

METALLI IN MEDICINA

A.A. 2016-2017

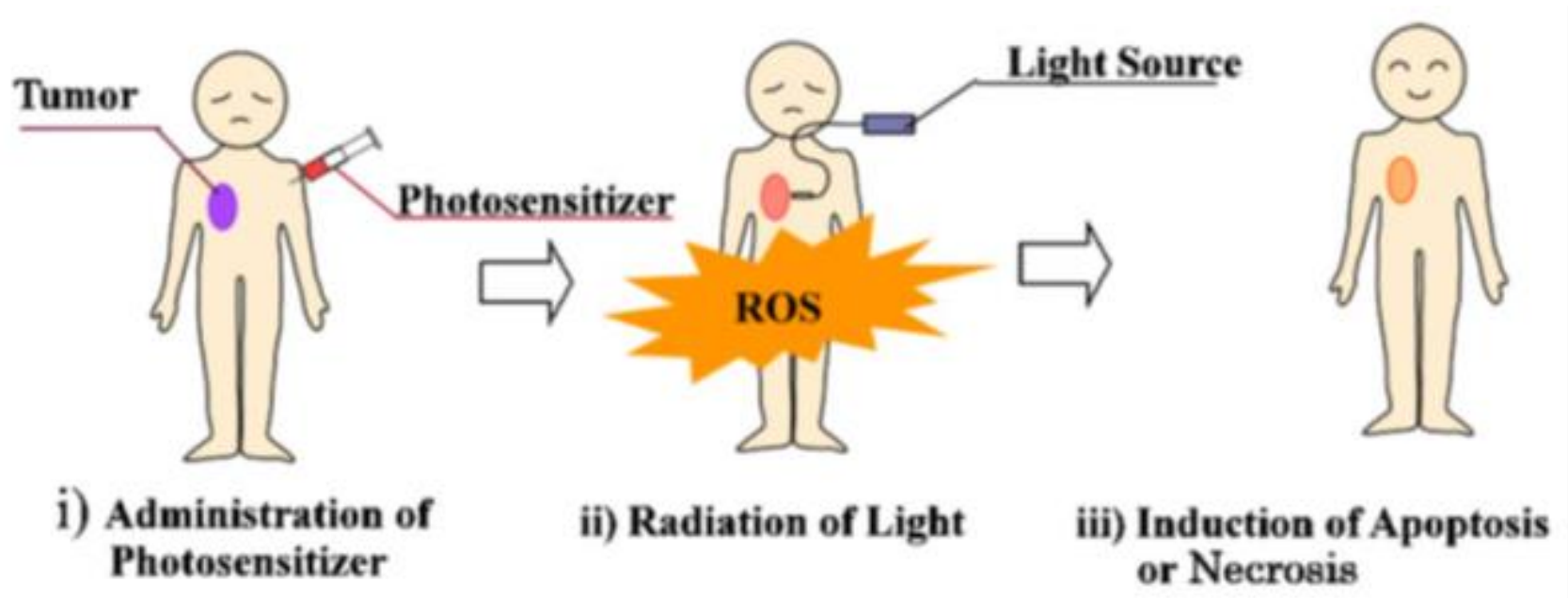
PARTE 3

Enzo Alessio

alessi@units.it

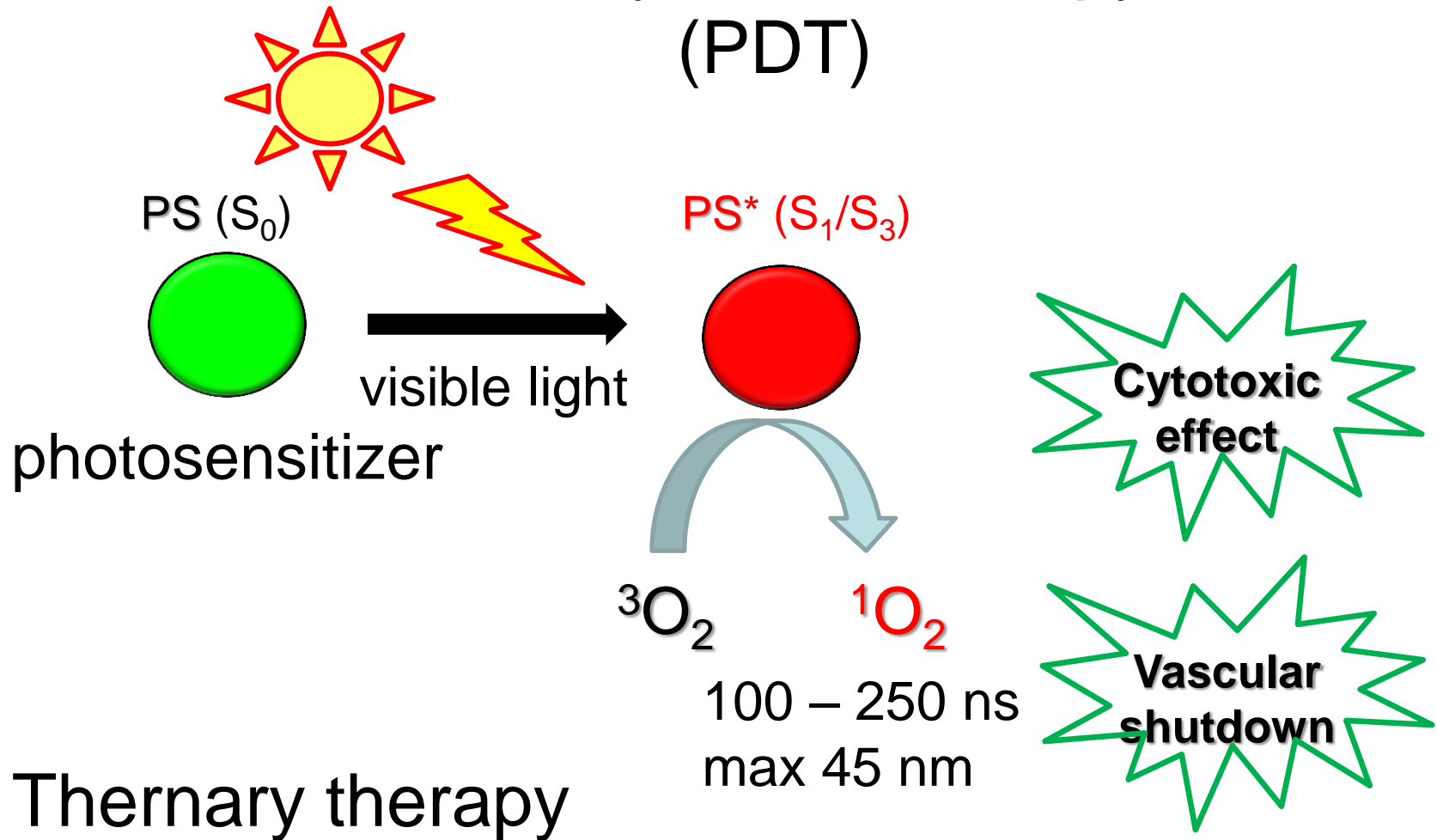


Photodynamic Therapy (PDT)



Spatio-temporal control

Photodynamic Therapy (PDT)



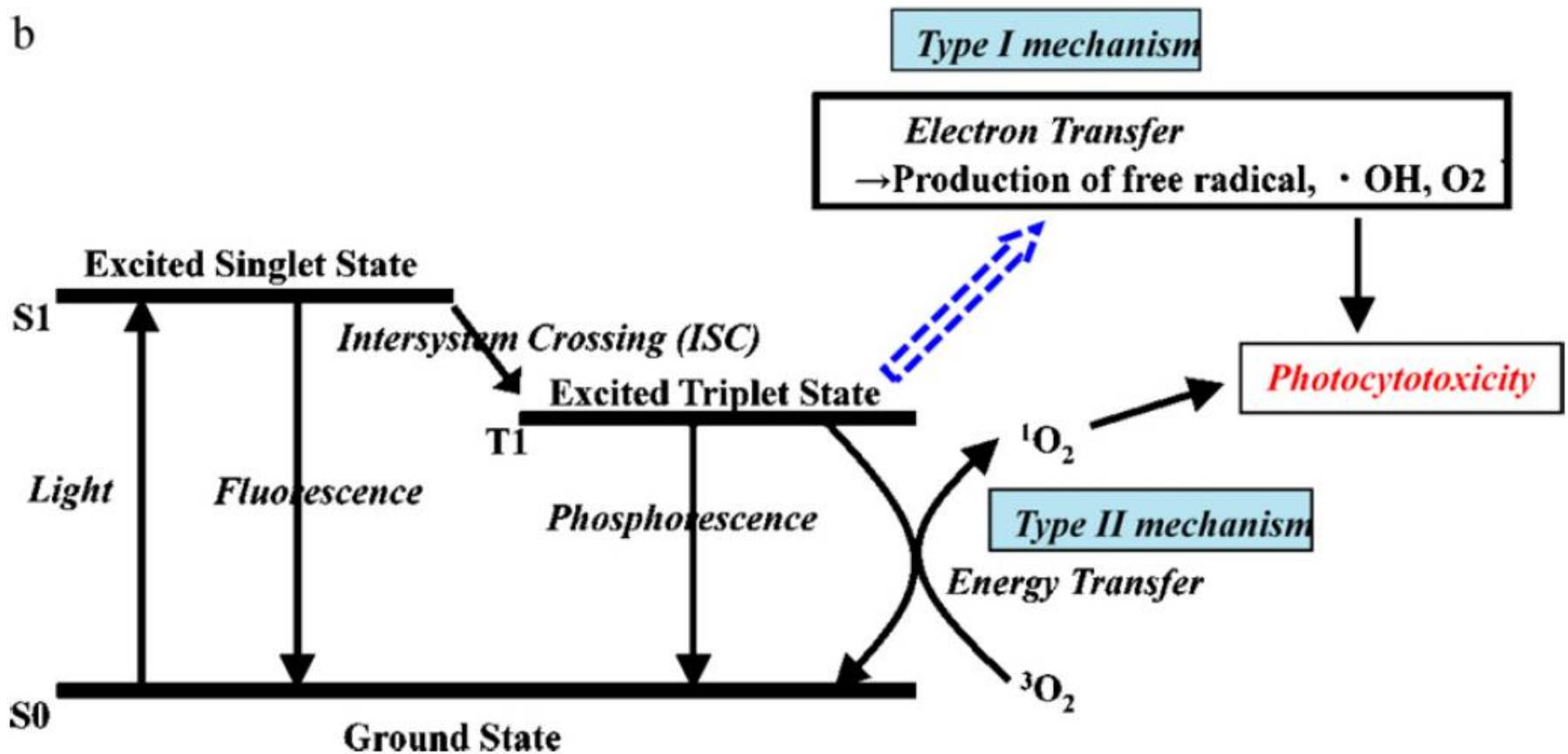
Thernary therapy

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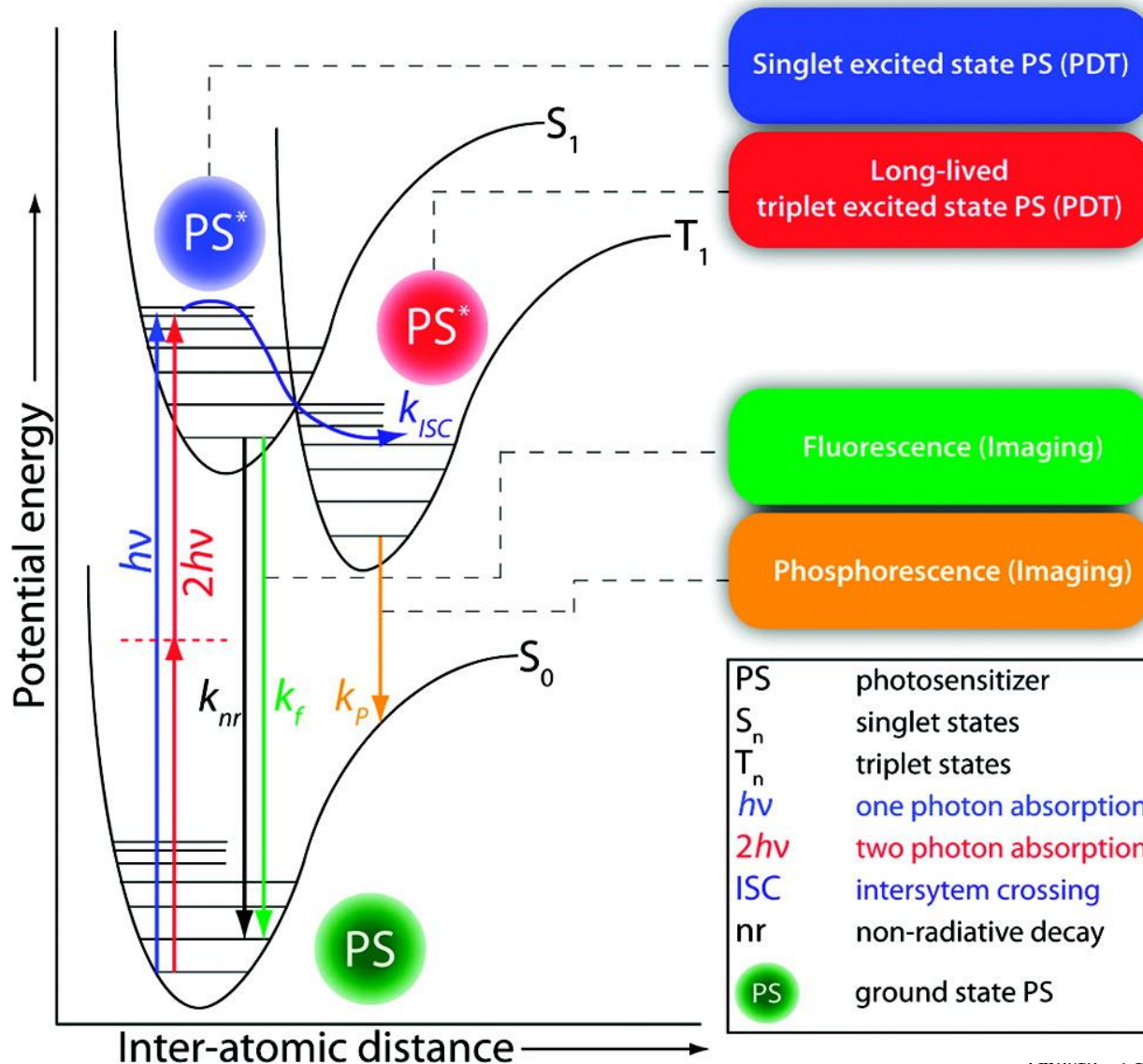


b

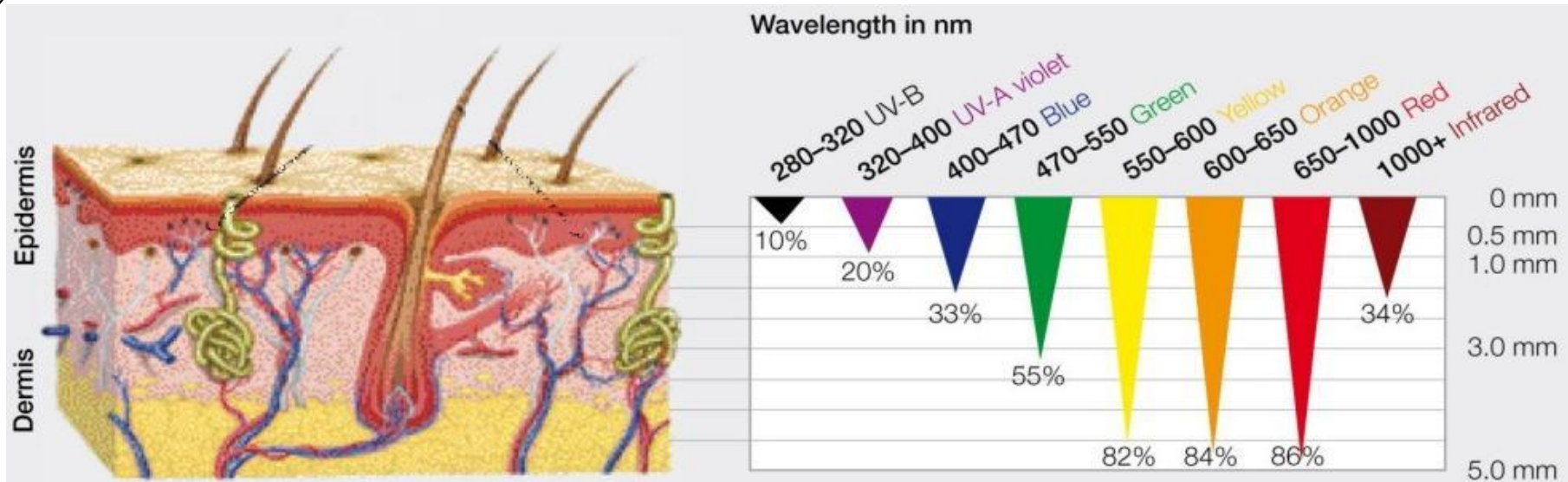


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Tissue penetration of light



PDT window

ΔE between 1O_2 and $^3O_2 = 22.5$ kcal/mol

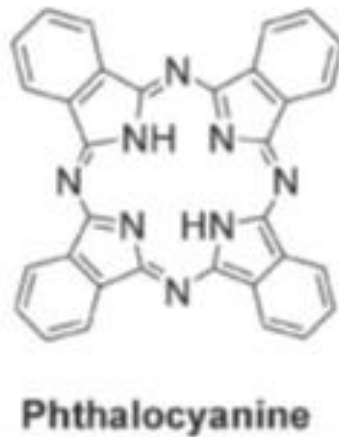
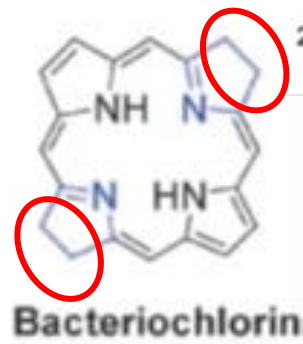
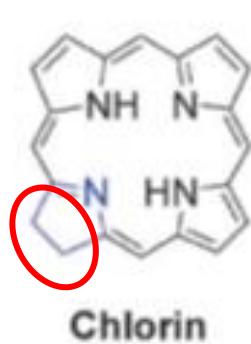
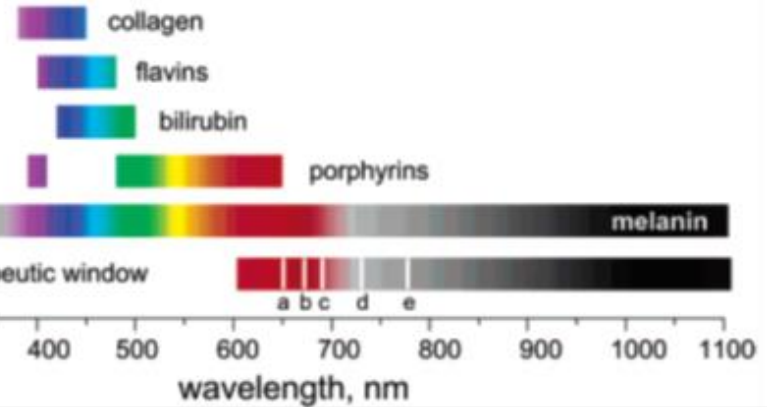
This energy gap is compatible with photosensitizers that have absorption maxima up to over 800 nm (their triplet excited state is still higher in energy than the ground state of 3O_2).

The Ideal photosensitizer

- Absorbs strongly in the PDT window (600 – 900 nm)
- Has a high $^1\text{O}_2$ quantum yield
- Is photostable (no photo-bleaching)
- Is non-toxic in the dark
- Localizes selectively in the diseased tissue
- Has a rapid clearance

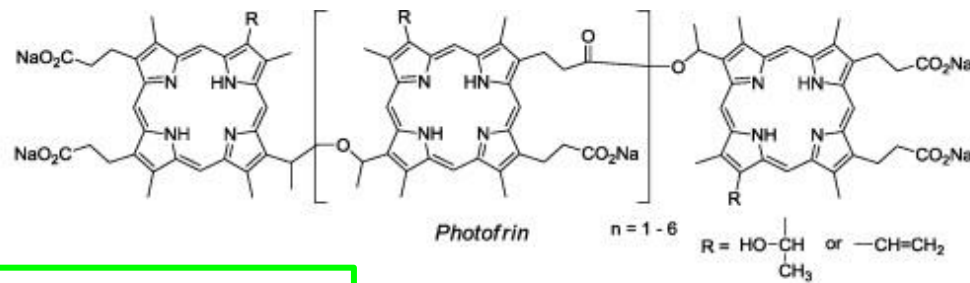
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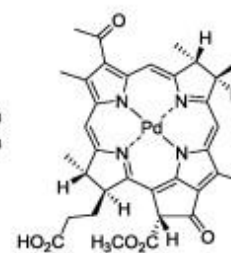
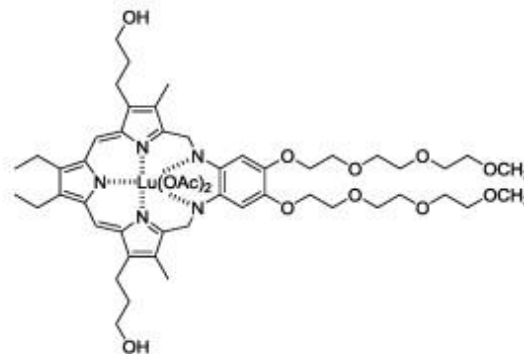
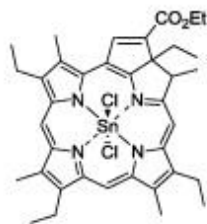
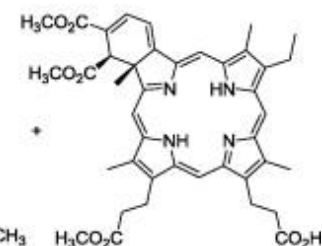
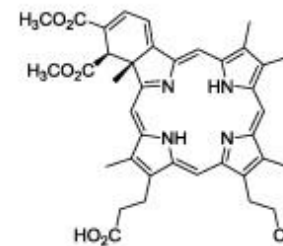
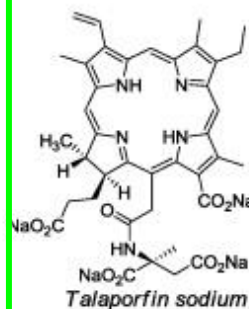
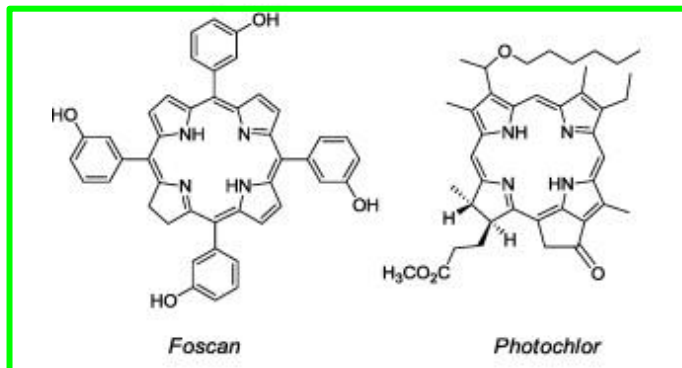


$$\lambda = 630$$

$$\varepsilon = 1170 \text{ M}^{-1}\text{cm}^{-1}$$

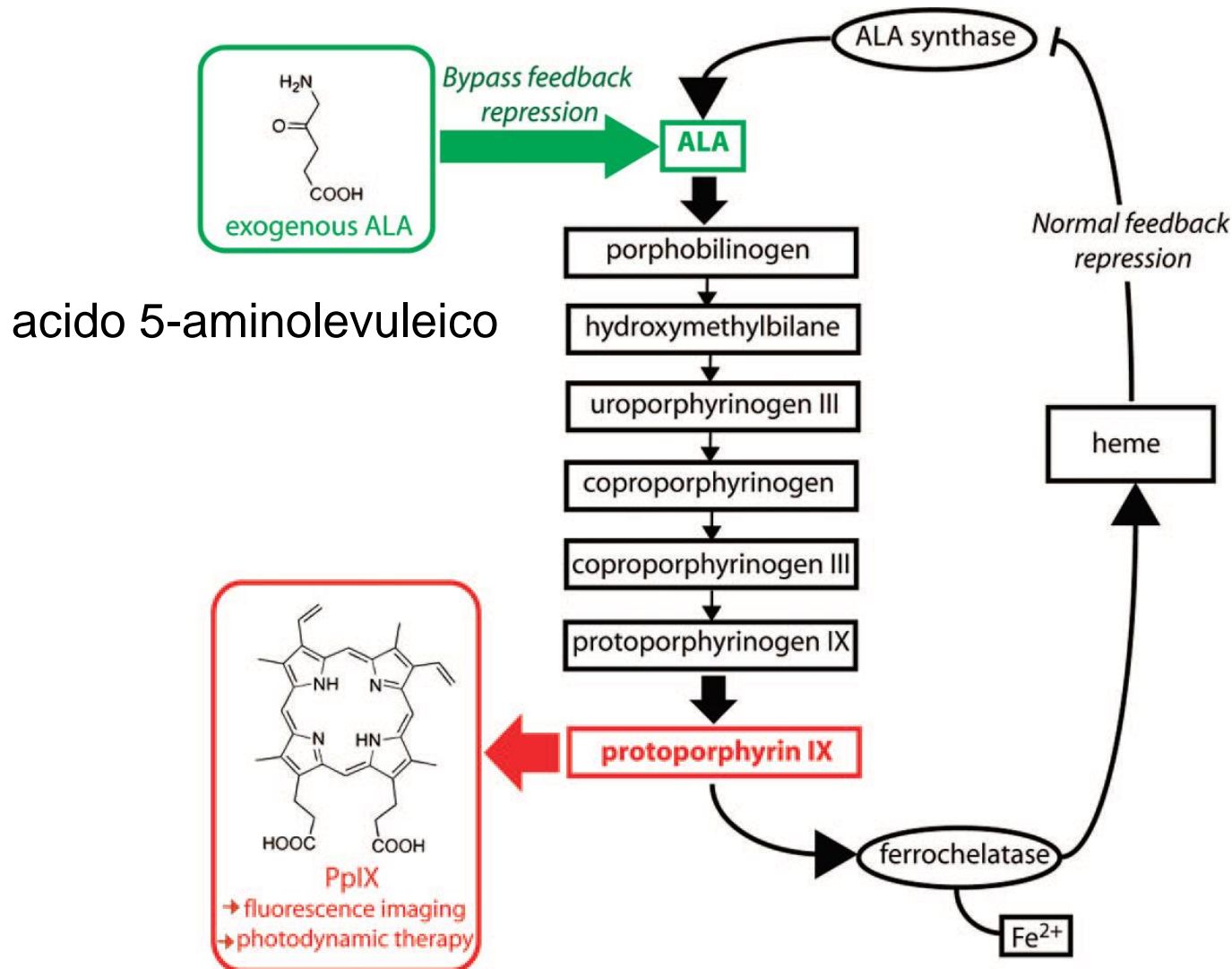
$$\lambda = 652$$

$$\varepsilon = 3 \times 10^4 \text{ M}^{-1}\text{cm}^{-1}$$



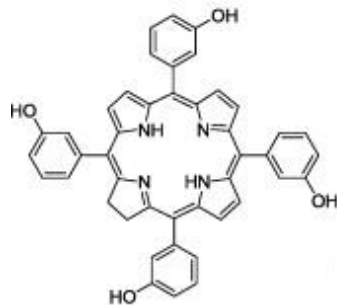
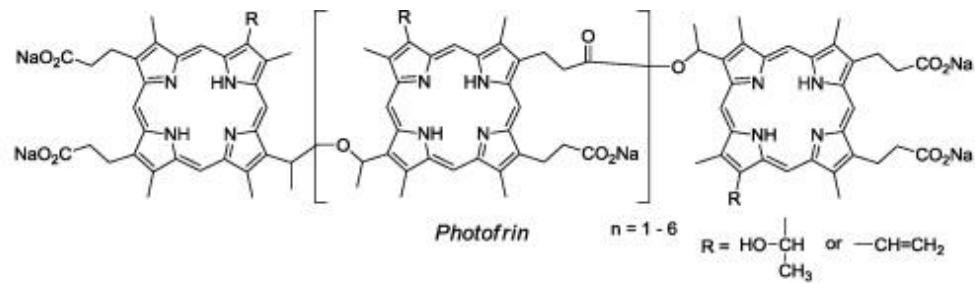
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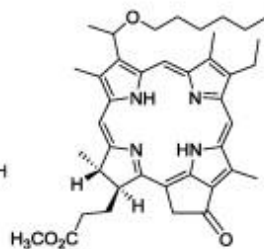


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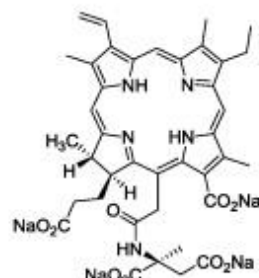
PARTE 3



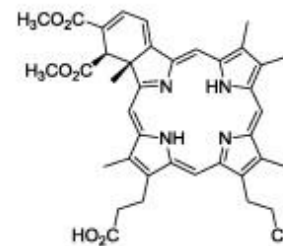
Foscan



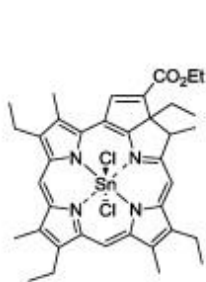
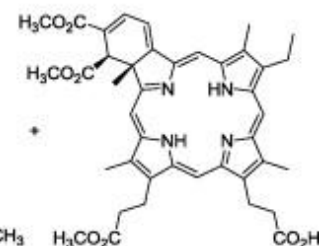
Photochlor



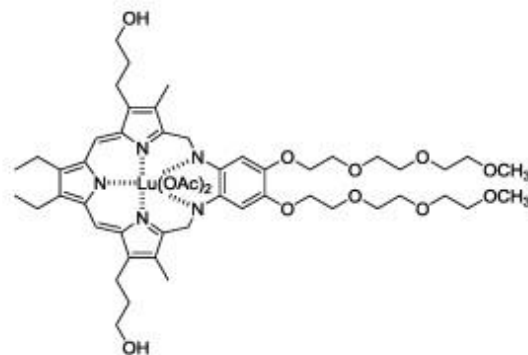
Talaporfin sodium



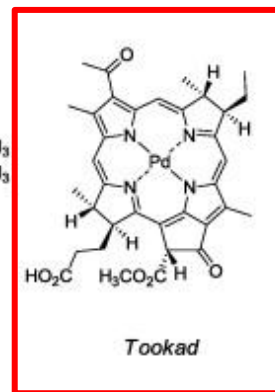
Visudyne



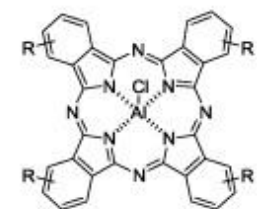
Purlytin



Lutrin



Tookad

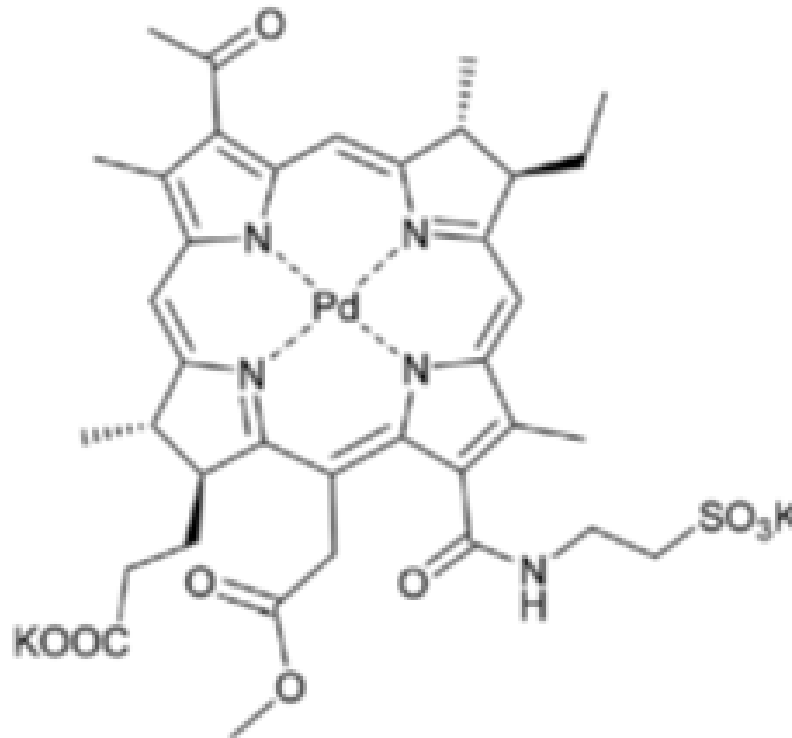


Photosens

$R = \text{H or } -\text{SO}_3\text{H}$

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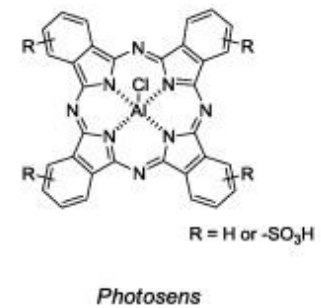
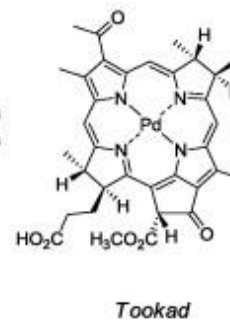
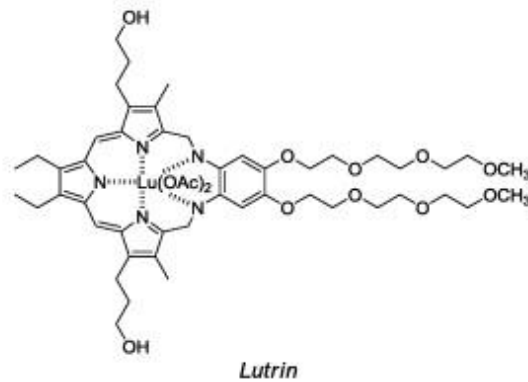
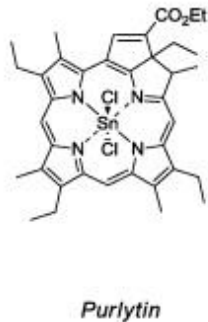
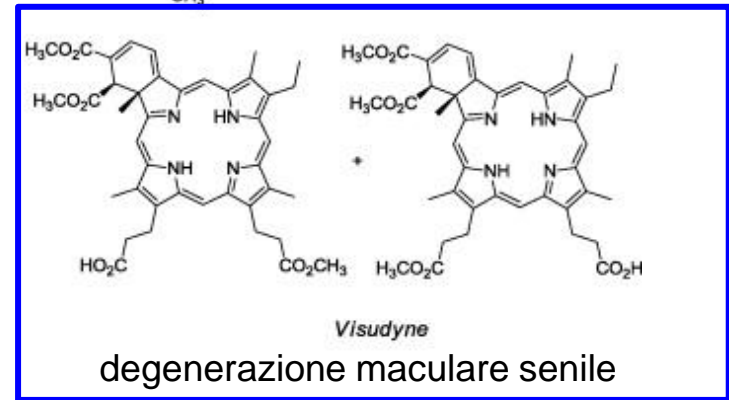
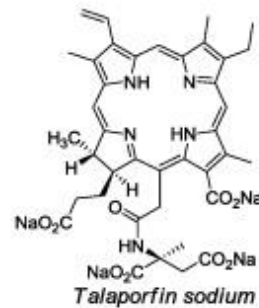
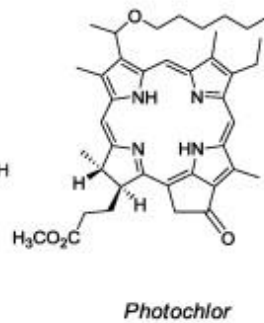
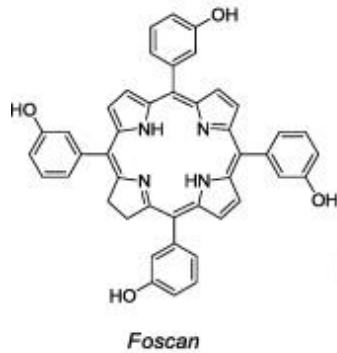
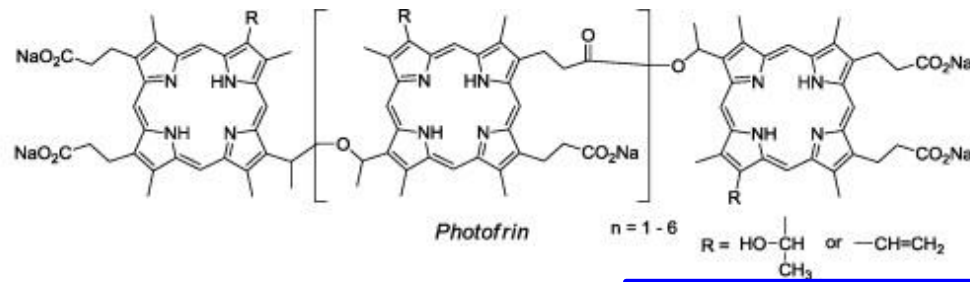
PARTE 3



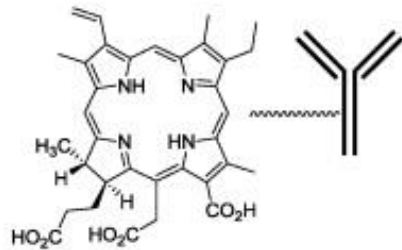
TOOKAD-solubile
(palladio-batteriofeoforbide)

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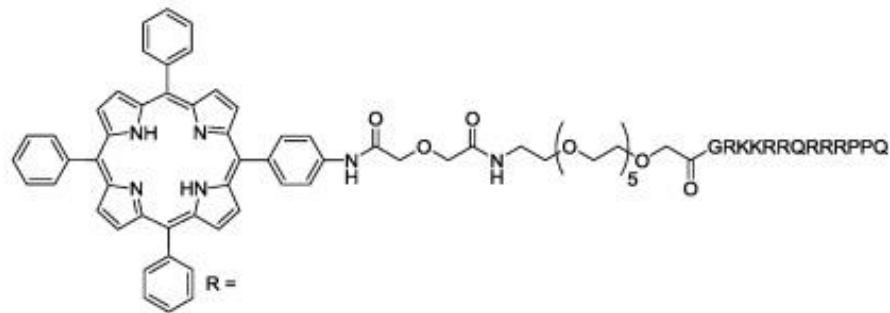
PARTE 3



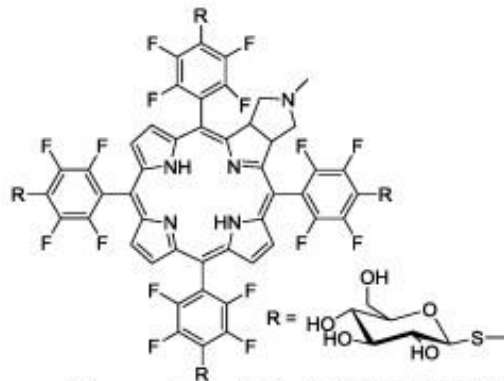
Third generation (targeted) PS's



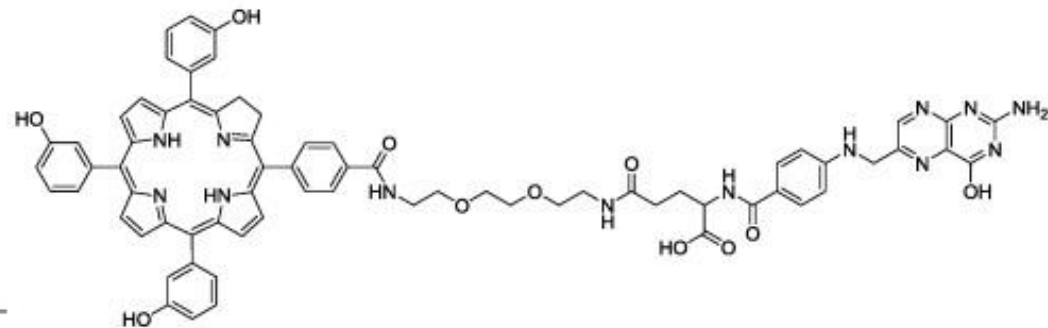
IgG conjugated chlorin



HIV-1 Tat peptide conjugated porphyrin

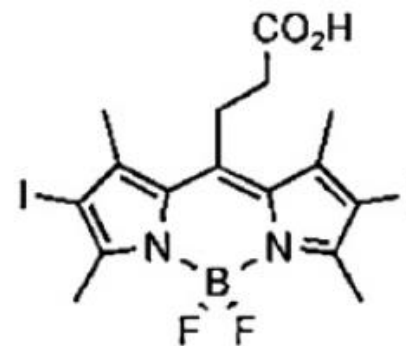
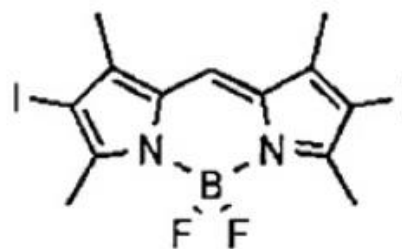
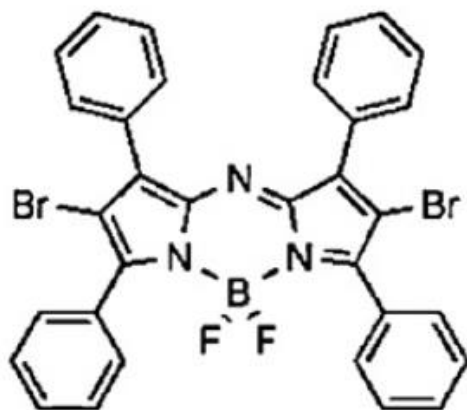


Glycoconjugated chlorin (H₂TFPC-SGlc)



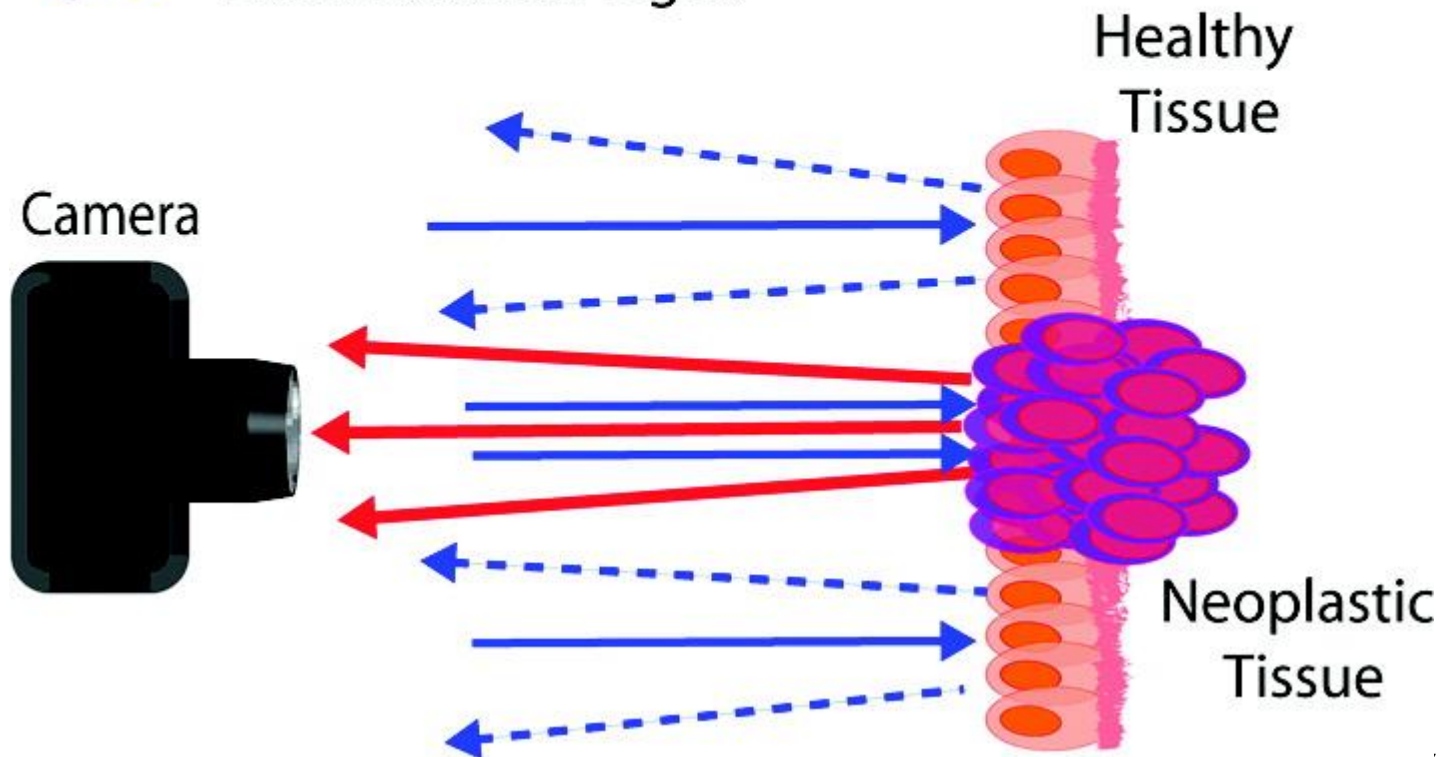
Folate conjugated temoporfin

BODIPY (*boron-dipyrromethene*) derivatives

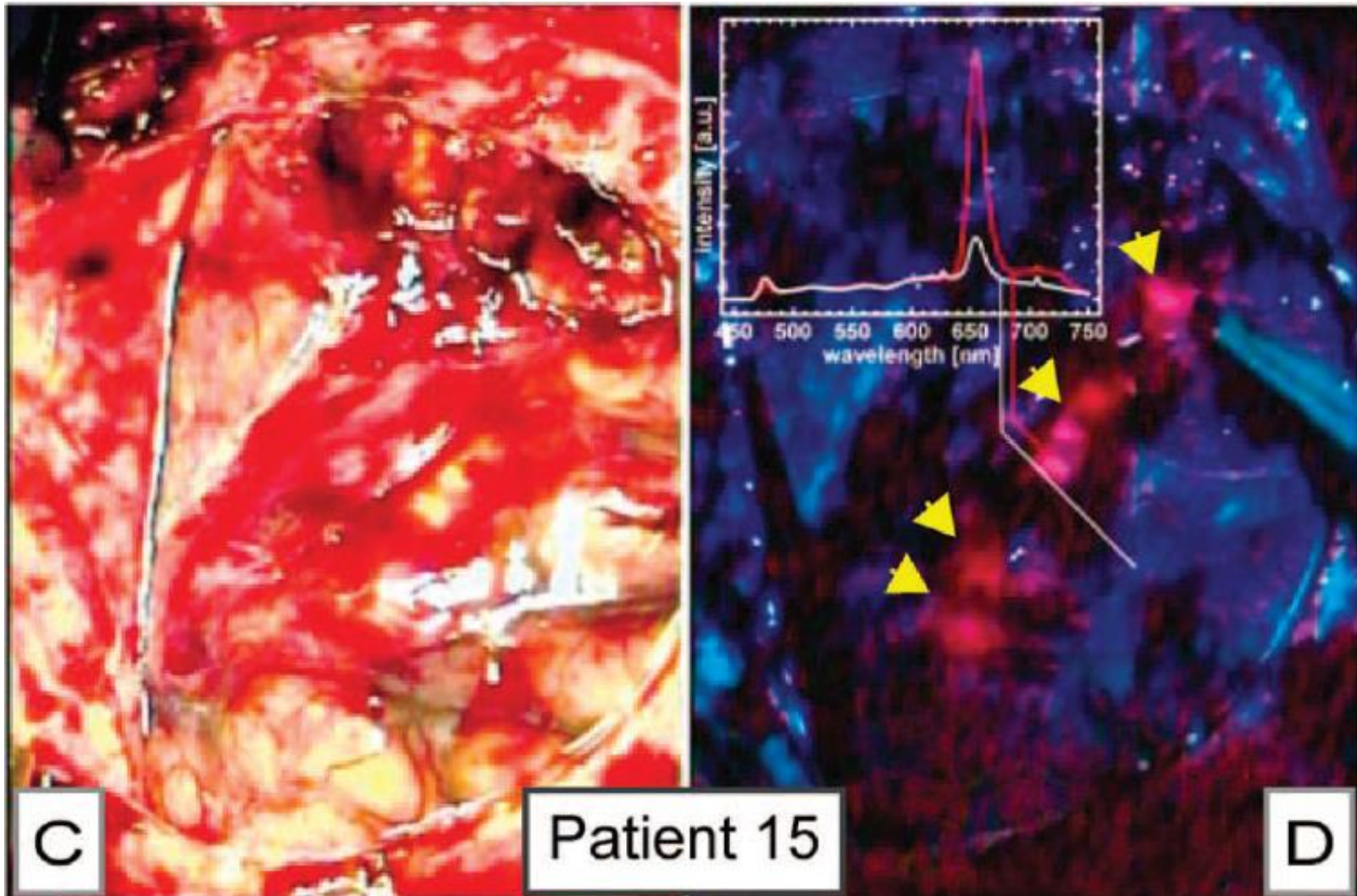


Tumor margin resection with *tumor avid* PS's

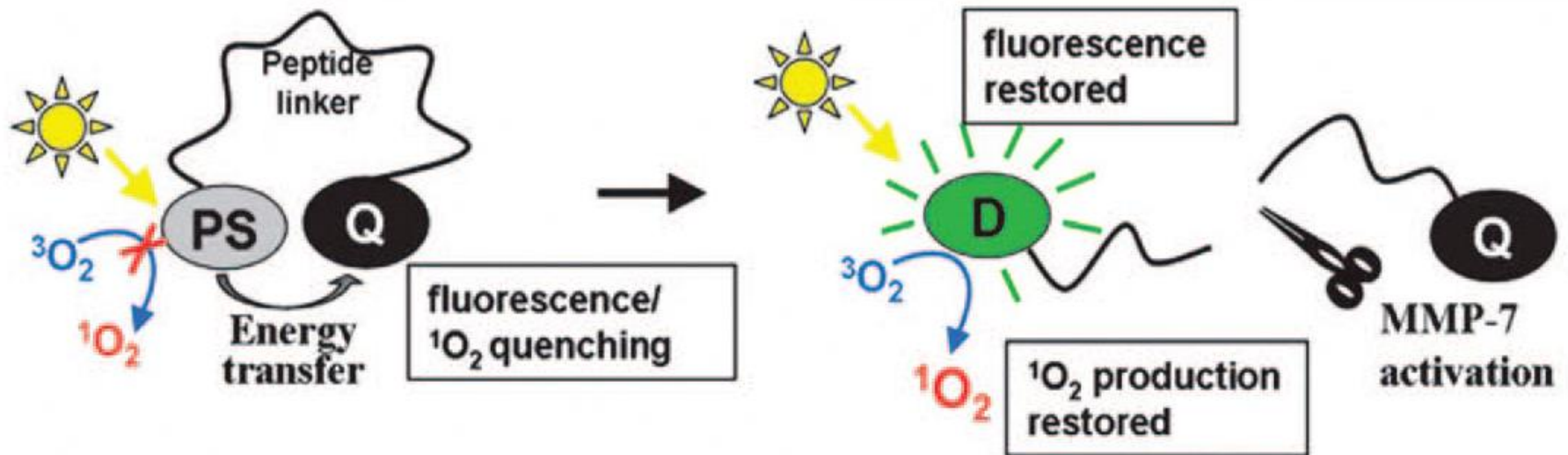
- = Excitation Light
- ← = Fluorescence Emission
- ← - - = Backscattered Light



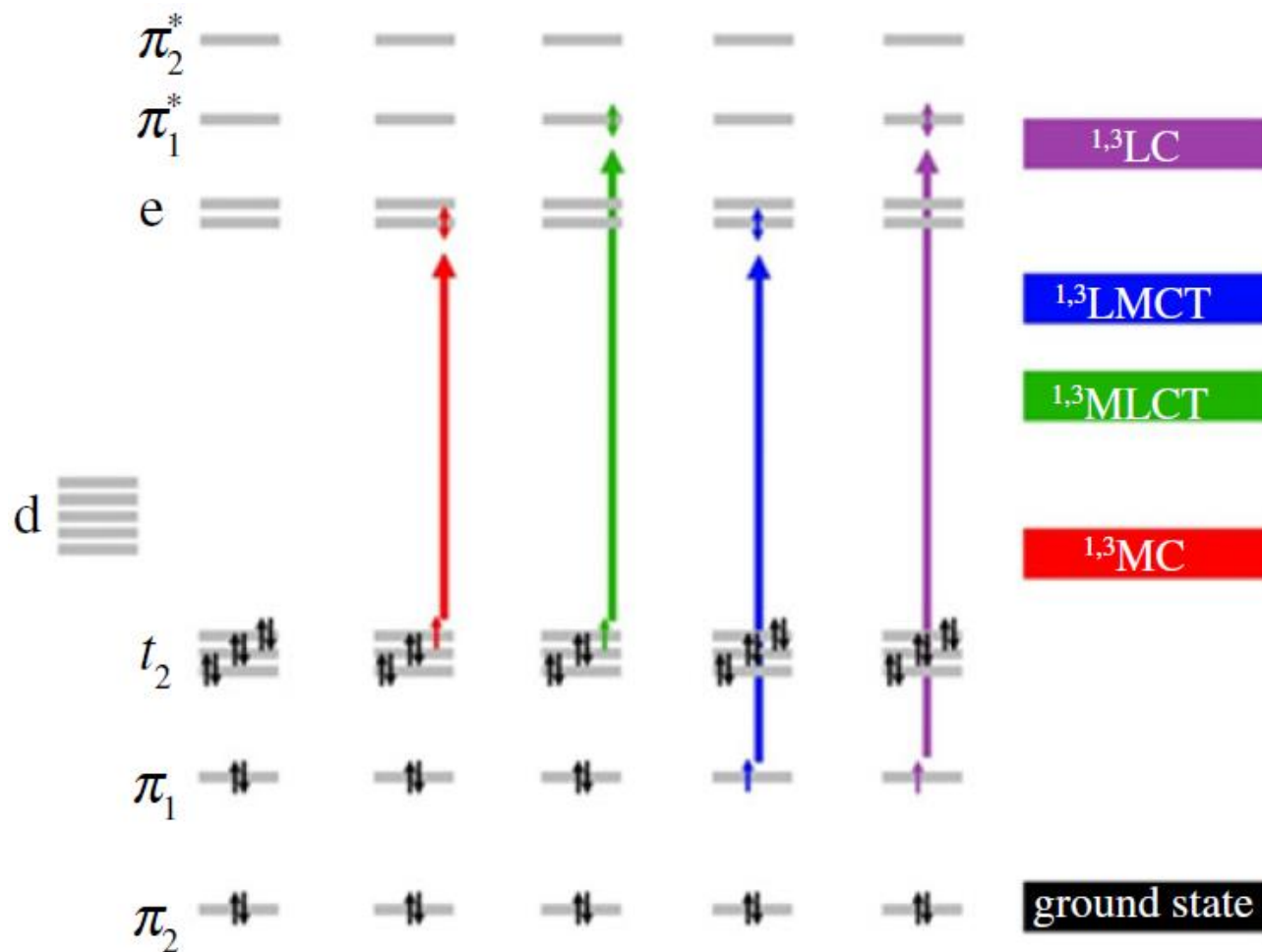
Brain tumor, patient treated with Foscan



Site-activated constructs



Photoactivatable metal compounds



Photoactivatable metal compounds

These complexes are inert and non-toxic to cells in the dark.

Upon irradiation at the tumor site, they undergo various **photochemical reactions**, including **isomerization**, **substitution**, and **reduction**.

The photoactivation pathway of metal complexes **does not rely on O₂**, which is a significant advantage over the photosensitizers used in current PDT.

Photoinduced ligand
dissociation

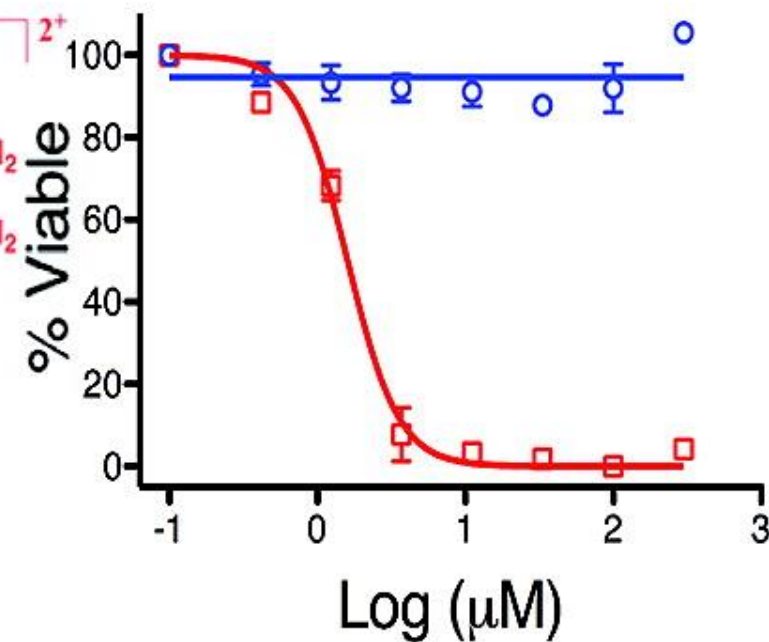
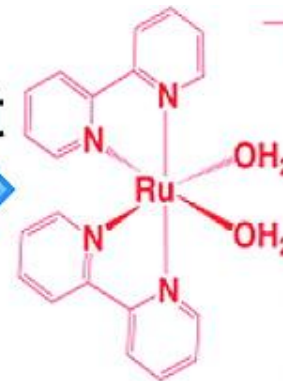
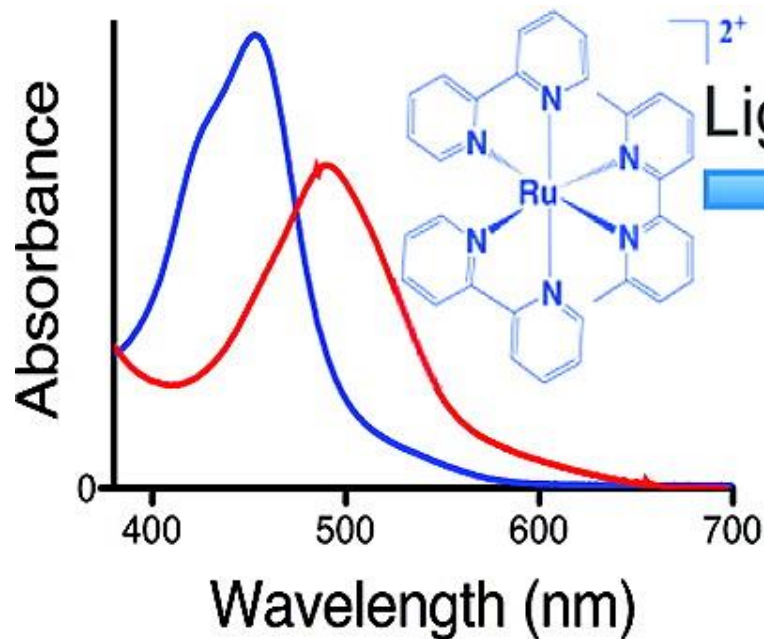


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graph TD; A[Photoinduced ligand dissociation] --> B[Activation of the metal center]; A --> C[Selective release of active ligands (photo-uncaging)];
```

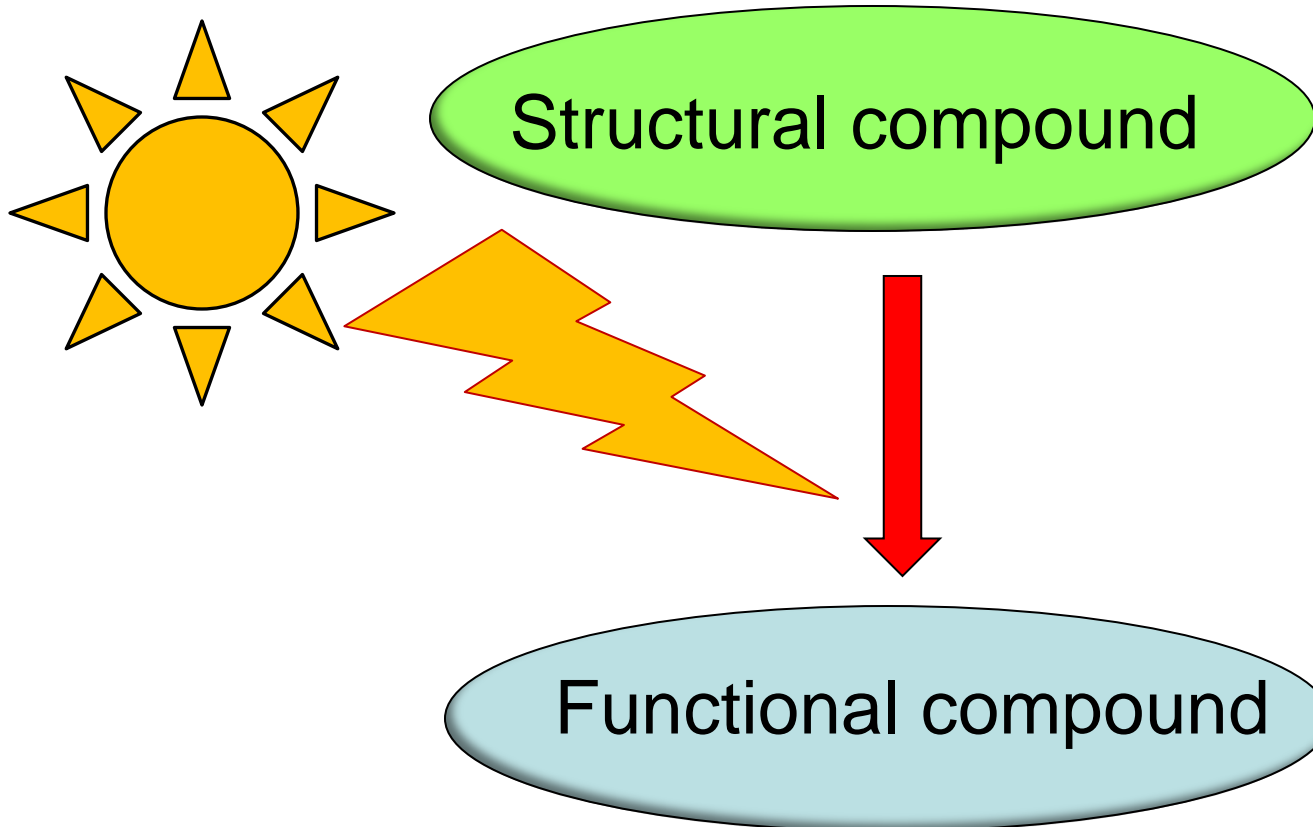
Activation of the
metal center

Selective release
of active ligands
(*photo-uncaging*)

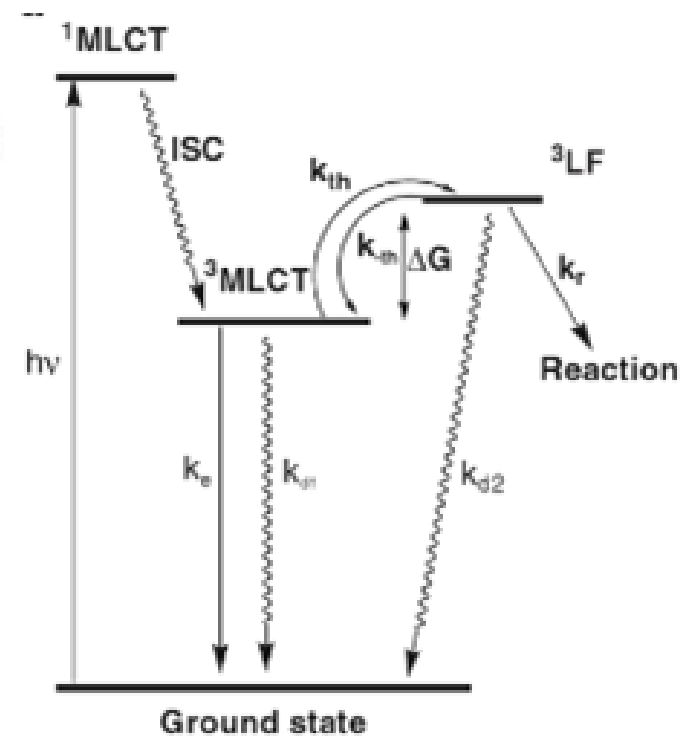
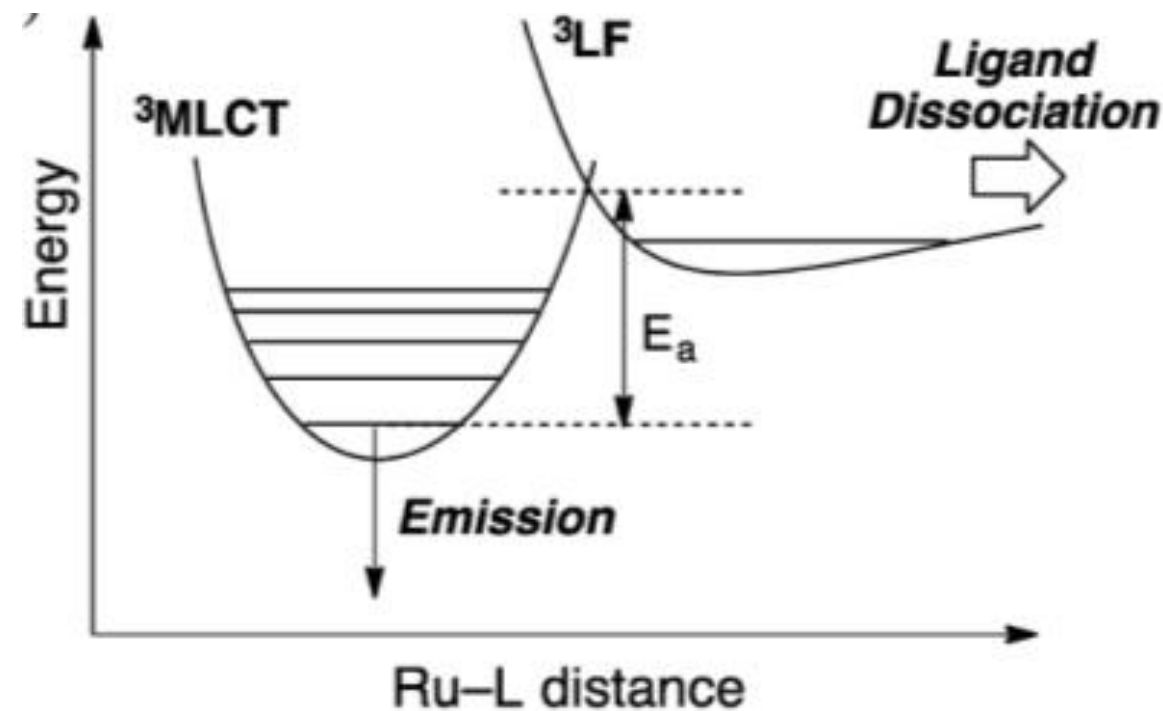
Photoactivatable Ru compounds



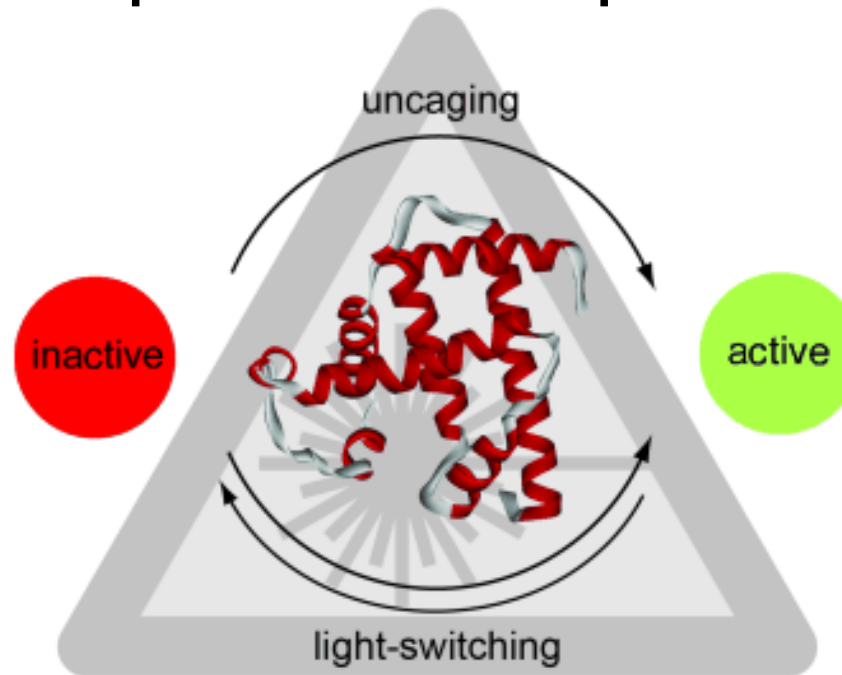
Phototoxicity Index, PI



Photoactivatable Ru compounds

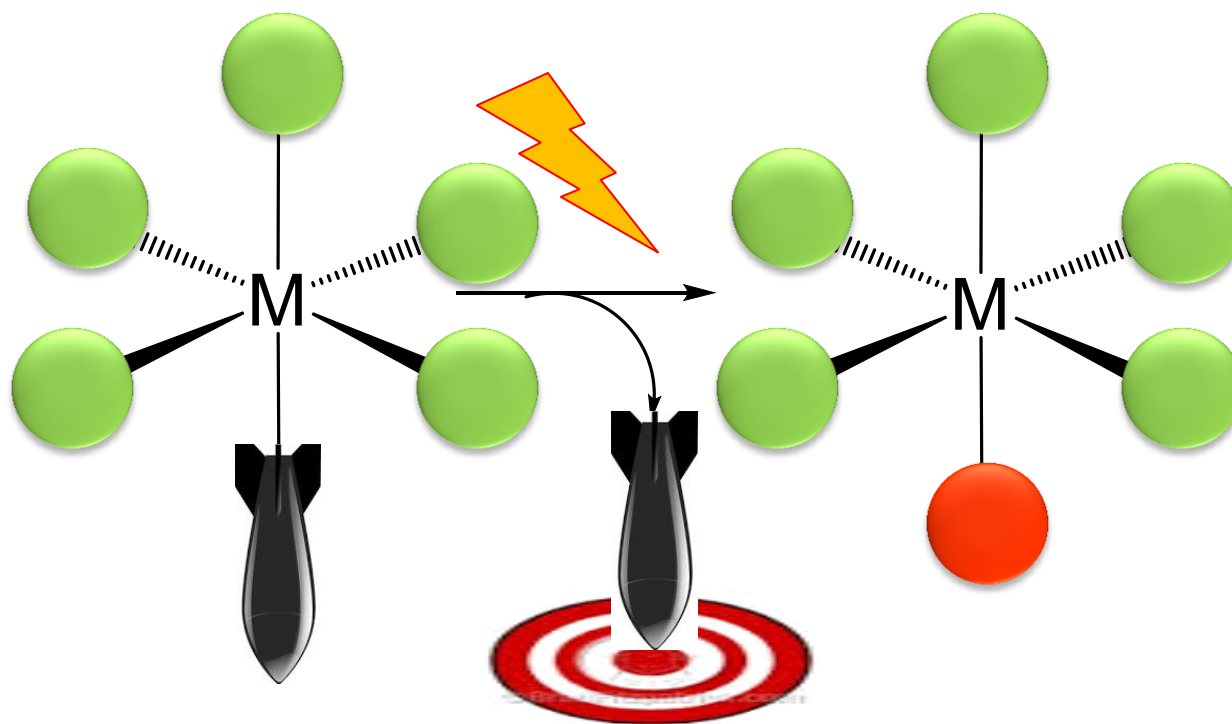


Caged compounds and photo-uncaging



Photolabile protecting groups, attached to a defined position of a molecule, can be used to gain spatio-temporal control over the concentration of the active form of a molecule.

Metal compounds for the delivery of active molecules



=

NO, CO, 4-aminopyridine (4-AP, K⁺ channel blocker), γ -aminobutyric acid (GABA, a neurotransmitter),...

Caged compounds and photo-uncaging

NO Releasing Molecules = NORM

CO Releasing Molecules = CORM

Photo-NORM

Photo-CORM



$h\nu$

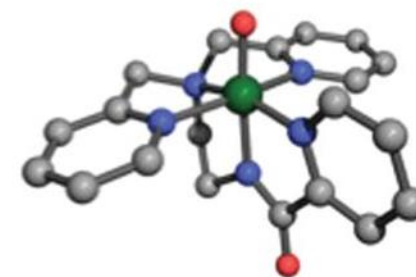
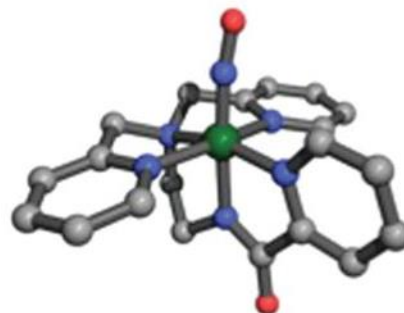
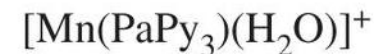
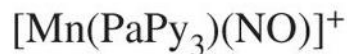
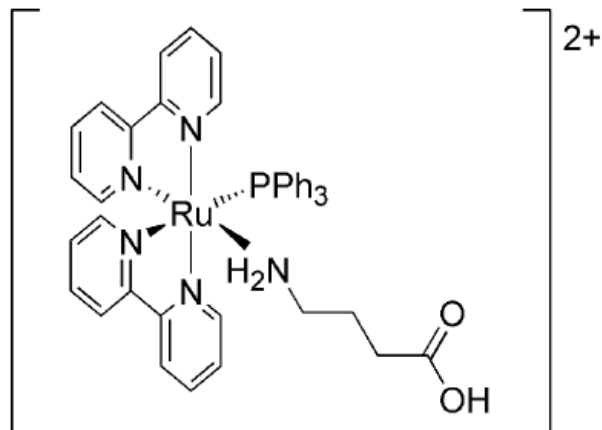
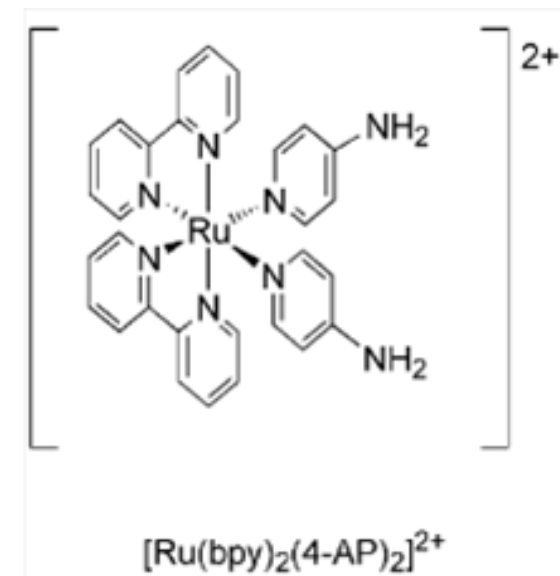
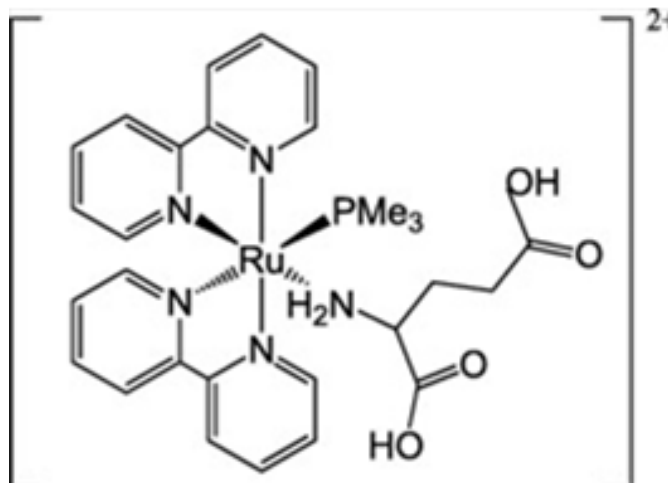


Photo-release of neurotransmitters



$[\text{Ru}(\text{bpy})_2(\text{PPh}_3)(\text{GABA})]^{2+}$



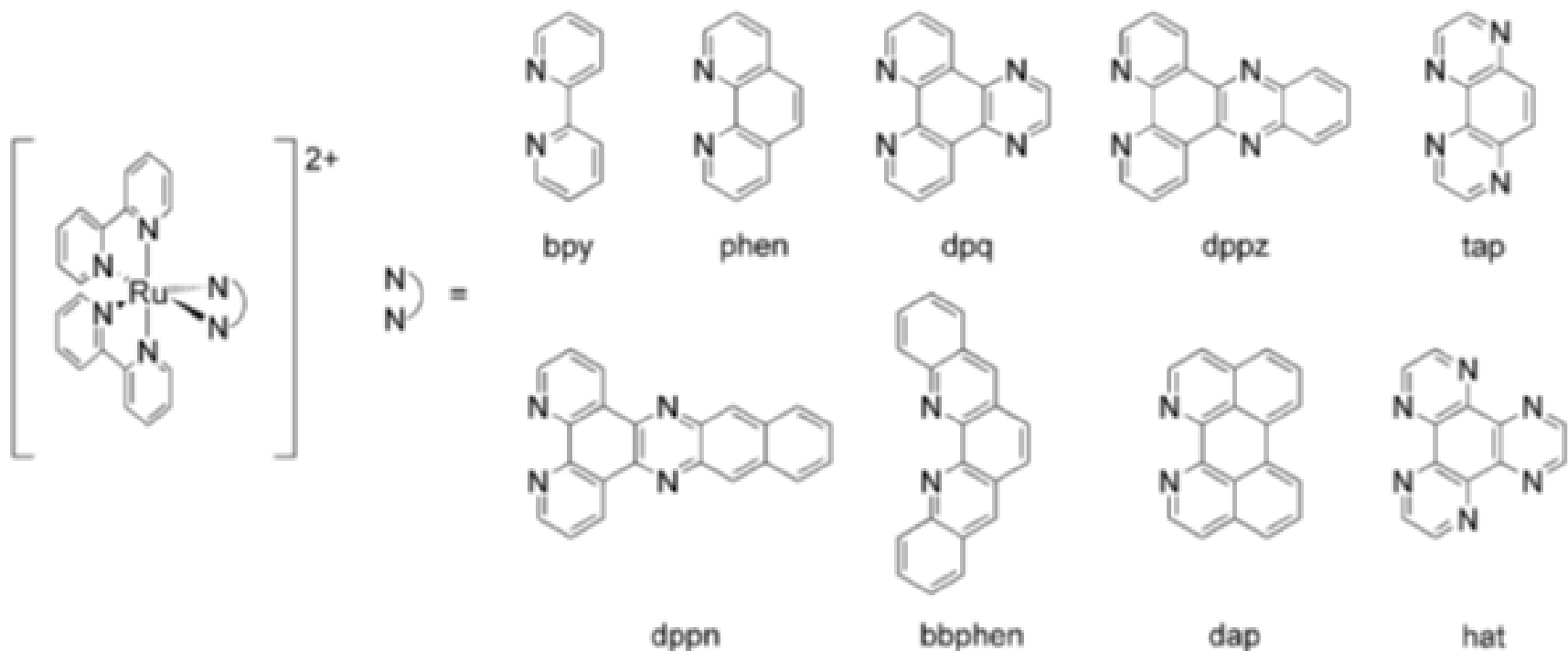
$[\text{Ru}(\text{bpy})_2(4\text{-AP})_2]^{2+}$

GABA = γ -aminobutyric acid: inhibitory neurotransmitter

Glutamic acid: excitatory neurotransmitter

4-AP = 4-aminopyridine: K^+ channel blocker

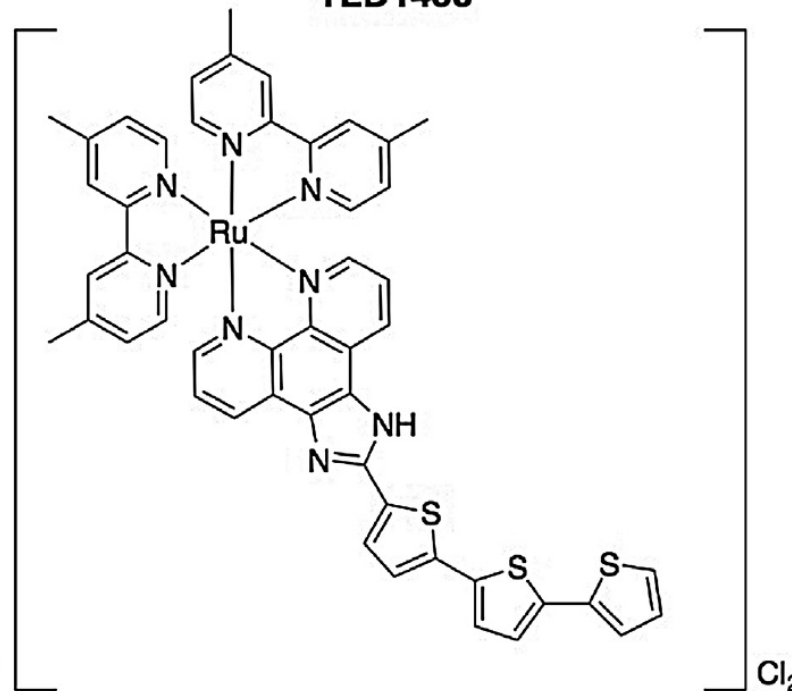
Metal compounds for PDT



Health Canada Approves Clinical Trial Application for Anti-Cancer Drug

Toronto, Ontario – December 17, 2015, Theralase Technologies Inc. (“Theralase” or the “Company”) (TLT:TSXV) (TLTFF:OTC), a leading biotechnology manufacturer focused on commercializing medical technologies to eliminate pain and destroy cancer, announced today that Health Canada has approved its next generation anti-cancer drug, TLD-1433, under Clinical Trial Application (“CTA”) for evaluation in a Phase Ib clinical trial for patients inflicted with Non-Muscle Invasive Bladder Cancer (“NMIBC”).

TLD1433



Cl₂

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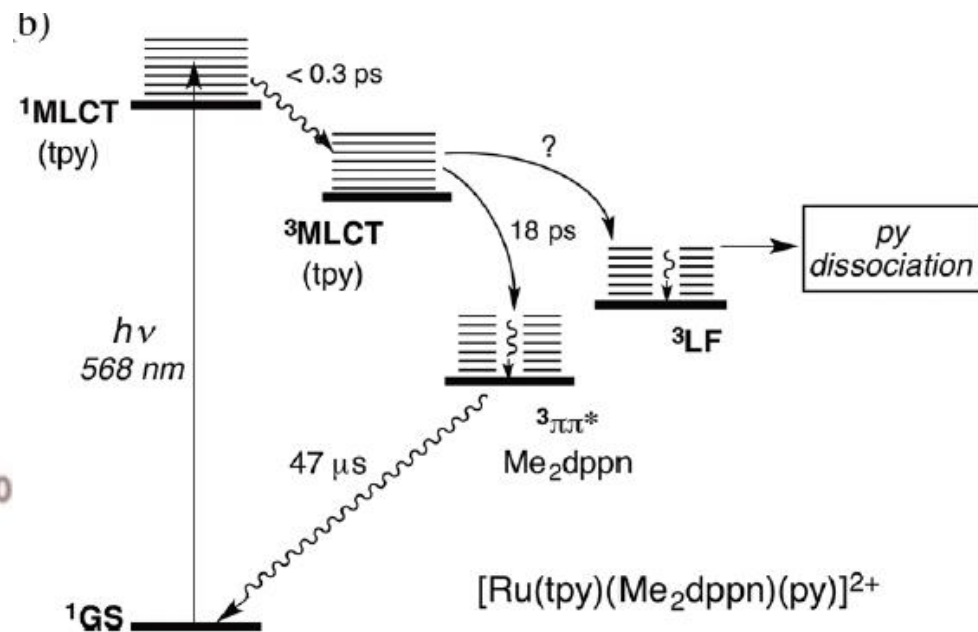
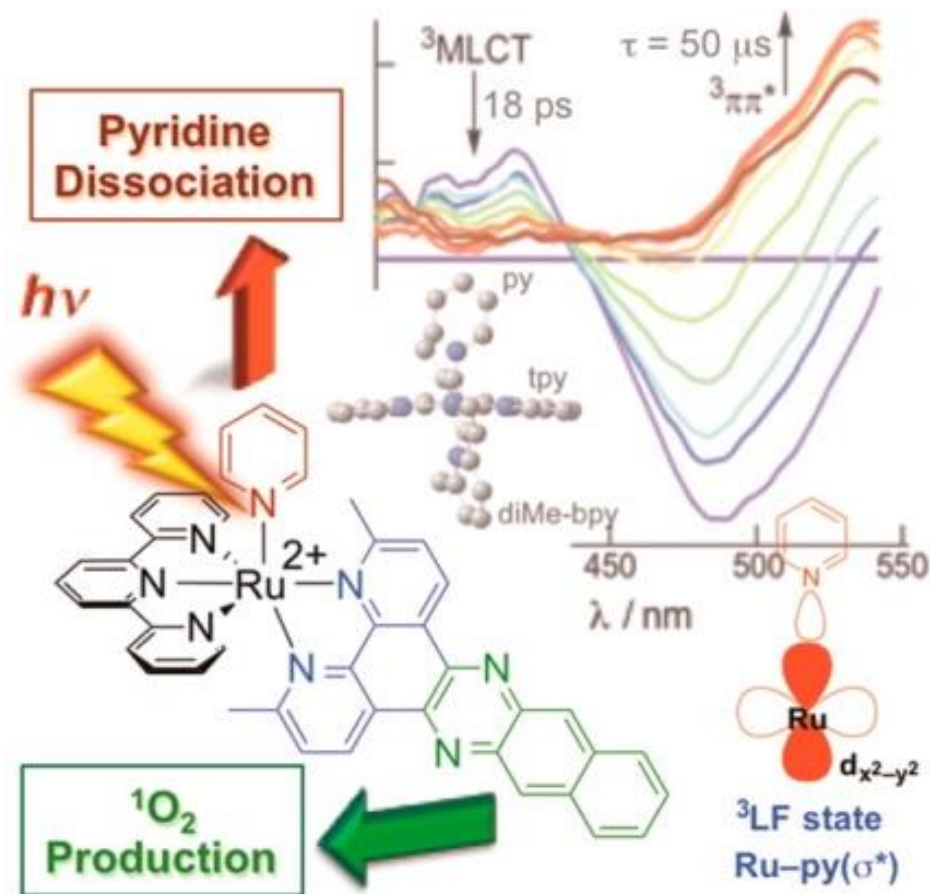


Photo-reduction of Pt(IV)-azido compounds

