# Developing Dendritic Drug Carriers

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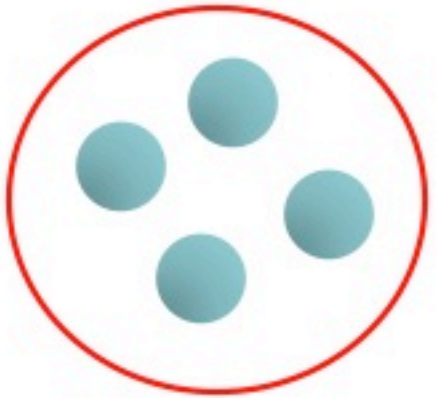
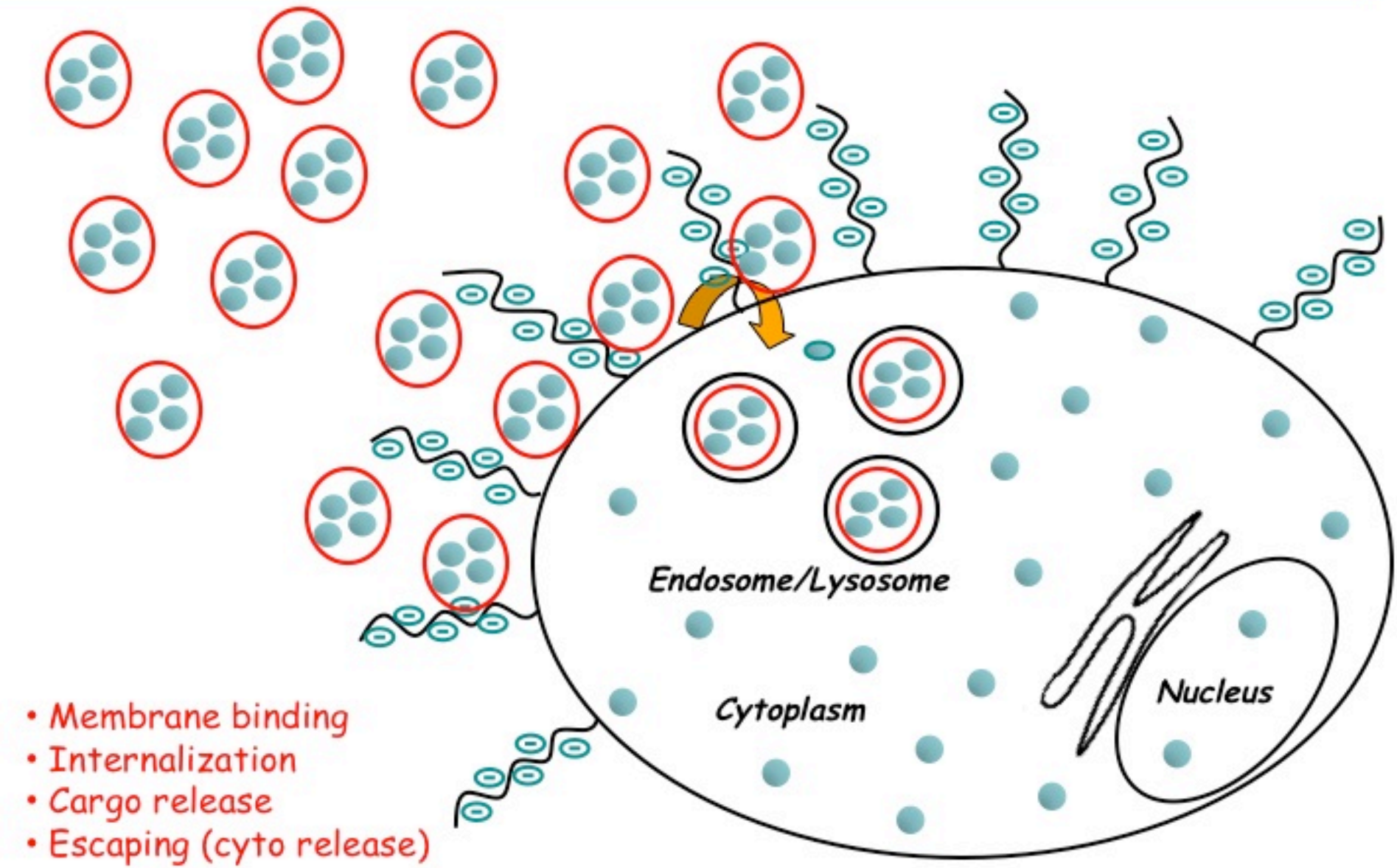
Funded by: NSF

# Developing Drug Carriers

- Our research goal was to develop a small trackable carrier loaded with cargo molecules that will go into cells and then release the cargo (drug, dye, etc.).



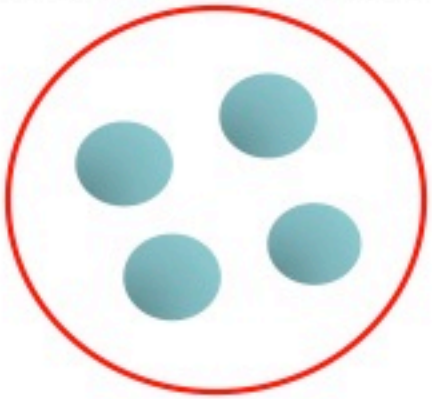
# A (very) simple picture

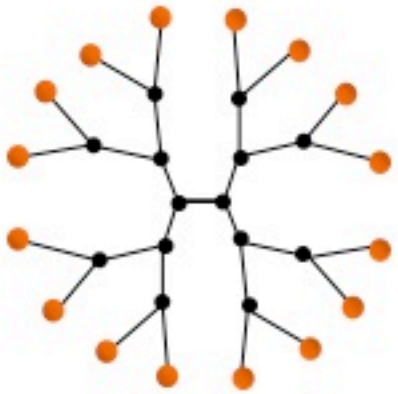



- Membrane binding
- Internalization
- Cargo release
- Escaping (cyto release)

# How did we accomplish our goal?

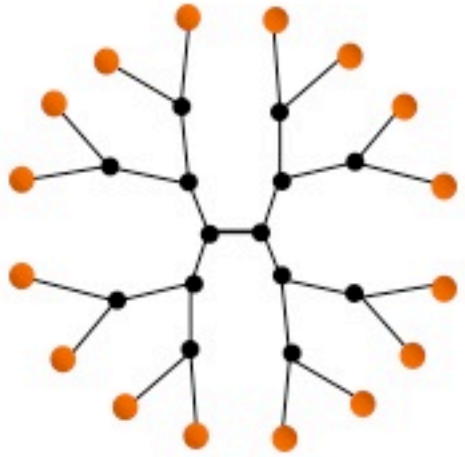
- Building a dendrimer as the carrier for the cargo
- Attach dyes that simulate a drug
- Trackable: monitor where dyes are released and what happens to dye and dendrimer in the cell





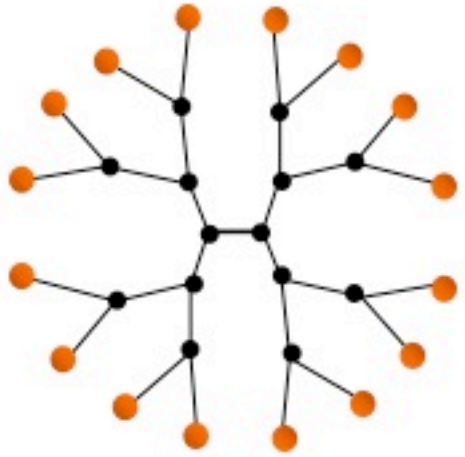
# What is a dendrimer?

- A branched synthetic macromolecule (polymer)
- Its architecture is based on molecular branches that spread out from a central core.
- A dendrimer is 'grown' in layers (or generations).

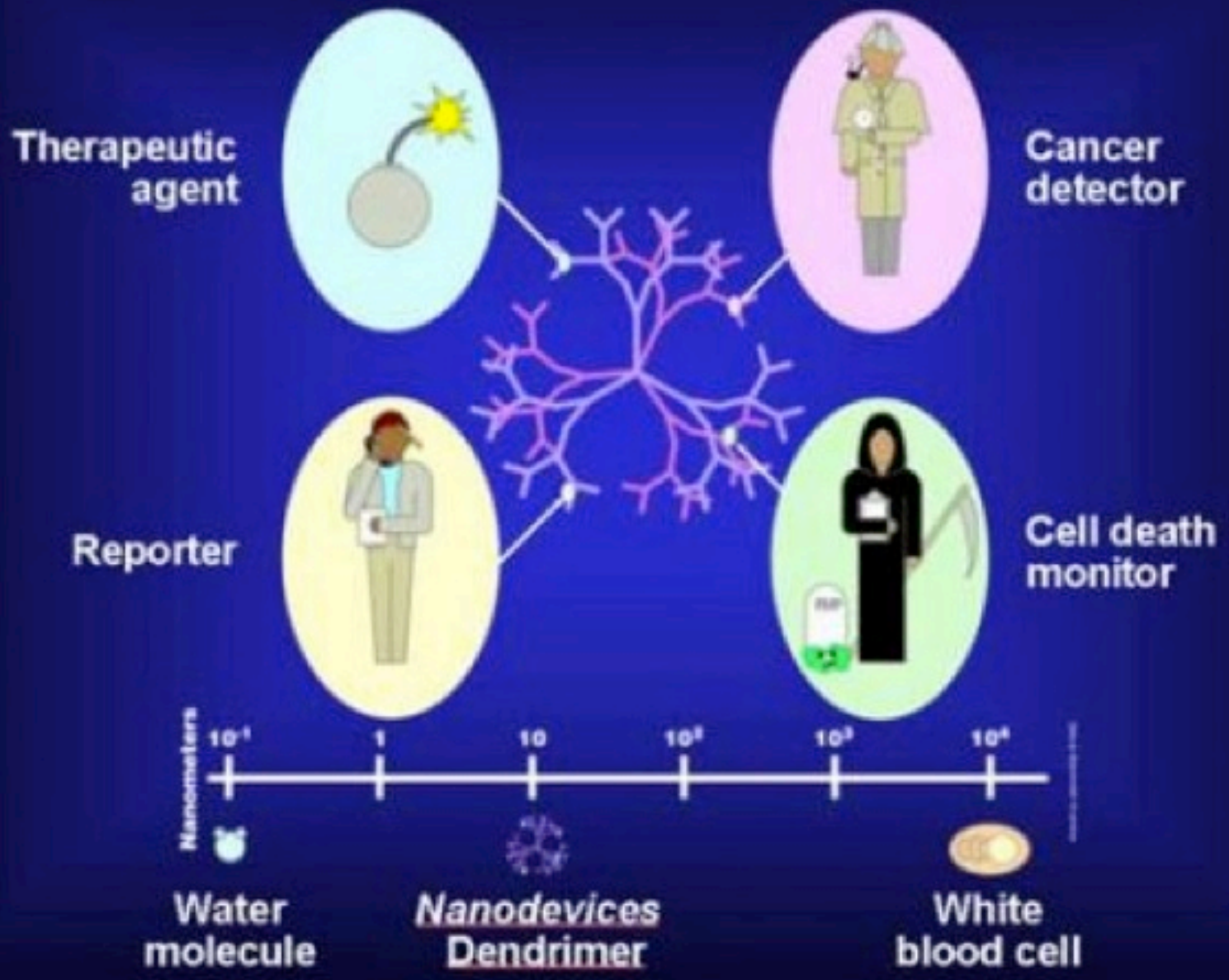


# Benefits of a dendrimer:

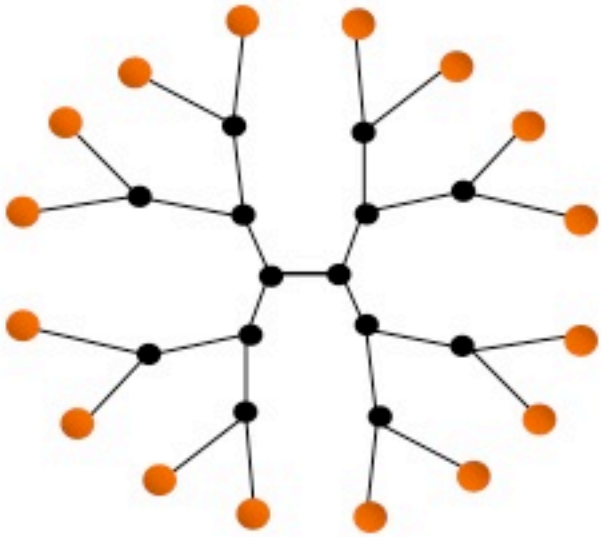
- Can control the surface and internal groups
- Many functional end groups
- Monodisperse (same molecular weight)



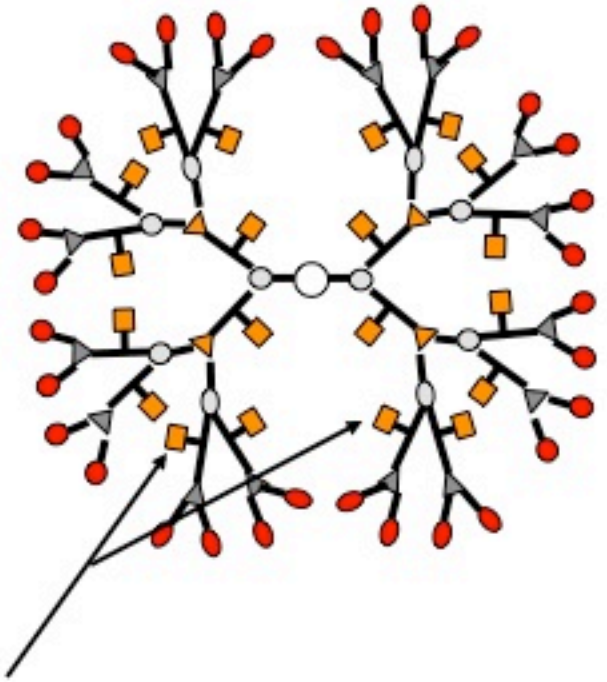
# Dendrimers as Cancer Therapy



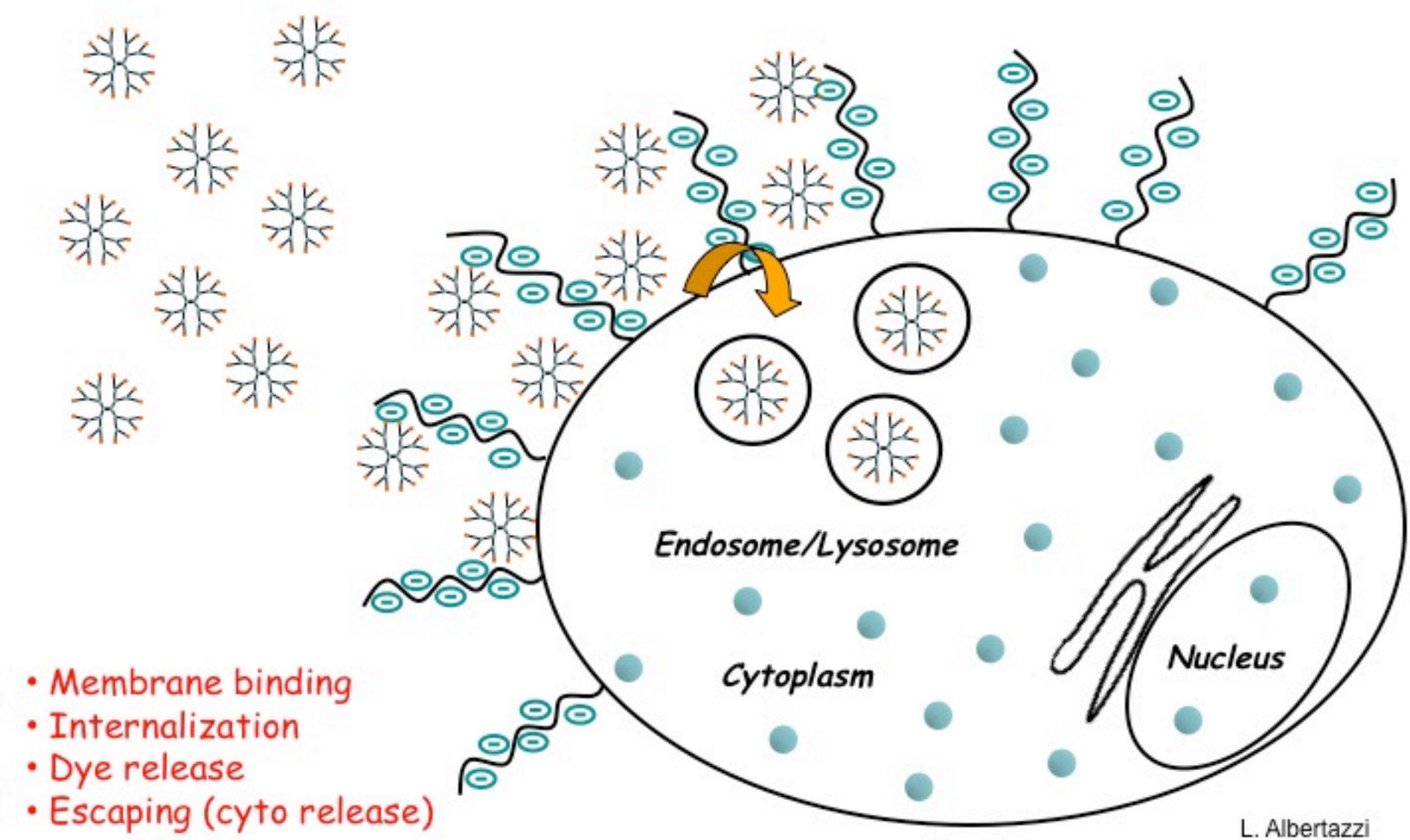
# Conventional design



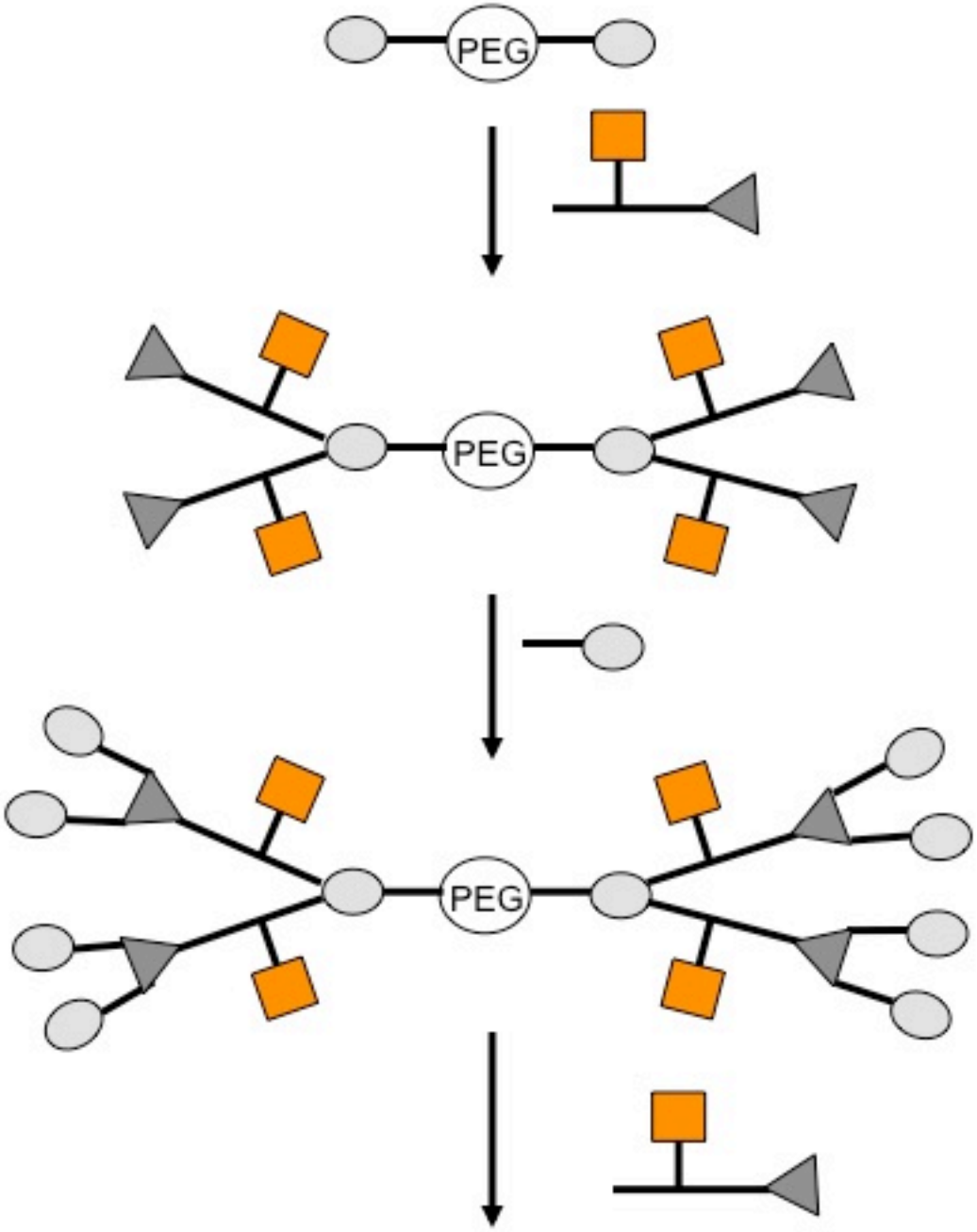
# Our design



Functional group inside




- Membrane binding
- Internalization
- Dye release
- Escaping (cyto release)


PEG
PEG
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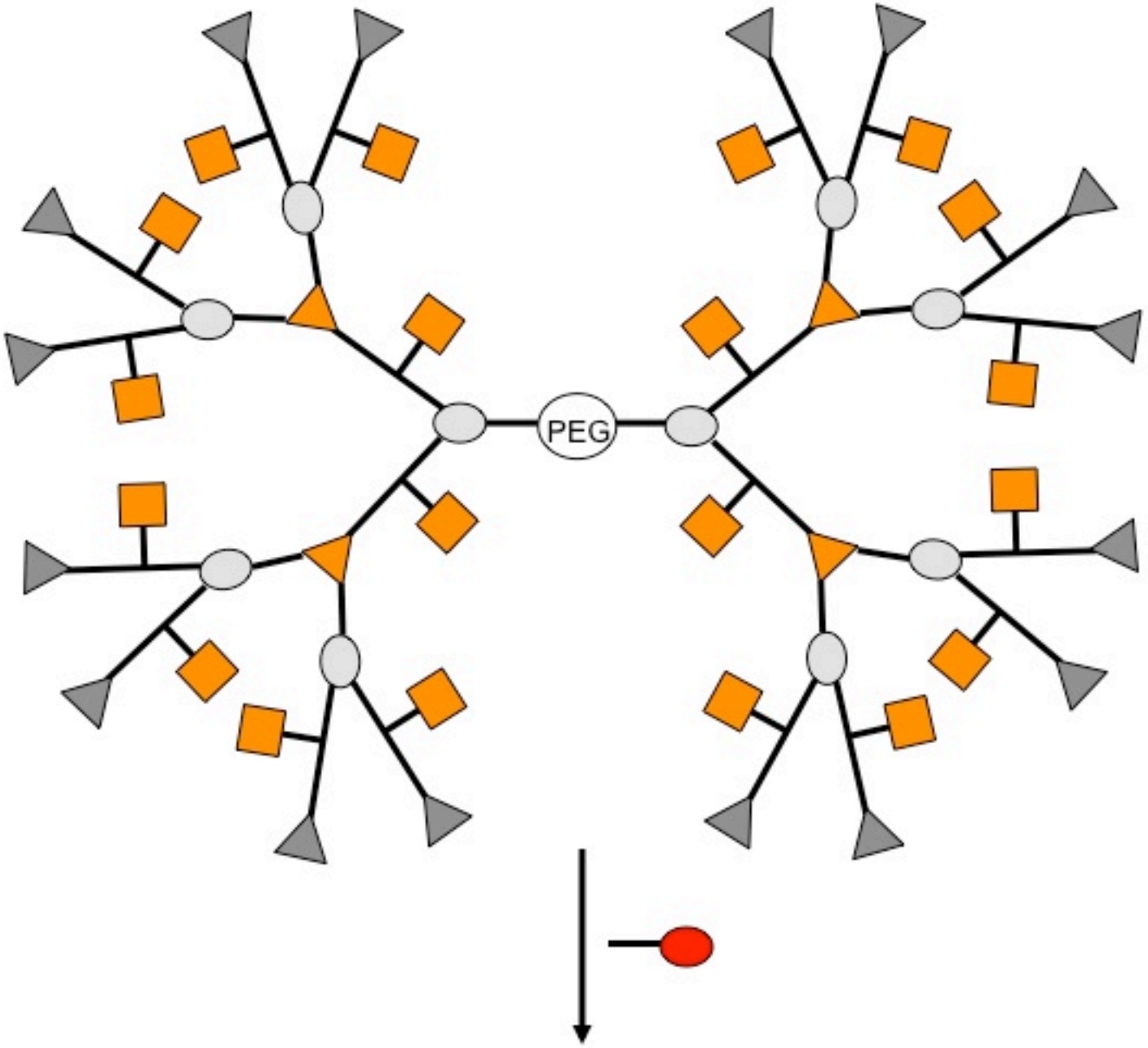
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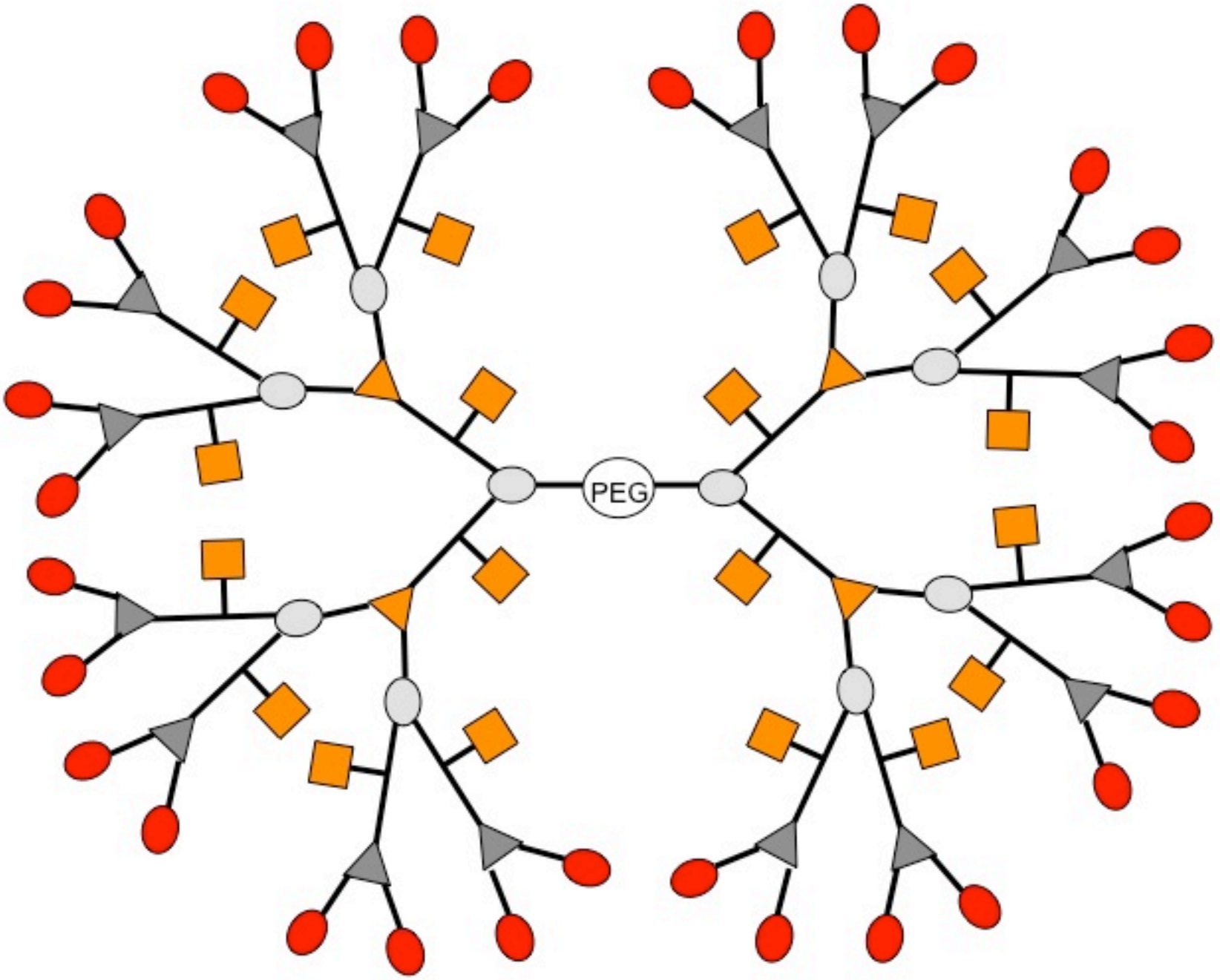
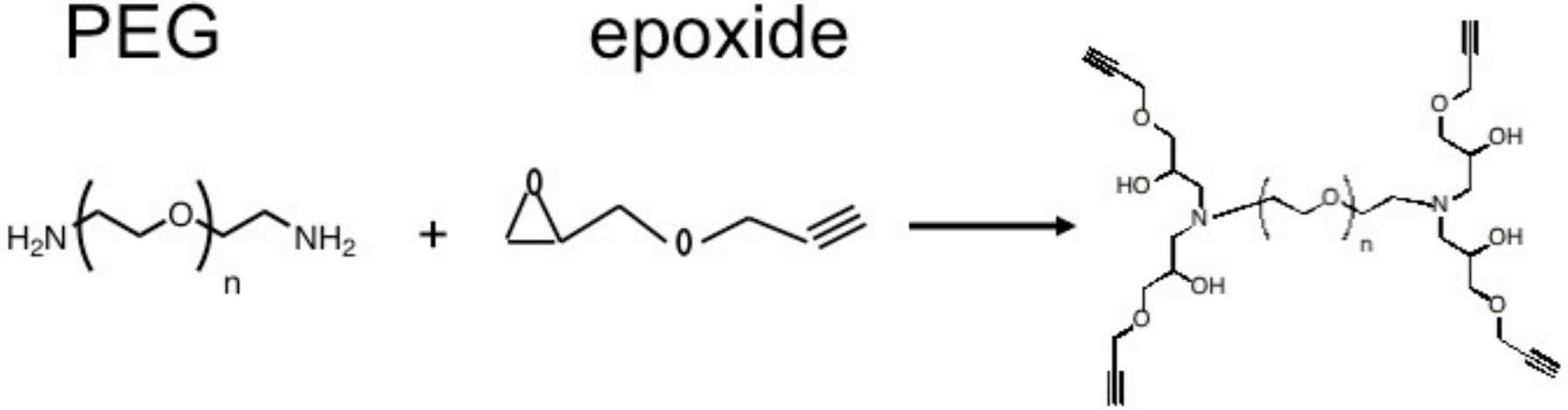

PEG

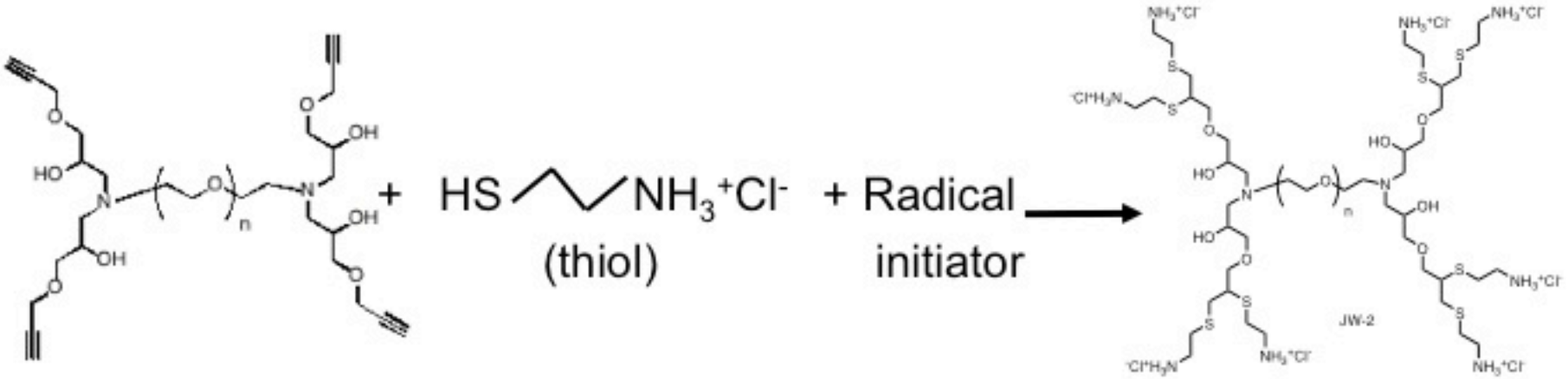
# Synthesis: 1st Generation

PEG epoxide




- Precipitate with ethyl ether to isolate product.
- Filter product to separate solid.
- Vacuum oven for 24hrs to dry product.

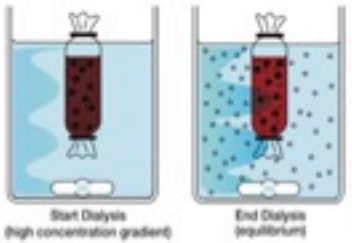
# Synthesis of 2nd Generation:



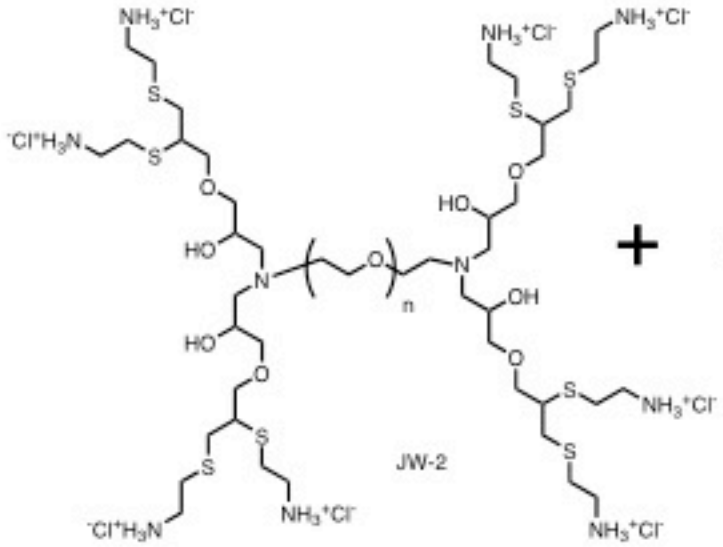

- Sparged with Ar: radical will not react with $O_2$

- Under UV light: 2 thiol radicals (S•) react with triple bond

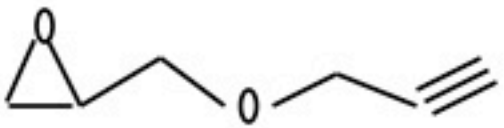
- Filter by dialysis with MeOH to get rid of excess thiol



# Synthesis of 3rd Generation:

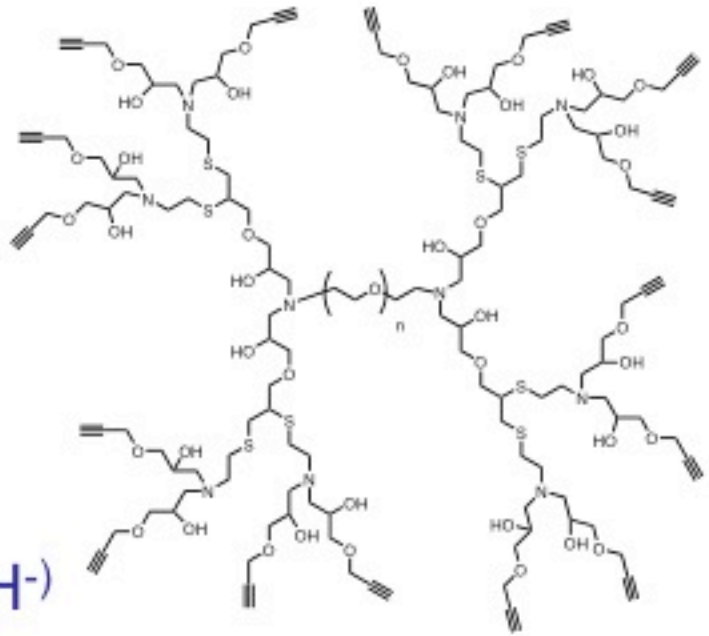



+



Base

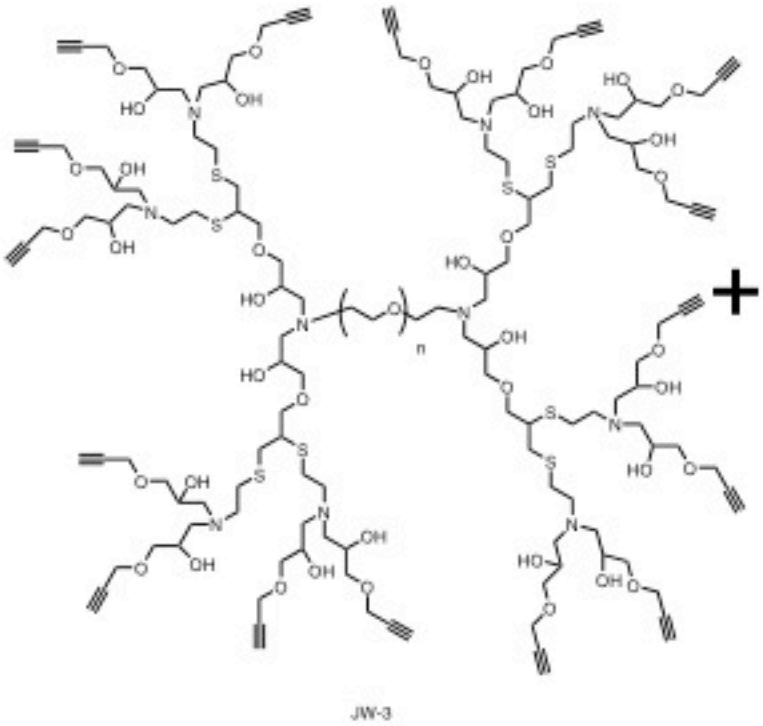
- Precipitate with ethyl ether
- Filter product
- Vacuum oven for 24hrs.



20 ($OH^-$)

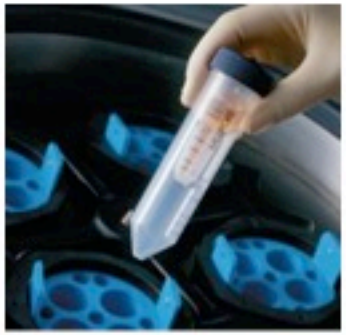
JW-3

# Synthesis of 4th Generation:

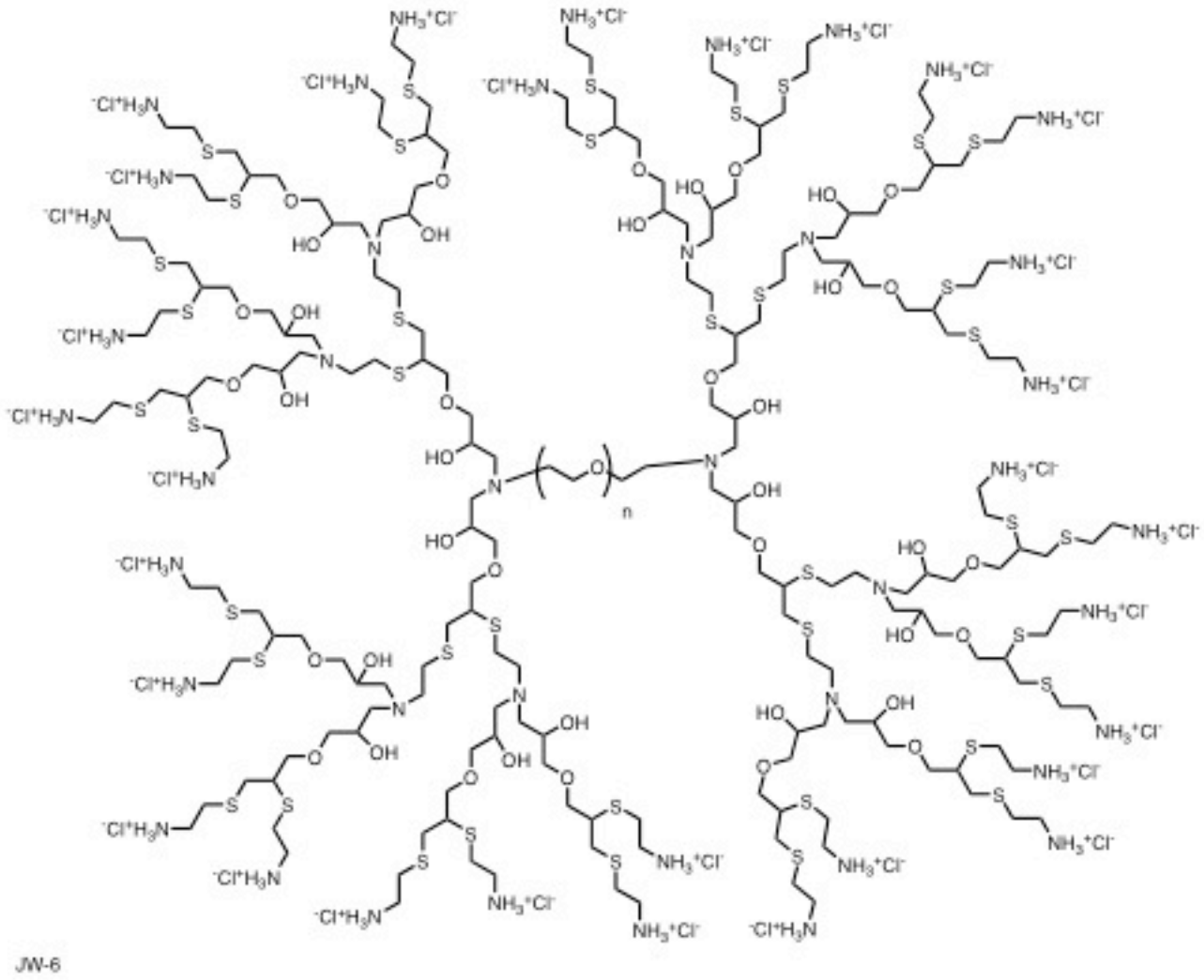



+ HS⁄⁄$NH_3^+Cl^-$ + Radical initiator ⟶

- Sparged with Ar
- Under UV light
- Filter by Dialysis with $H_2O$ in centrifuge tube (cut-off 3000) to remove excess



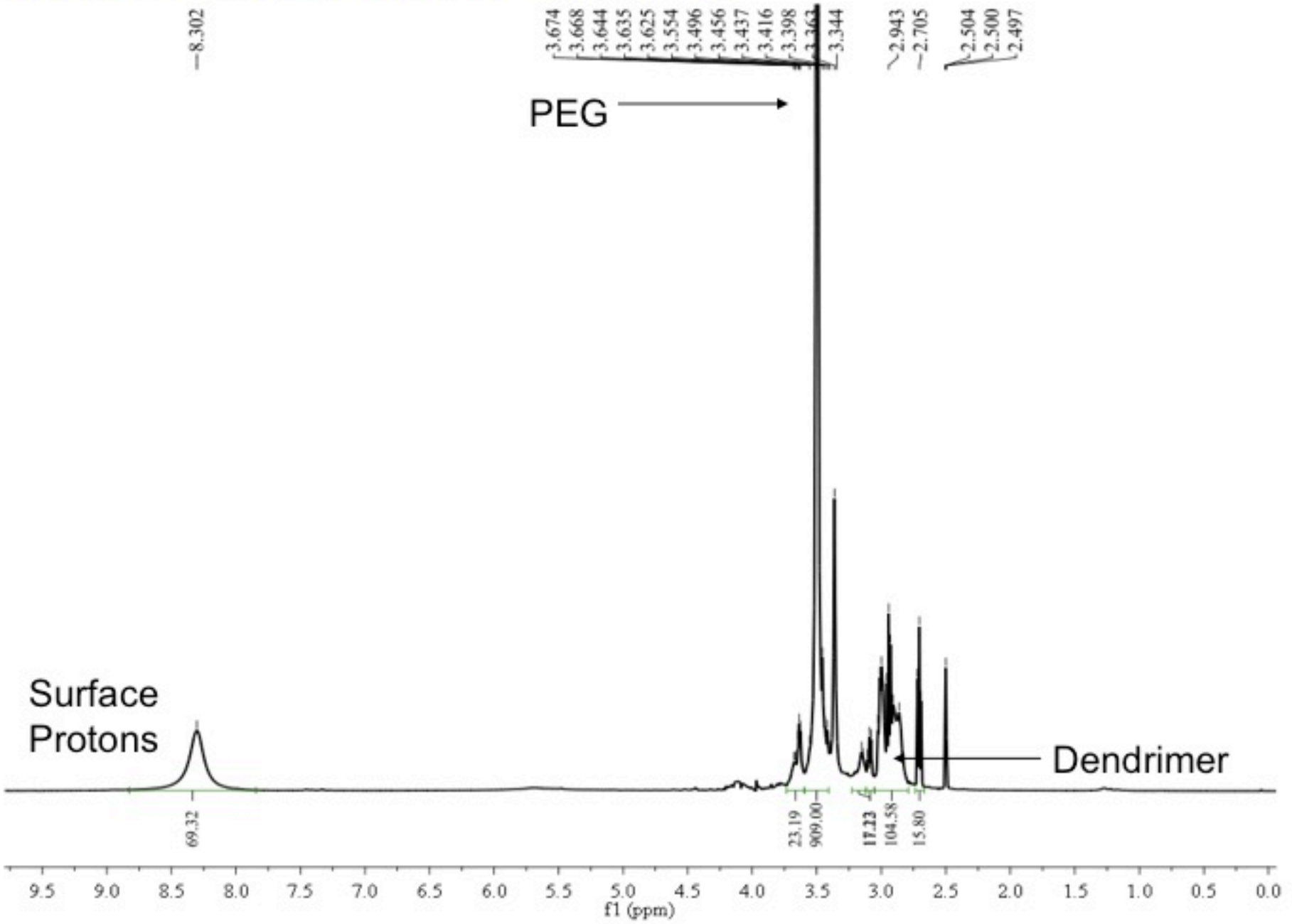
# Dendridic platform without the dye



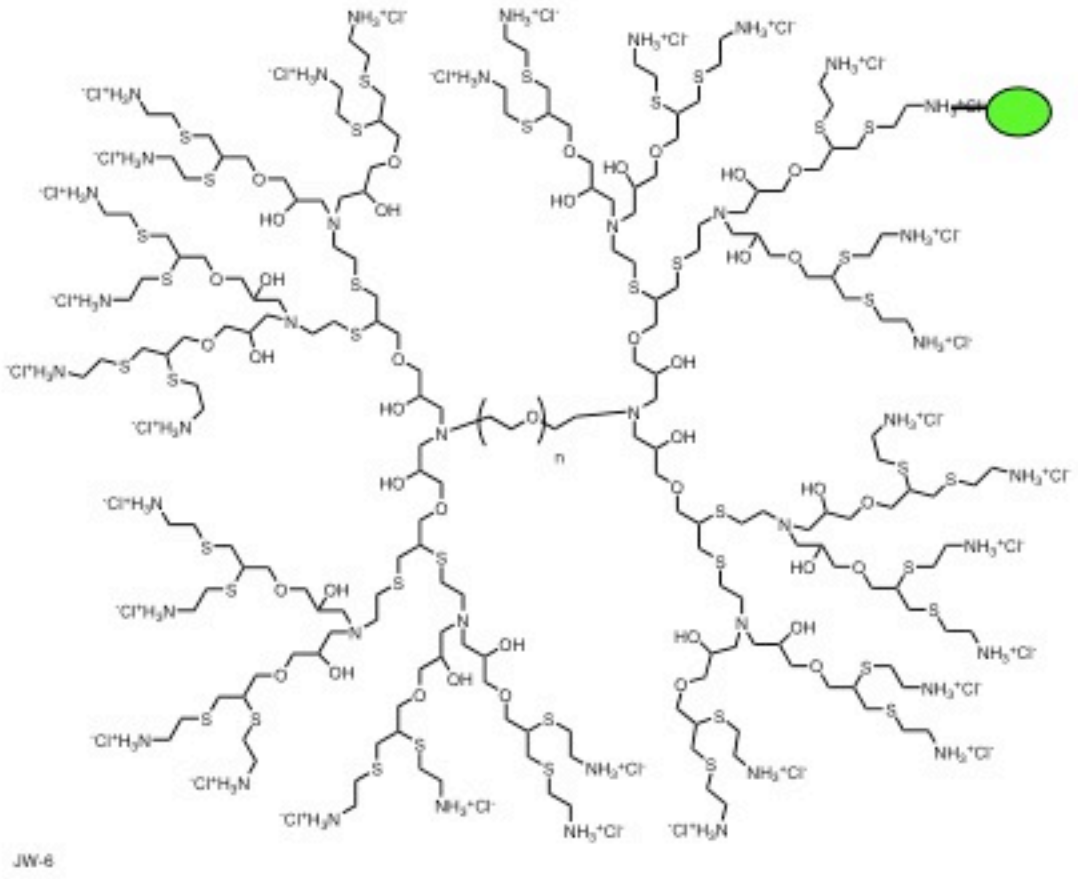

32 ($NH_3^+Cl^-$)

20 ($OH^-$)

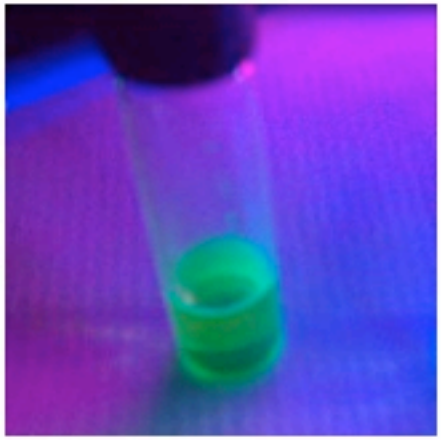
# Nuclear Magnetic Resonance (NMR)

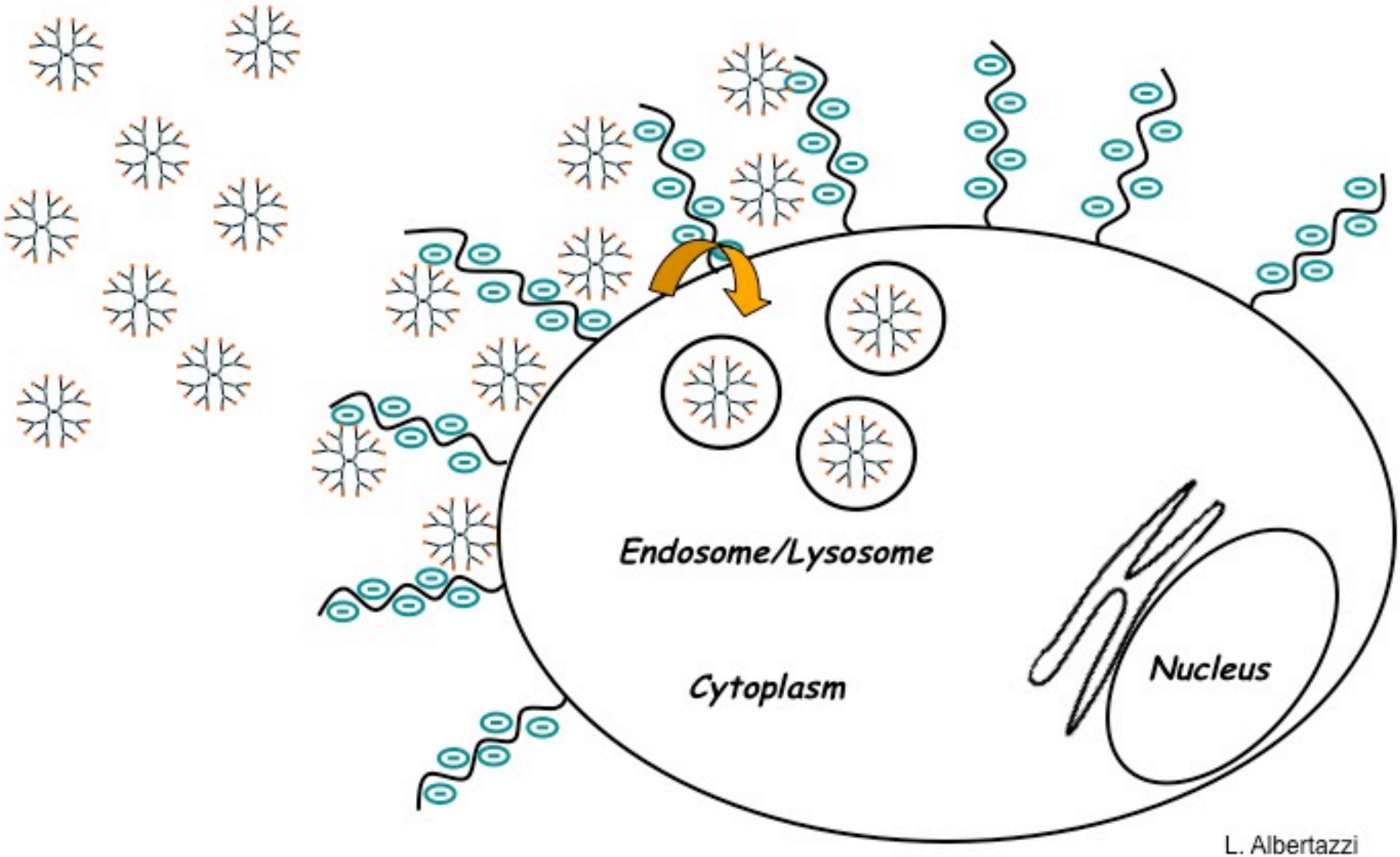


# Adding dye to periphery: checking surface groups

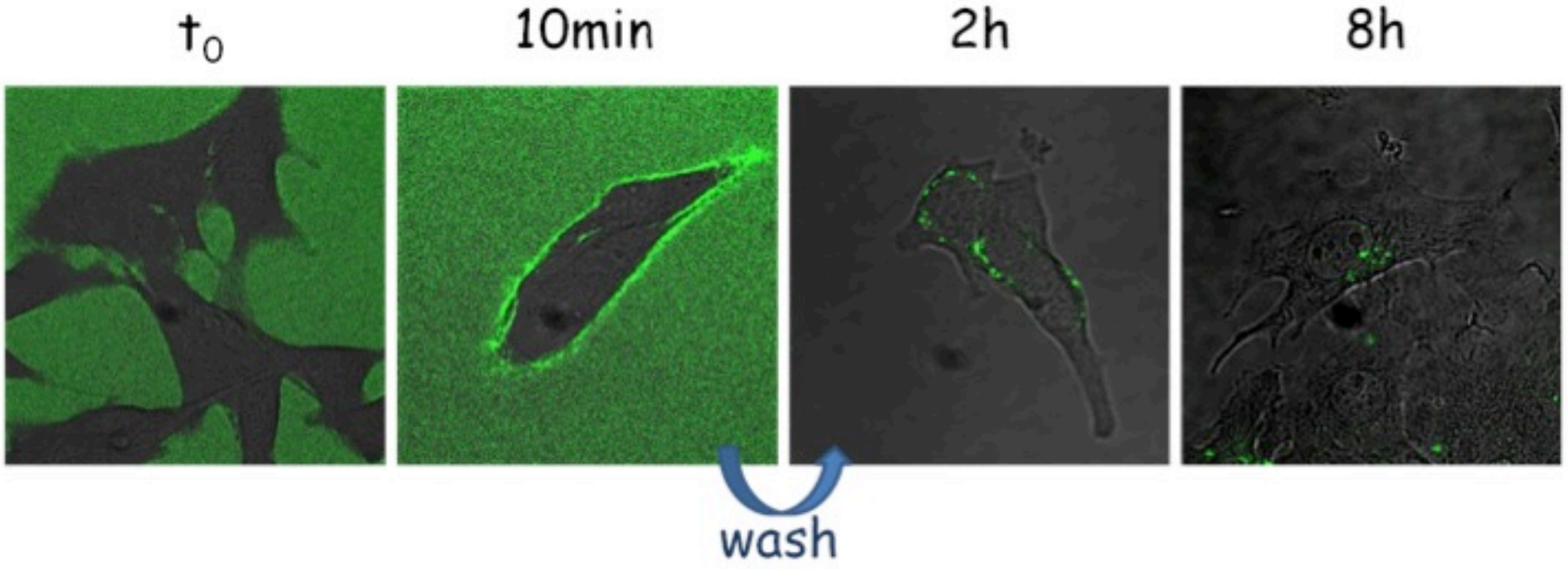



Flouroscene (FITC)

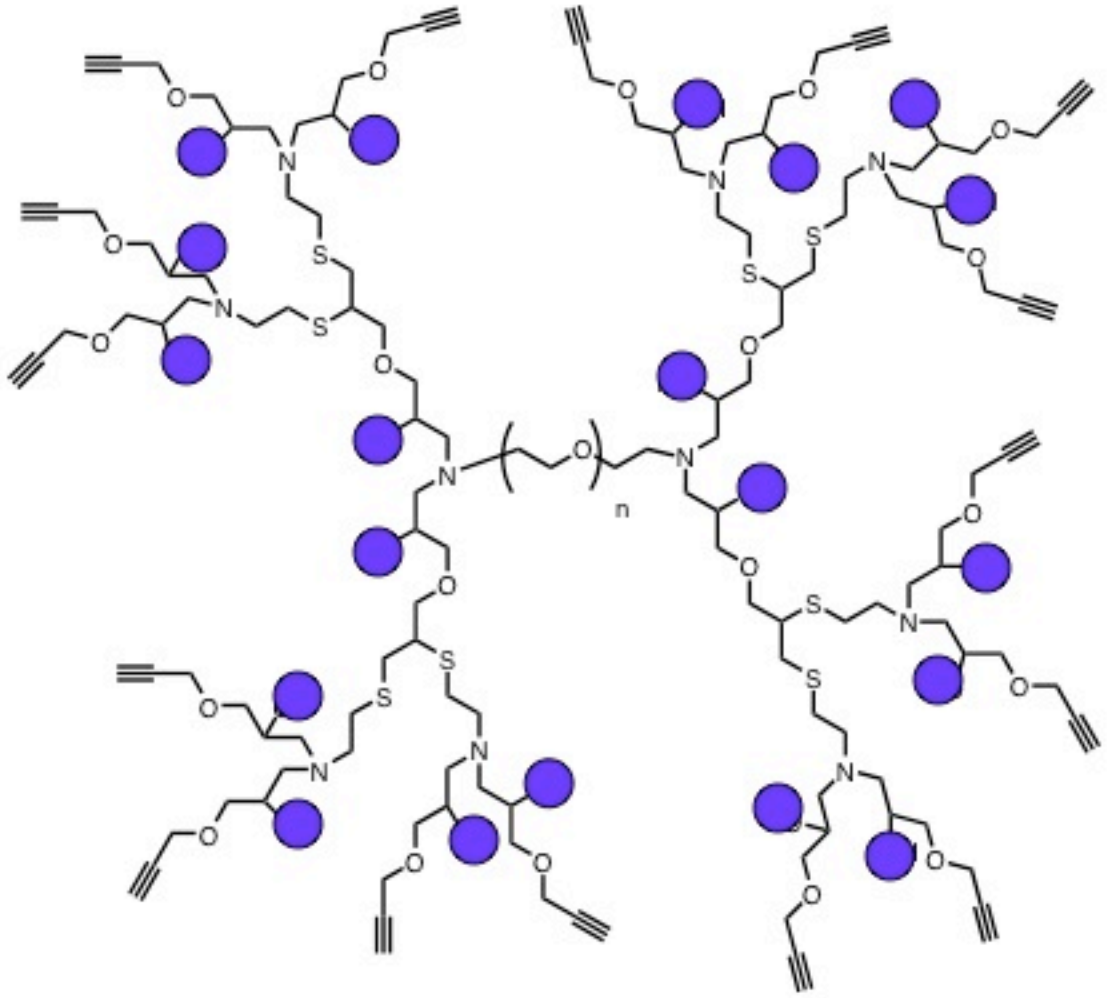



Endosome/Lysosome
Cytoplasm
Nucleus
L. Albertazzi

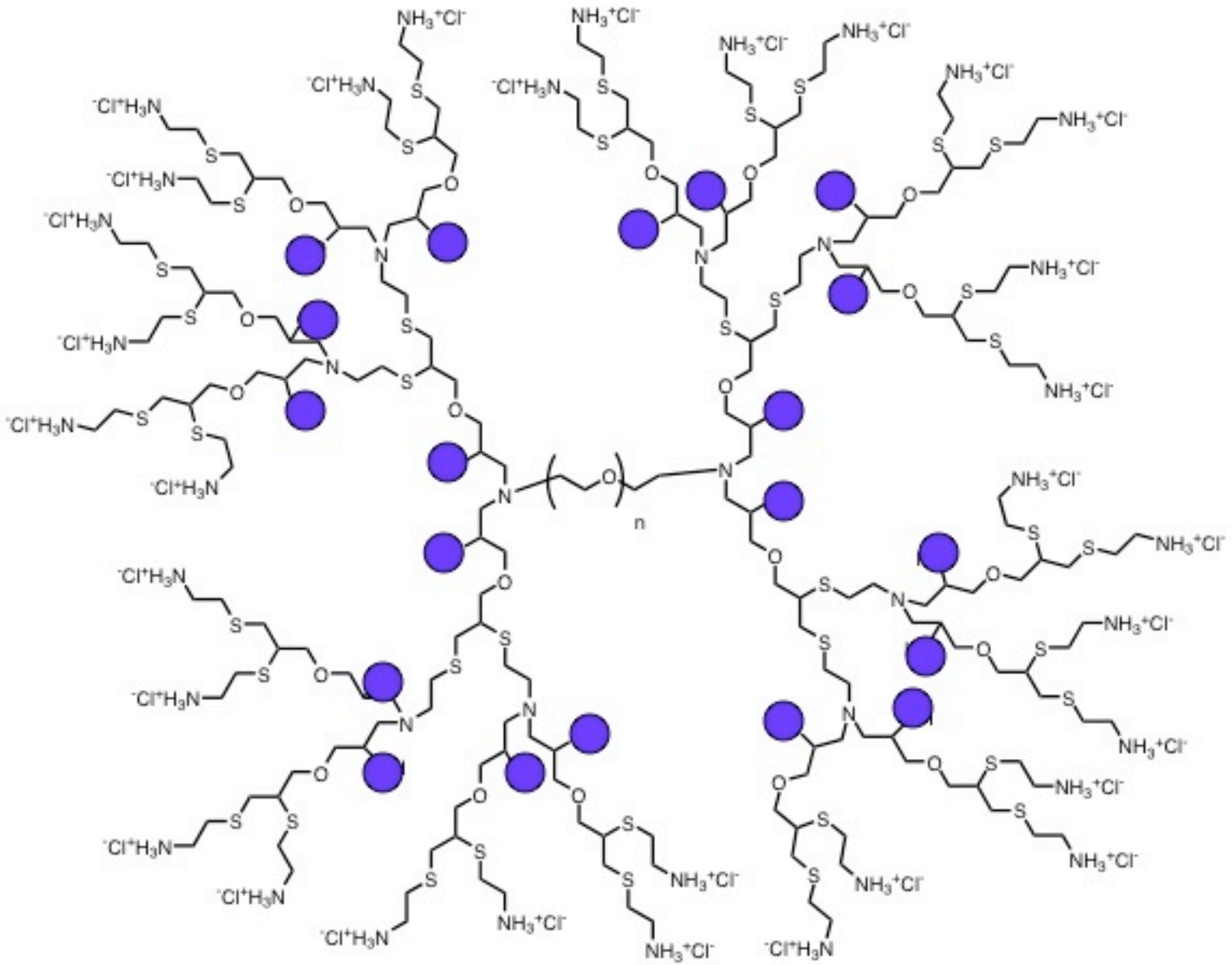
# Internalization of the dye on periphery. (fluorescence)



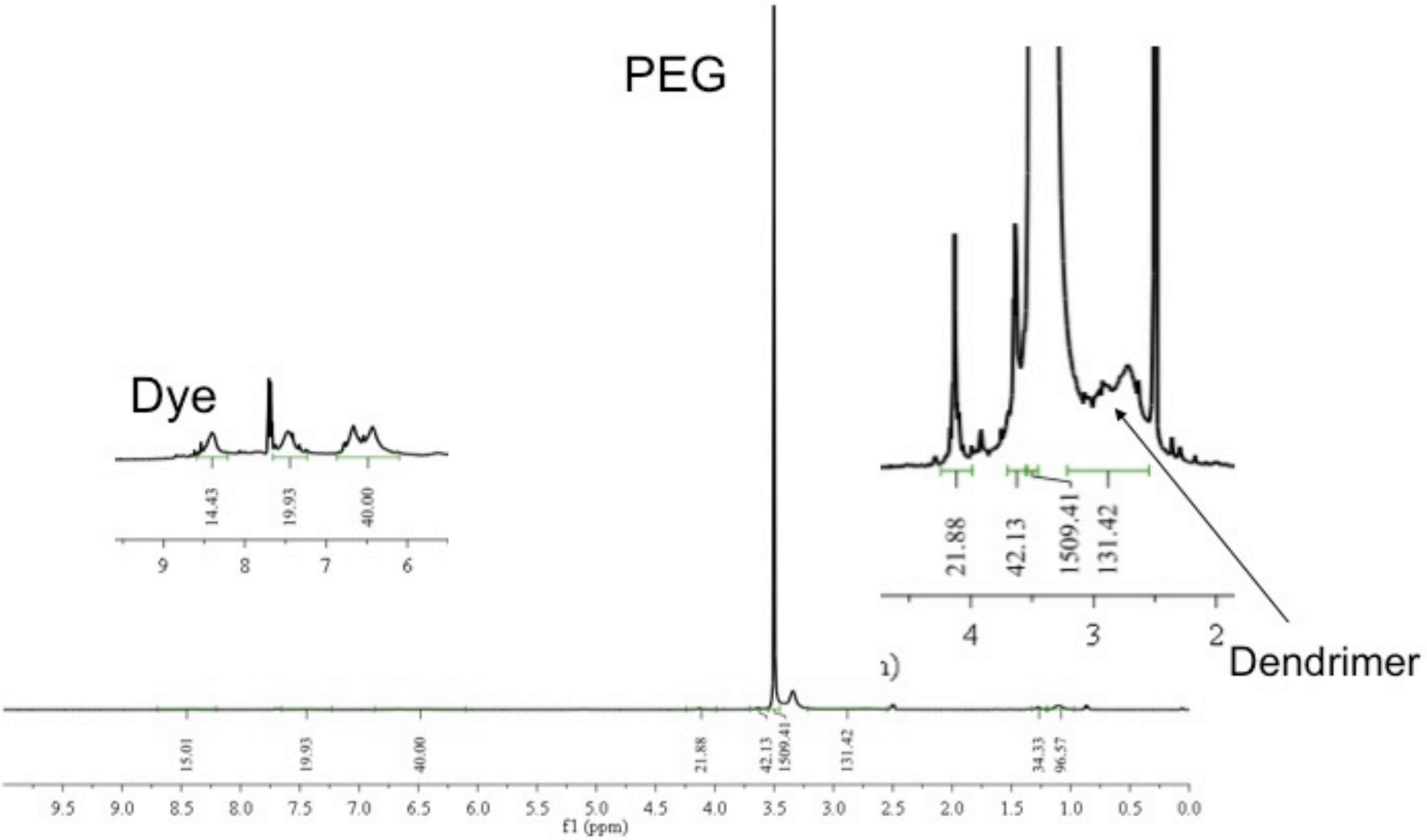
# Attaching the dye (coumarine):



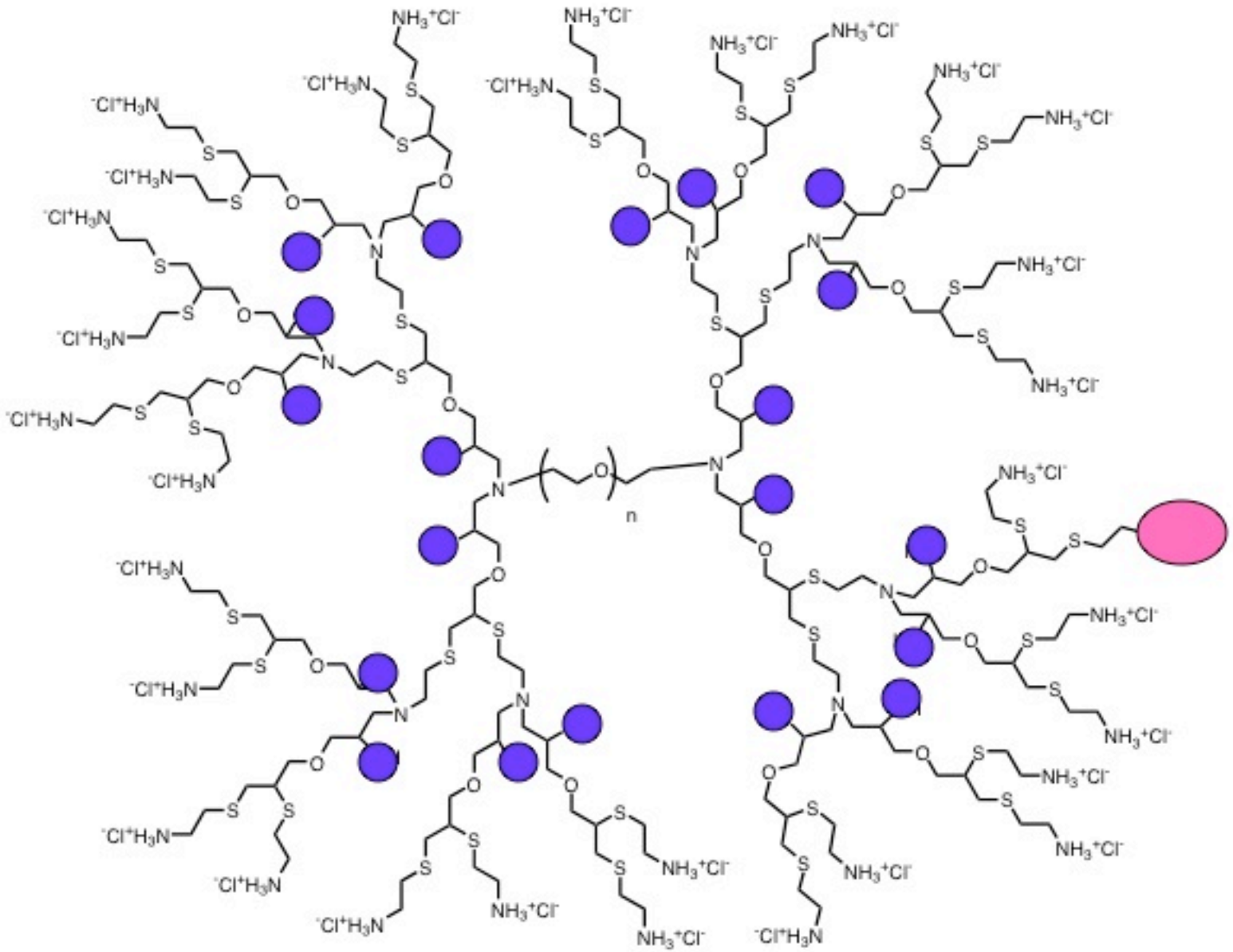
# Adding surface groups:



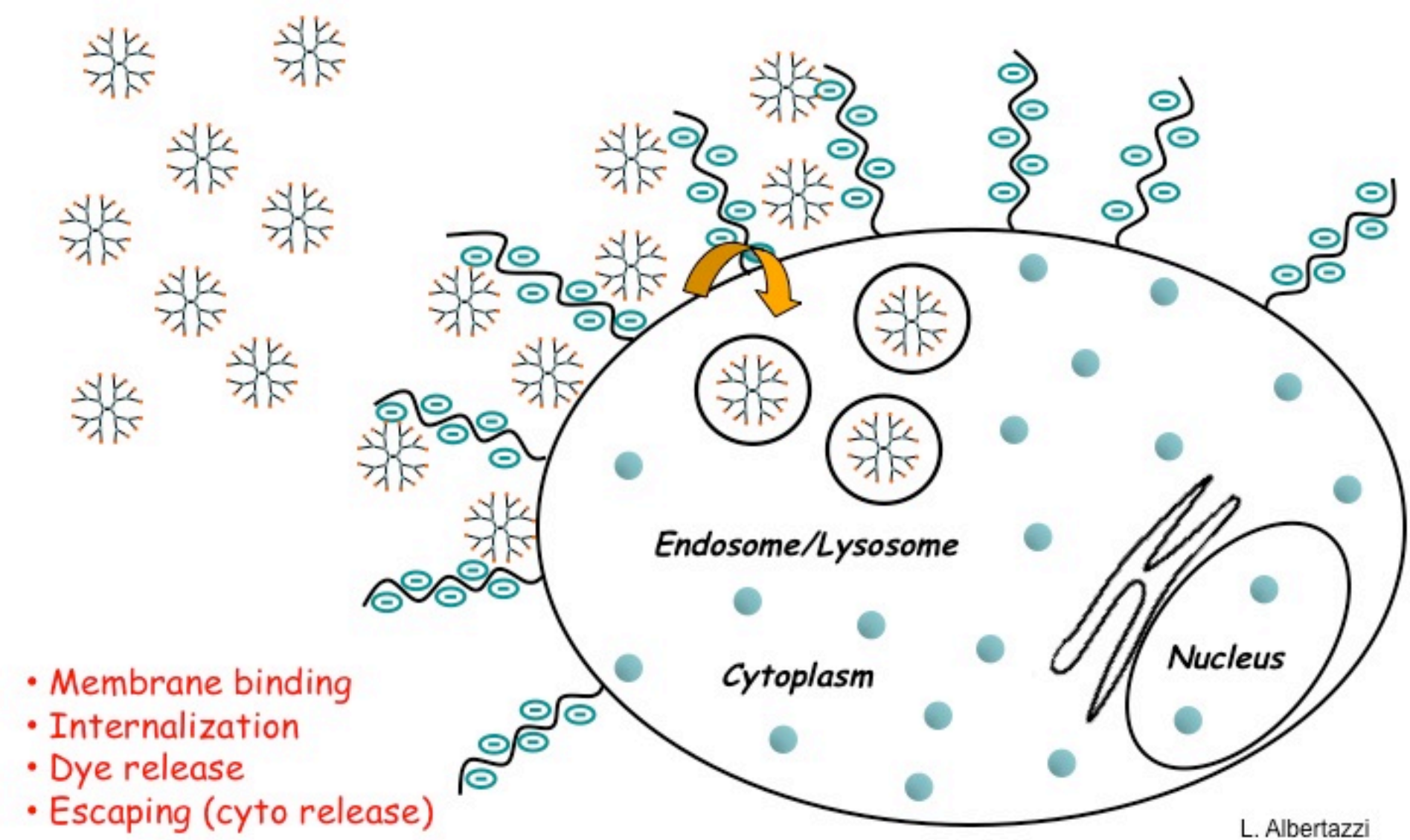
# Nuclear Magnetic Resonance (NMR)



# Attaching Alexa647 (infrared dye):

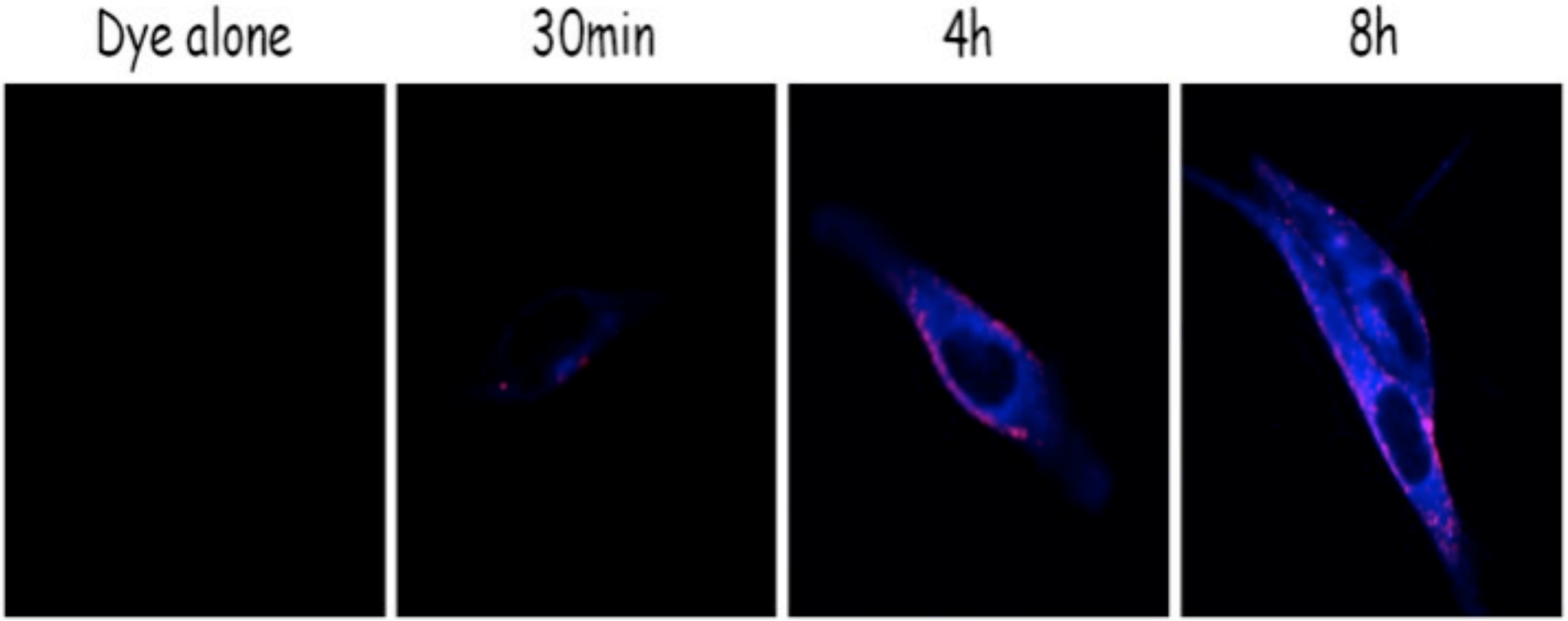



JW-6




- Membrane binding
- Internalization
- Dye release
- Escaping (cyto release)

# Results: Internalization of both dyes attached to dendrimer.



# Conclusion:

- We were able to successfully internalize the dendrimer with the dyes inside melanoma cells.
- Possible future applications: **Drug carriers**