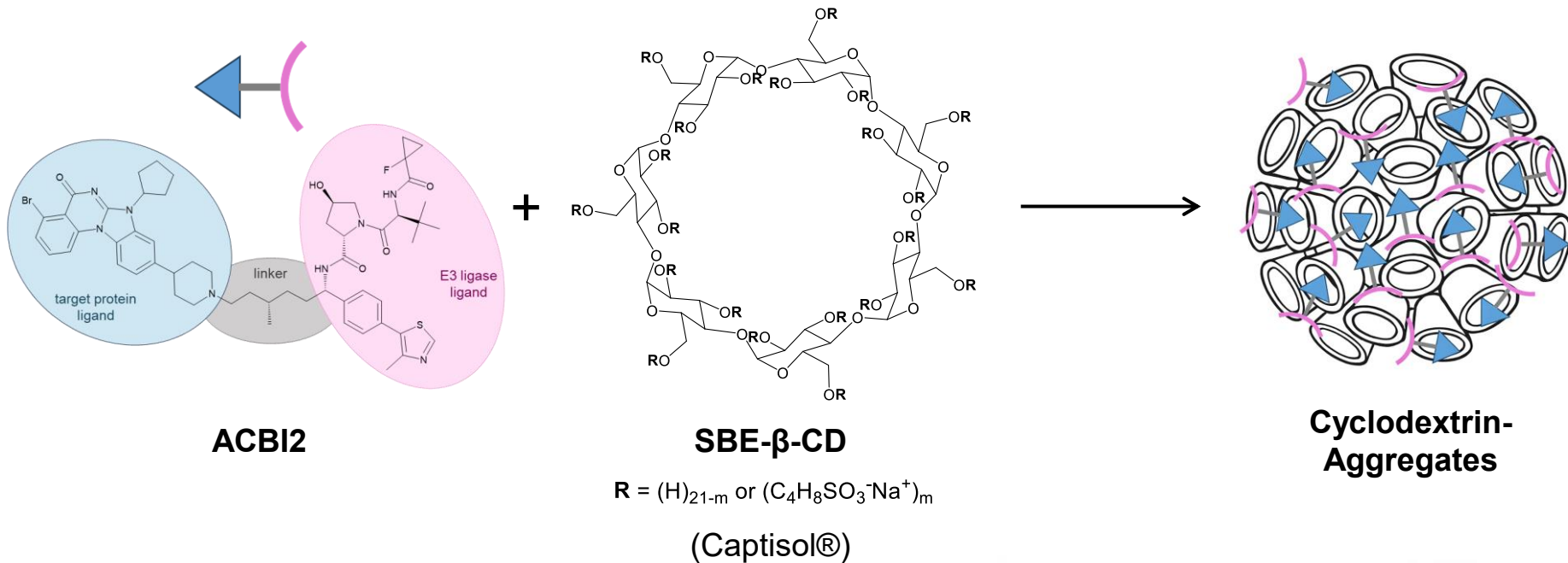


Cyclodextrin-  
Aggregates

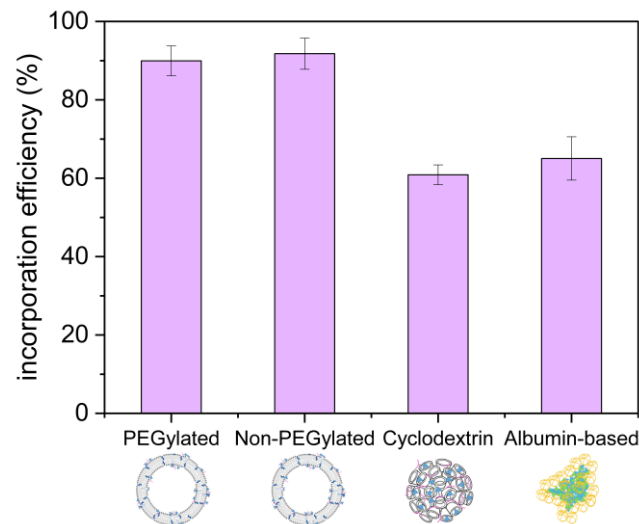
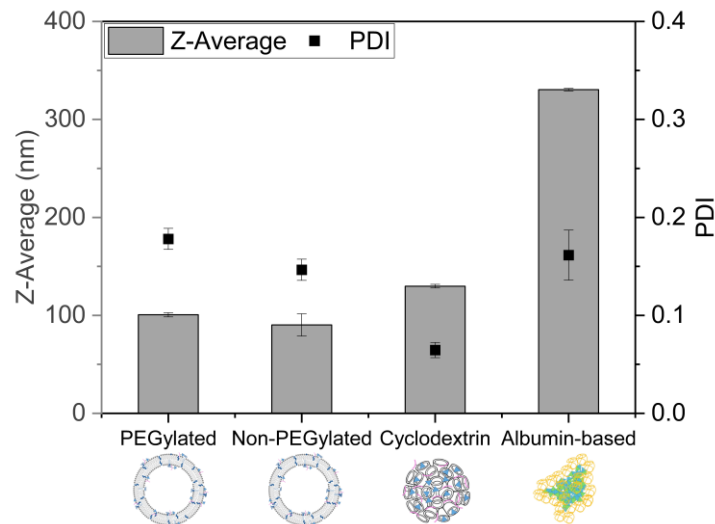


Albumin-based  
Nanoparticles

# Cyclodextrin-Aggregates



# Characteristics of All Drug Loaded Carriers



Liposome composition: DOPC / DOPG / Cholesterol / DSPE-mPEG<sub>2000</sub> (%)

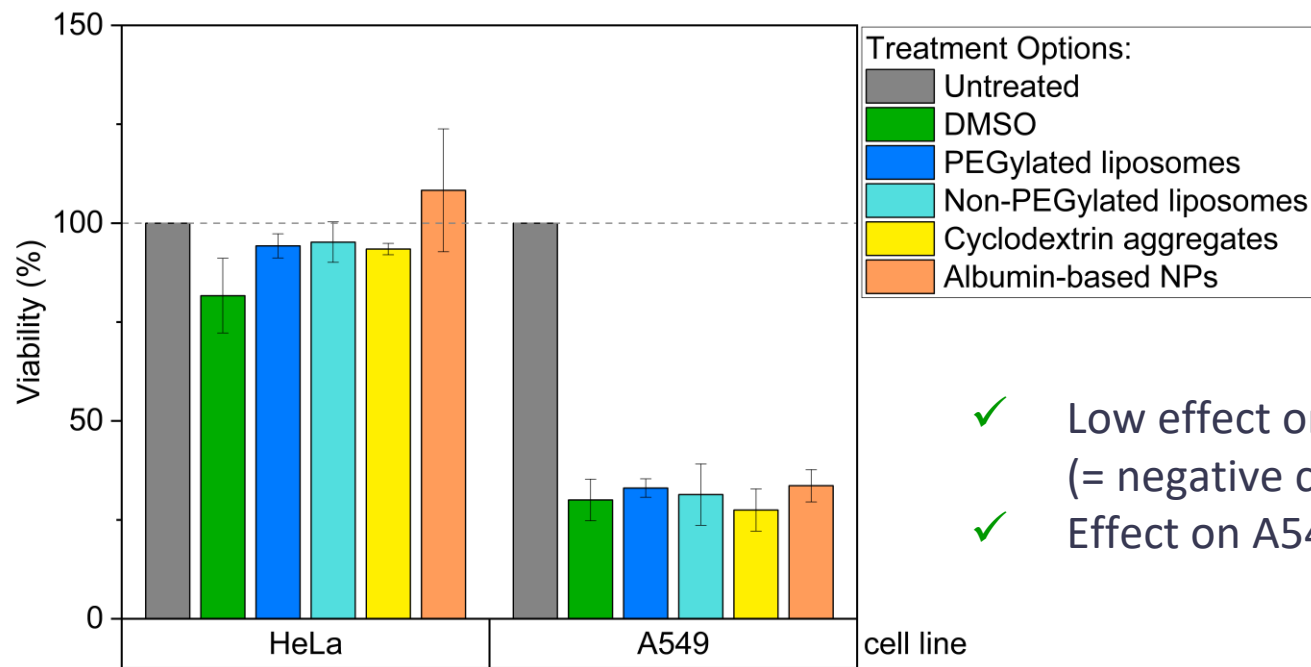
PEGylated liposomes 50.6 / 42.0 / 2.4 / 5

Non-PEGylated liposomes 46.9 / 41.3 / 11.8 / 0

(data shown as mean  $\pm$  SD, n = 3)

# Cell Viability

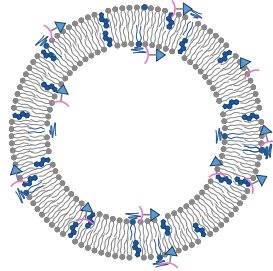
CellTiter-Glo® Assay  
treatment with 250 nM ACBI2 for 2 hrs  
incubation for 6 days



- ✓ Low effect on HeLa cells  
(= negative control)
- ✓ Effect on A549 cells

(data shown as mean  $\pm$  SD, n = 3)

## Liposomes



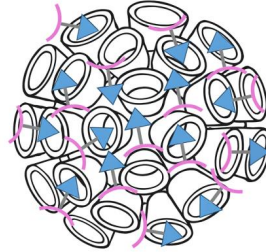
High drug load



Advantages

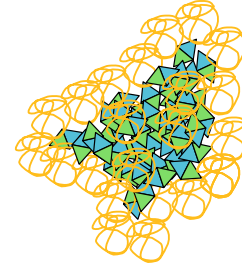
Modular

## Cyclodextrin-Aggregates



Easy manufacturing

## Albumin-based Nanoparticles



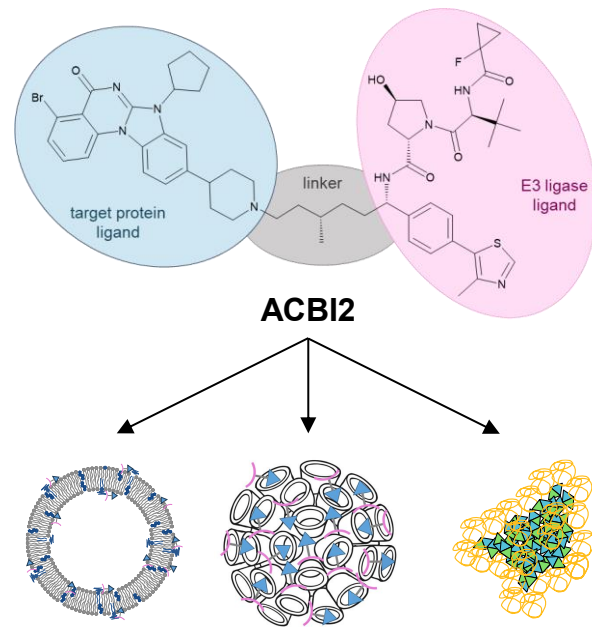
*Built-in* active targeting via  
SPARC receptor

# Conclusion

- Formulation of ACBI2 into nanocarriers was feasible  
→ Relevant drug concentrations
- Electrostatic interactions play important role

## Outlook

- 3D cell culture models
- *In vivo* studies
- Transferability to other PROTACs



# Acknowledgement

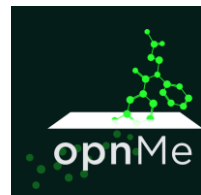


universität freiburg

Prof Regine Süss



Maximilian Wittmann, PhD



Luca Dari

