National Nanotechnology Coordinated Infrastructure

# Enhancing Cell Death Using Targeted Photoactivable Multi-Inhibitor Liposomes (TPMIL)

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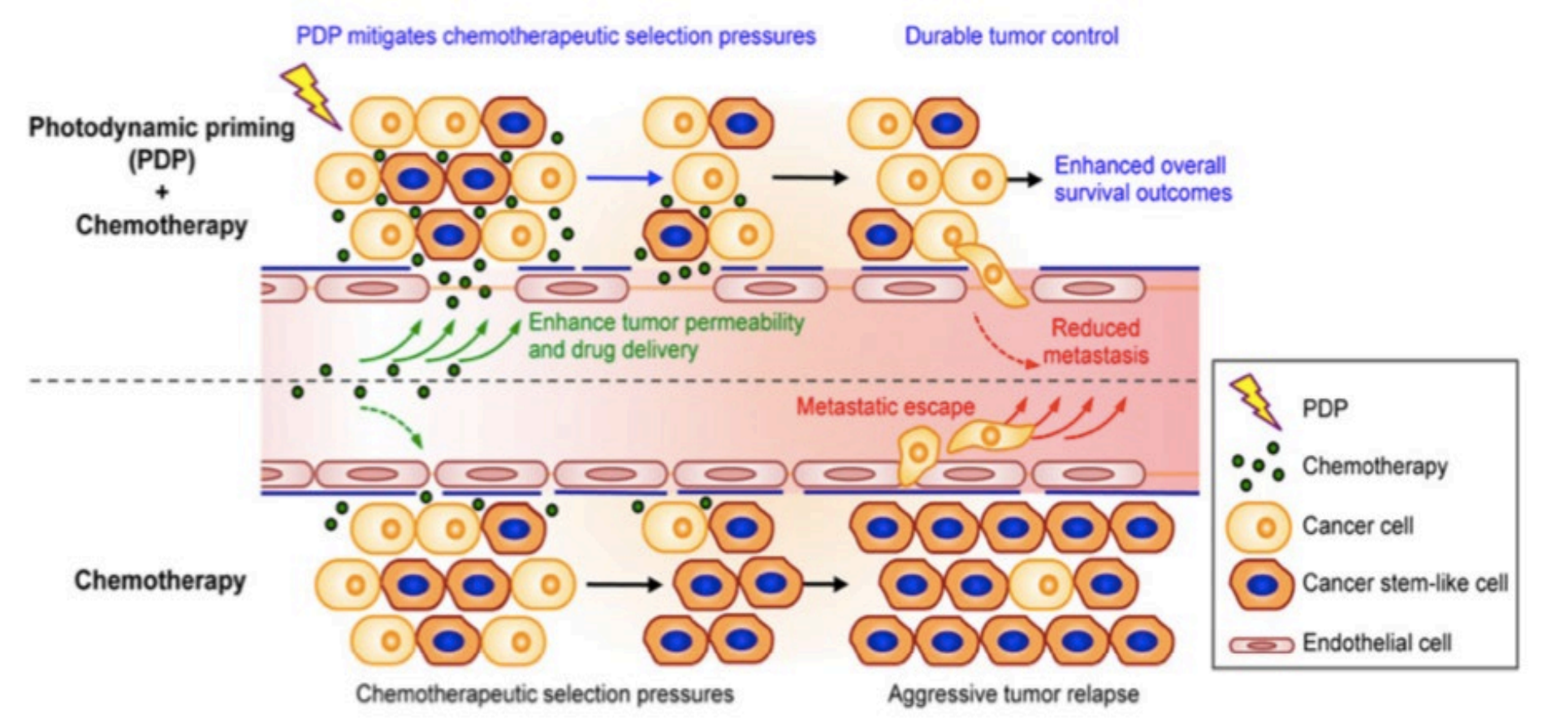
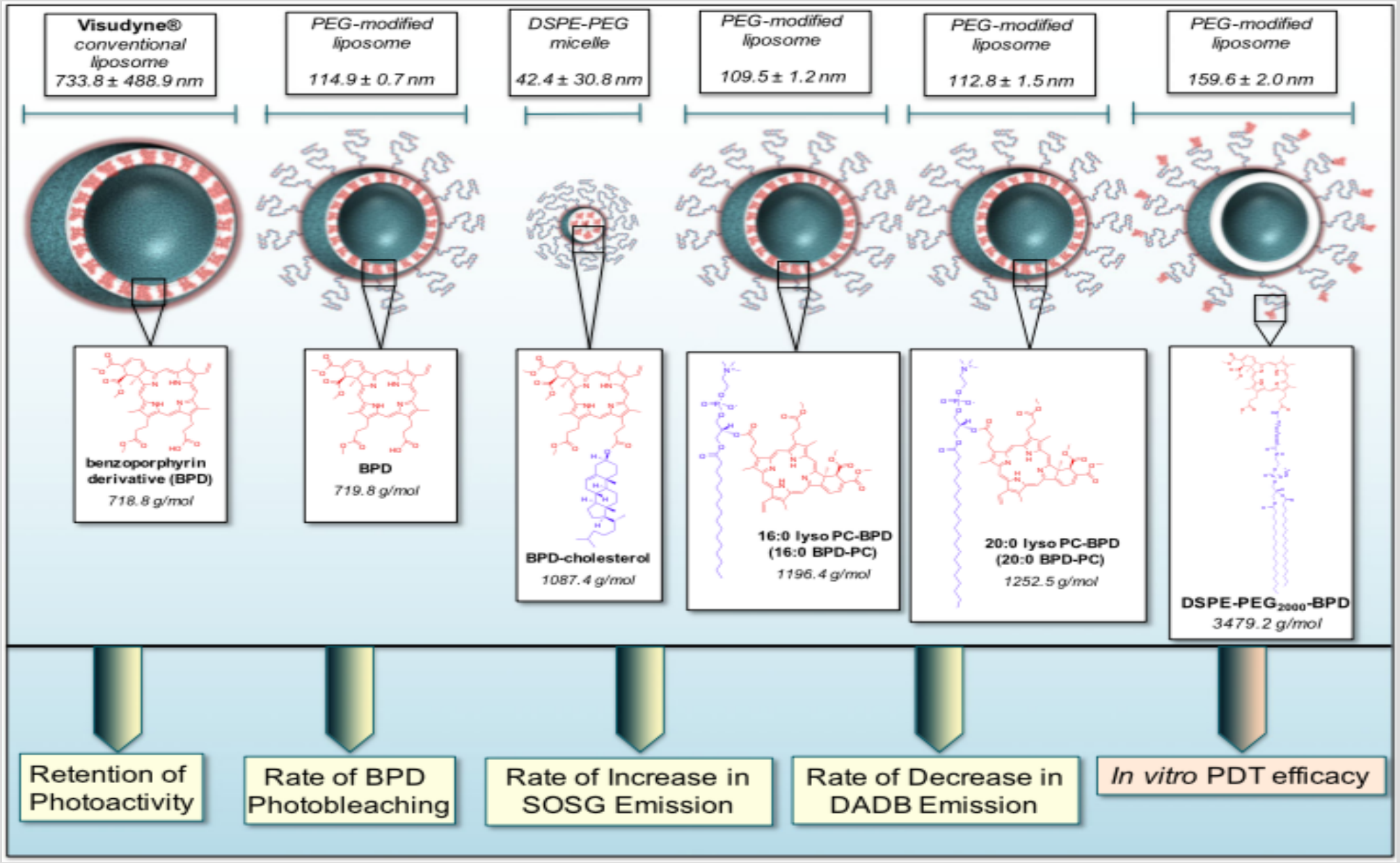
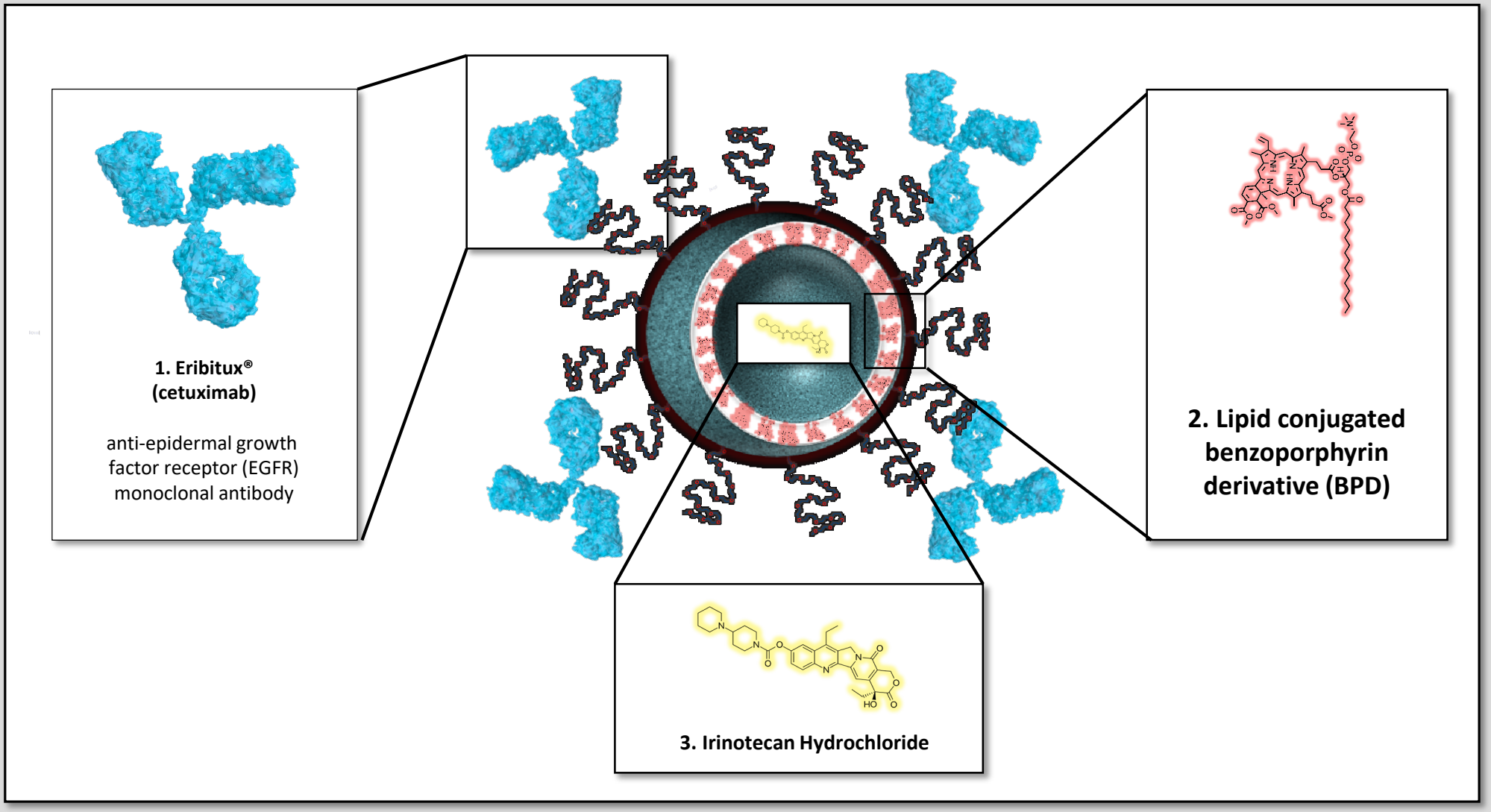
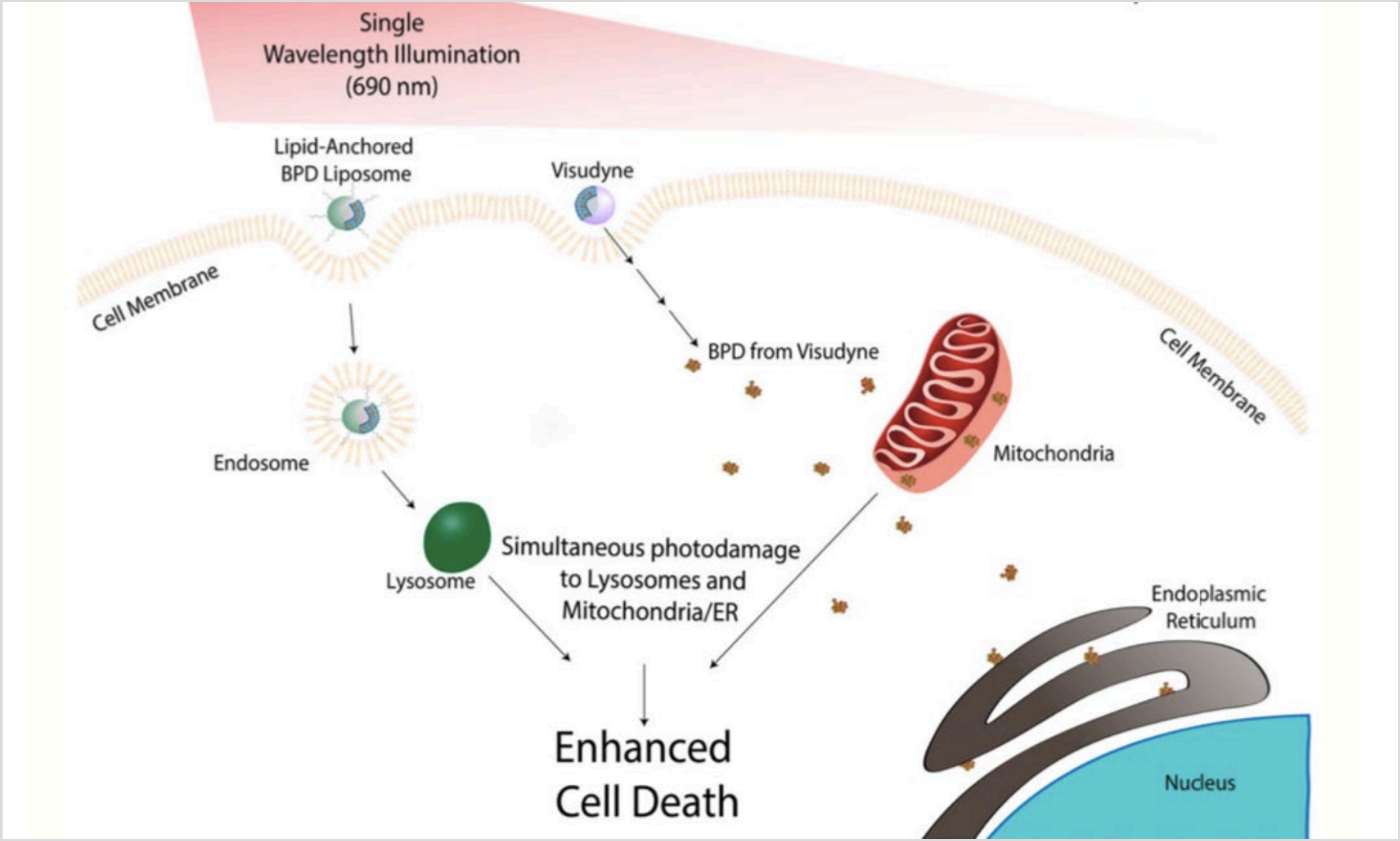
# Photodynamic Priming



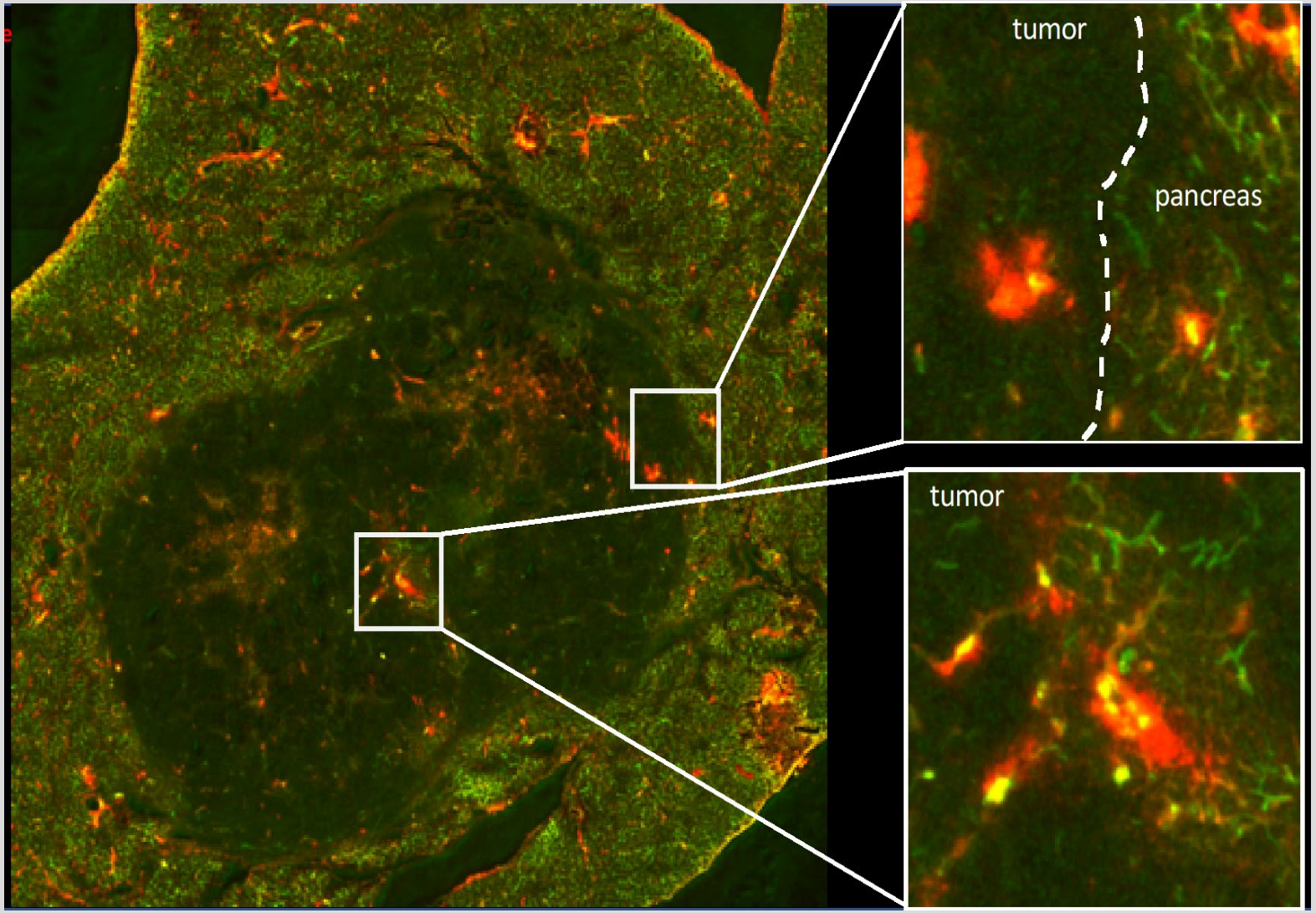

Visudyne®
conventional liposome
733.8 ± 488.9 nm
PEG-modified liposome
114.9 ± 0.7 nm
DSPE-PEG micelle
42.4 ± 30.8 nm
PEG-modified liposome
109.5 ± 1.2 nm
PEG-modified liposome
112.8 ± 1.5 nm
PEG-modified liposome
159.6 ± 2.0 nm
benzoporphyrin derivative (BPD)
718.8 g/mol
BPD
719.8 g/mol
BPD-cholesterol
1087.4 g/mol
16:0 lyso PC-BPD
(16:0 BPD-PC)
1196.4 g/mol
20:0 lyso PC-BPD
(20:0 BPD-PC)
1252.5 g/mol
DSPE-PEG2000-BPD
3479.2 g/mol
Retention of Photoactivity
Rate of BPD Photobleaching
Rate of Increase in SOSG Emission
Rate of Decrease in DADB Emission
In vitro PDT efficacy

# Targeted phototoxic multi-inhibitor liposomes (TPMIL)




Single
Wavelength Illumination
(690 nm)
Lipid-Anchored
BPD Liposome
Visudyne
Cell Membrane
BPD from Visudyne
Cell Membrane
Endosome
Mitochondria
Lysosome
Simultaneous photodamage
to Lysosomes and
Mitochondria/ER
Endoplasmic
Reticulum
Nucleus
Enhanced
Cell Death

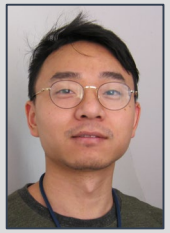
# Pancreas and Tumor Accumulation of TPMIL

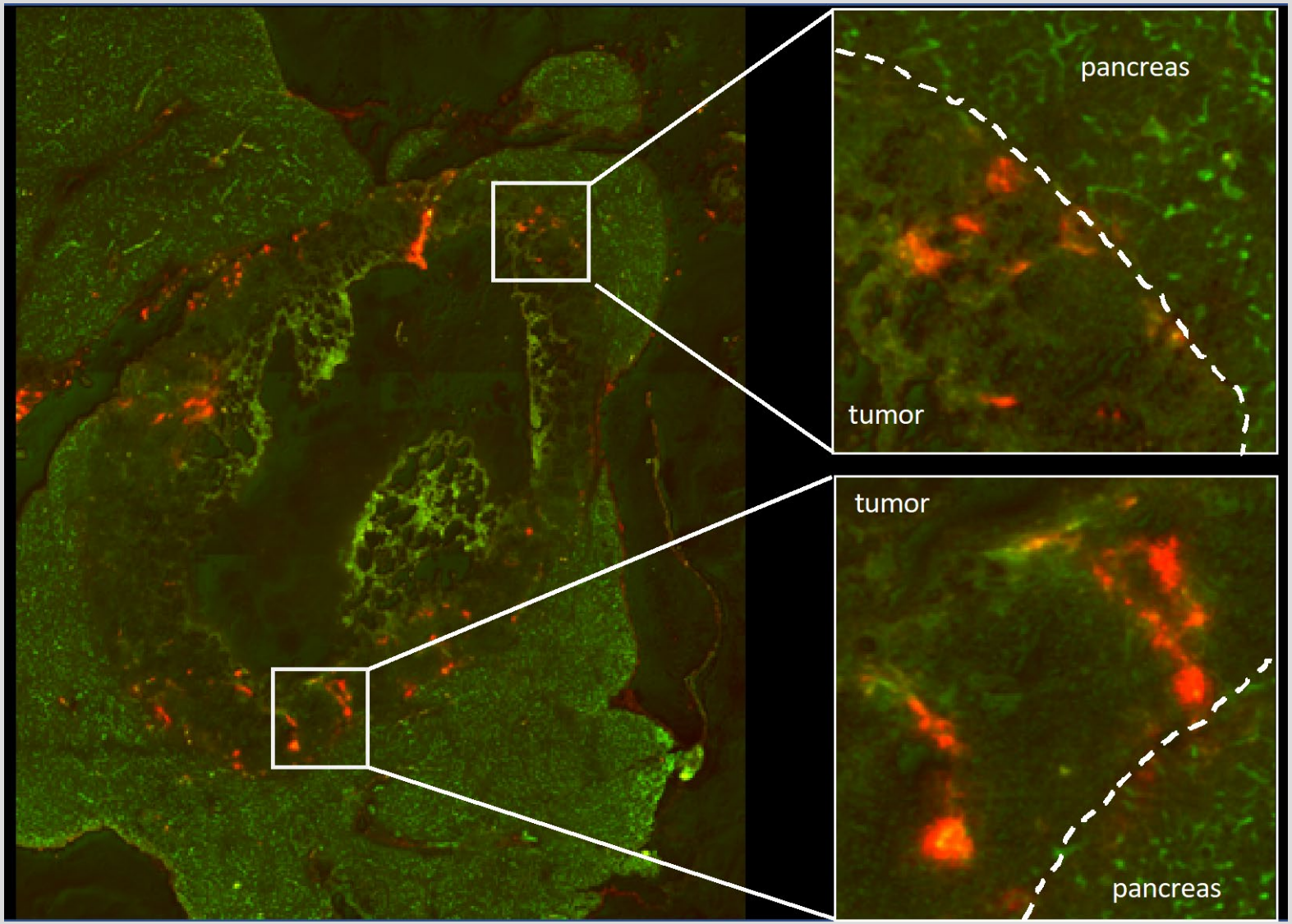



**Blood Vessels- Tomato Lectin**
**TPMIL-BPD Fluorescence**

Six hours after injection of the TPMIL constructs, the targeted nanoconstructs can be seen in both the healthy pancreatic tissue and the tumor.

# Pancreas and Tumor Accumulation of TPMIL






**Blood Vessels- Tomato Lectin**
**TPMIL-BPD Fluorescence**

At 24 hours after the injection of TPMIL, the targeted nanoconstructs are no longer present in the healthy tissue but remain bound in the tumor.

# Conclusions

- The TPMIL construct has the potential to be of great use in cancer treatment
- Further research on the mechanisms behind the photo-induced cell damage is required to fully understand the synergistic effects between autophagy, mitochondrial apoptosis, and lysosomal photodamage.
- Despite the increased efficacy of the TPMIL design, it is still limited to localized tumors that are accessible by an endoscope.

# Future Efforts

Research must be done to understand the mechanisms of the cell death pathways induced by the TPMIL constructs. The future goals of this project are to develop an increased awareness of:

1. The mechanisms behind the synergistic effects of lysosomal and mitochondrial photodamage.
2. Where lysosomal and mitochondrial photodamage converge with chemotherapy.
3. When the treatments converge with lysosomal photodynamic therapy.

# Questions?