FROM RESEARCH TO INDUSTRY

nanoSAFE 18

TOWARDS LESS TOXIC QUANTUM DOTS

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INTRODUCTION

Quantum dots (QDs):

- Colloidal fluorescent semi-conductor nanocrystals
- Unique optical properties
- To enhance the purity and accuracy of color reproduction

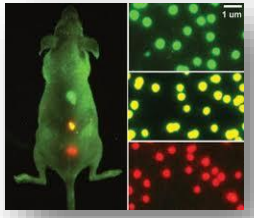
Applications:

Optoelectronics

Display screens

Photovoltaic cells

Biomedical imaging



Fluorescent markers

QDs market:

- CdSe (Cd classified carcinogenic by IARC and banned)
- Alternatives to reduce toxicity

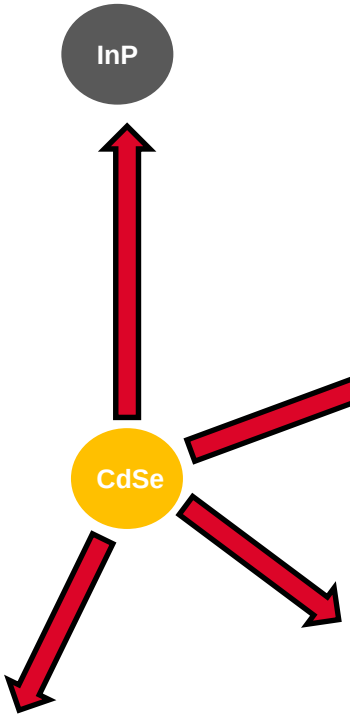
➡ **Indium based QDs**

➡ **Toxic effects of such alternative QDs are poorly documented**

STRATEGY FOR SAFER-BY-DESIGN QDS

To replace CdSe by InP

- ❑ To reduce the toxicity
- ❑ To improve the stability



Doping of the core (InPZn, InPZnS)

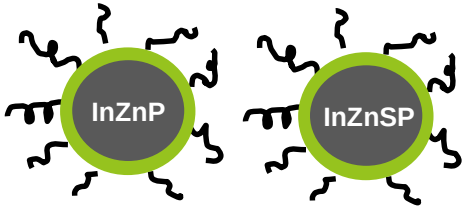
- ❑ To reduce In content
- ❑ To improve optical properties

Adding of a shell ZnSe-ZnS

- ❑ To limit the release of toxic metal ions from the core
- ❑ To increase the QDs stability
- ❑ To improve optical properties

Functionalization with a ligand

- ❑ To limit interaction with cell surface
- ❑ To allow the phase transfer



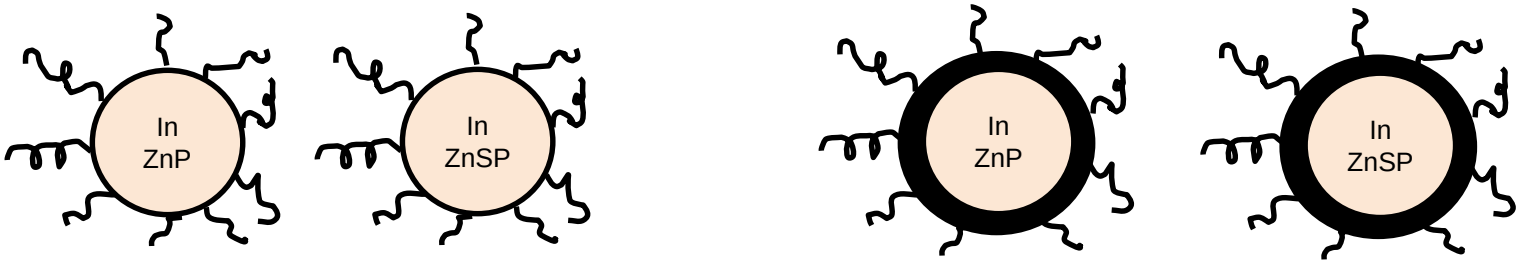
Penicillamine
Glutathione
PEG-ligand
Etc.

PREVIOUS RESULTS

Dissolution **Stability**

Low High

InZnP < InZnSP < InZnP@ZnSeZnS = InZnSP@ZnSeZnS



Toxicity **Safety**

Penicillamine
= GSH

STRATEGY FOR SAFER-BY-DESIGN QDS

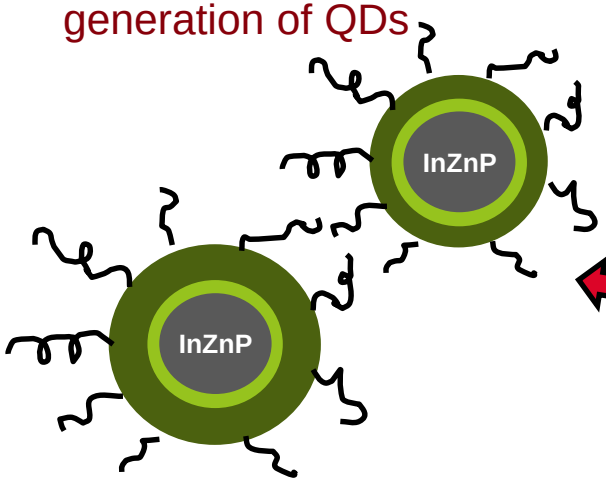
Replace CdSe by InP

- ❑ To reduce the toxicity
- ❑ To improve the stability

InP

Adding of a second shell ZnS (thin or thick)

- ❑ To improve the previous generation of QDs



Doping of the core (InPZn, InPZnS)

- ❑ To reduce In content
- ❑ To improve optical properties

InZnP InZnSP

CdSe

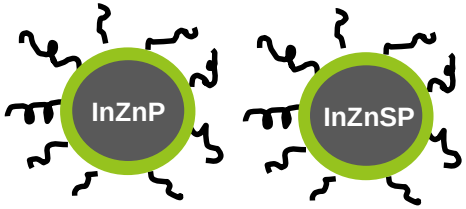
Adding of a shell ZnSe-ZnS

- ❑ To limit the release of toxic metal ions from the core
- ❑ To increase the QDs stability
- ❑ To improve optical properties

InZnP InZnSP

Functionalization with a ligand

- ❑ To limit interaction with cell surface
- ❑ To allow the phase transfer

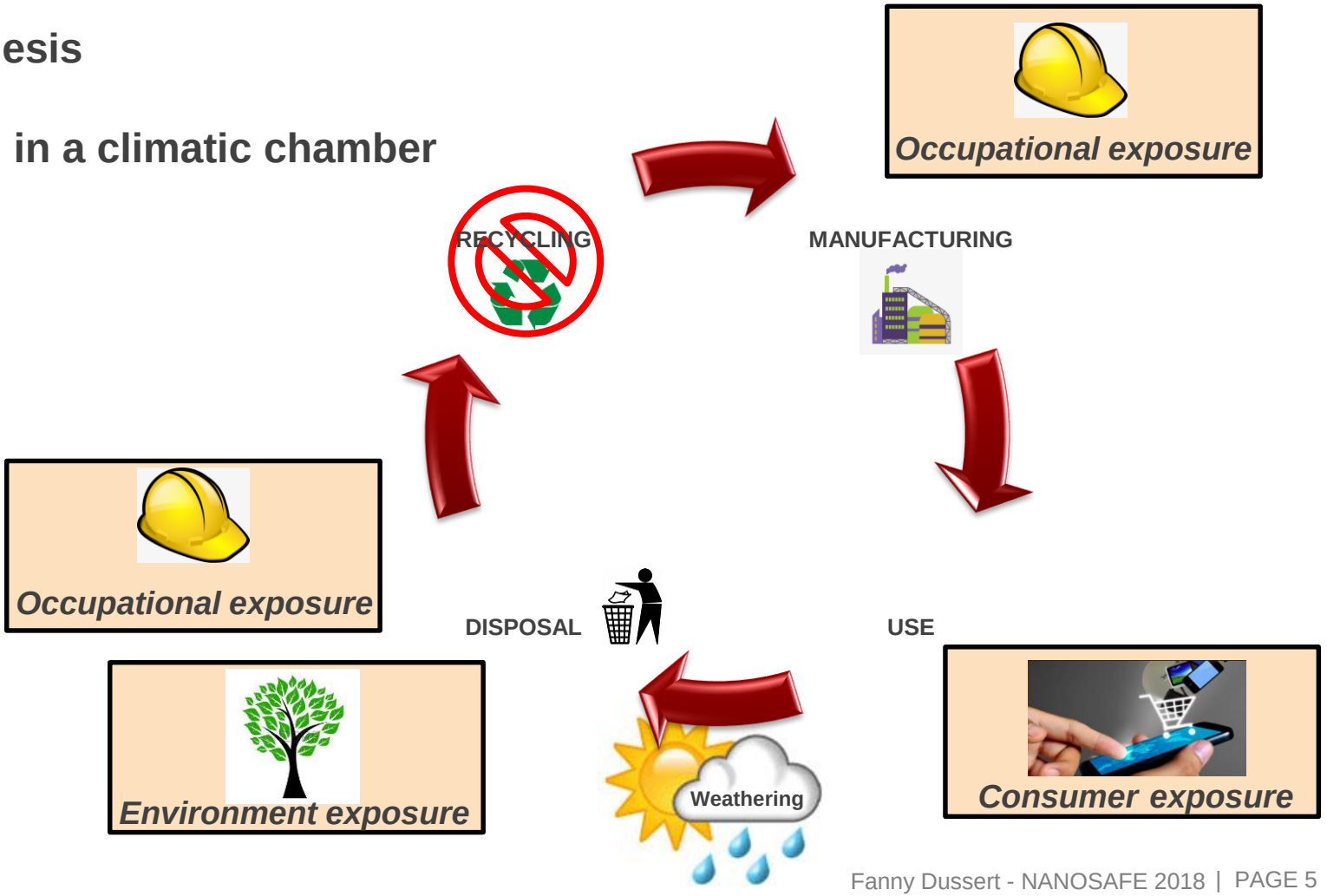


Penicillamine
Glutathione
PEG-ligand
Etc.

OBJECTIVES

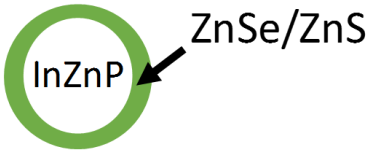
To evaluate the toxic effects and fate of these new generations of QDs throughout their life cycle:

- ❑ **After synthesis**
- ❑ **After aging in a climatic chamber**

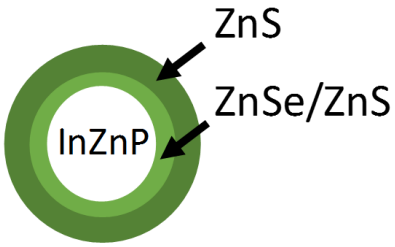


QDs DESIGN

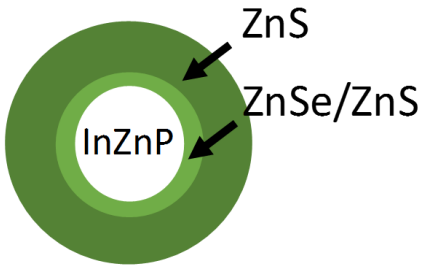
Synthesis:



Core/shell
Gradient shell*



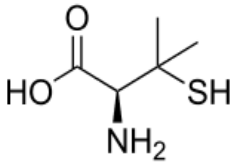
Core/shell/shell
Thin shell



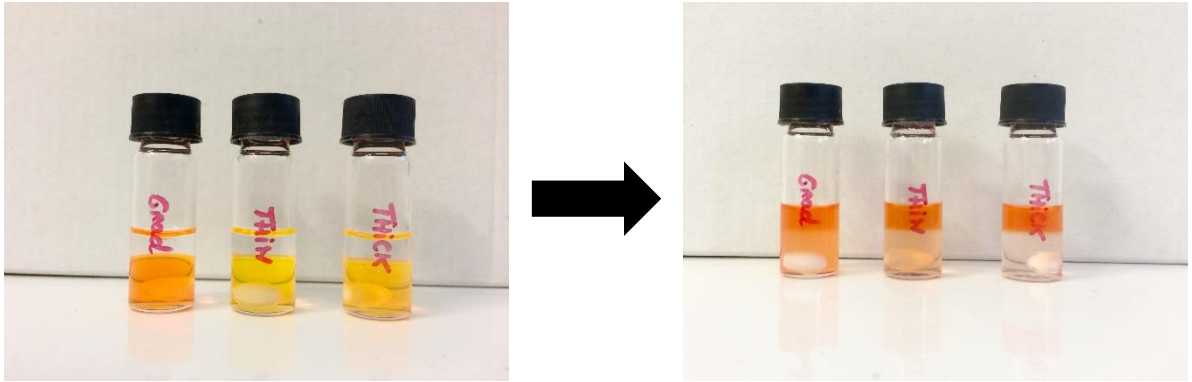
Core/shell/shell
Thick shell

**Shell of zinc (Zn) and selenium (Se) which are gradually substituted during synthesis with Zn and sulfur (S)*

Ligand exchange:

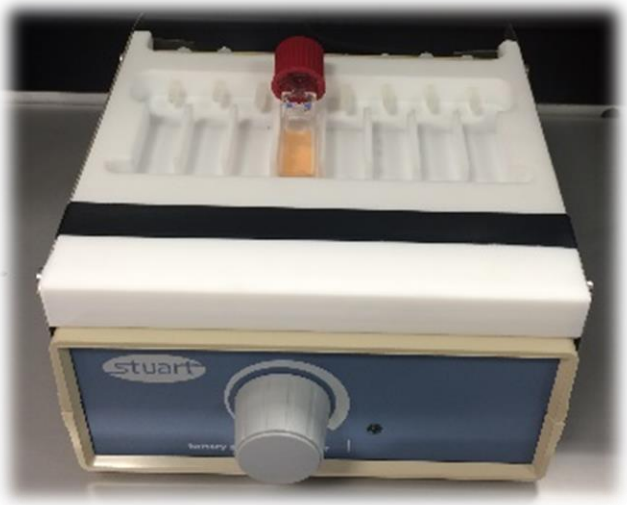


Penicillamine

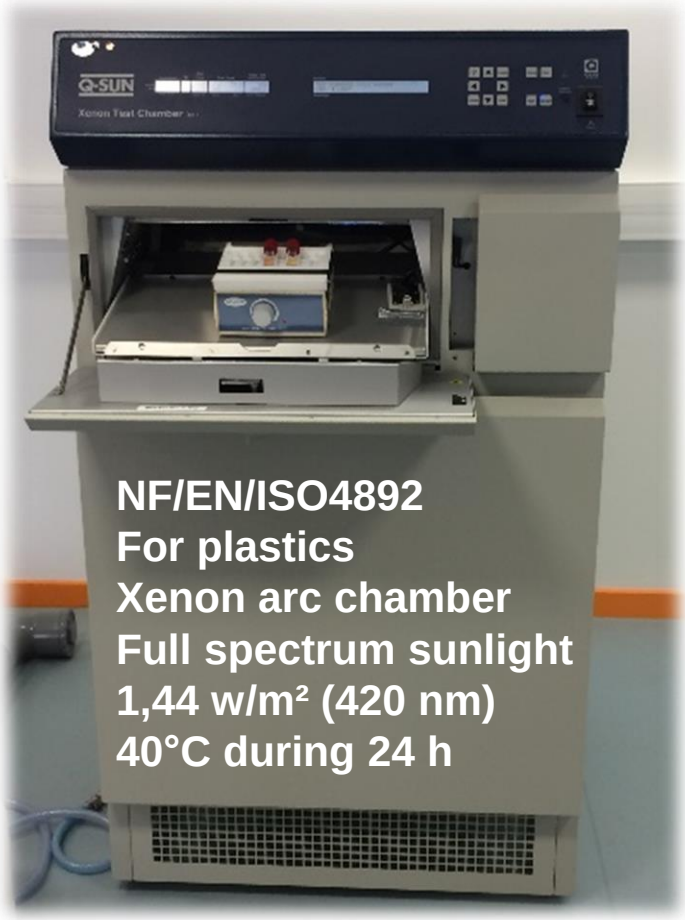


CLIMATIC CHAMBER

Aging of QDs solutions:



QDs 1µM (PBS) + CTL PBS

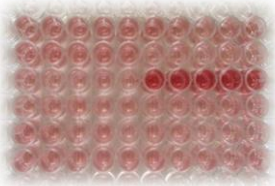


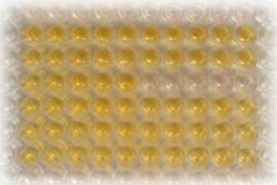
Model: QSUN Xe-1 BC with xenon arc lamp (Plateforme HYBRIDEN)

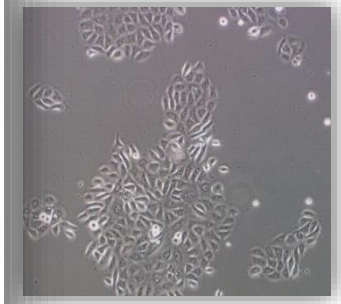
➡ PL and UV-vis measurements

CELL EXPOSURES

Primary keratinocytes extraction from skin explants:

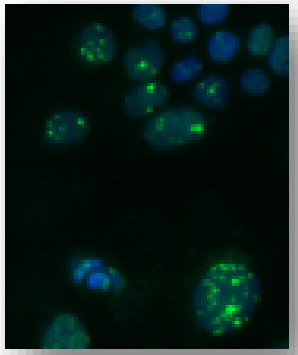


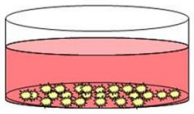




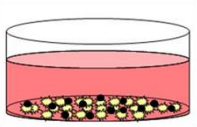
Pristine QDs

Aged QDs





24h



24h

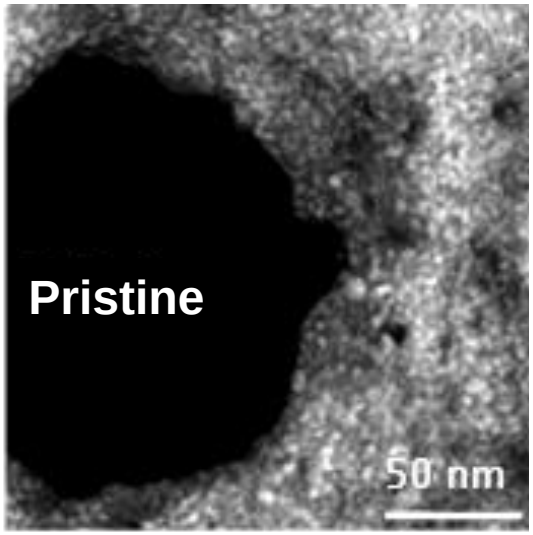
Cell seeding (human primary keratinocytes)

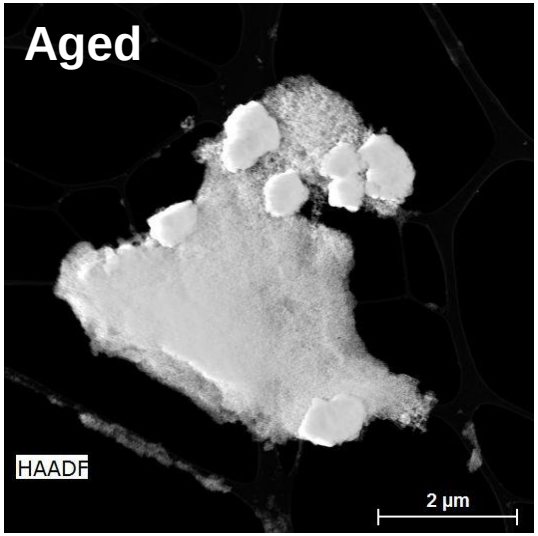
QDs Exposure

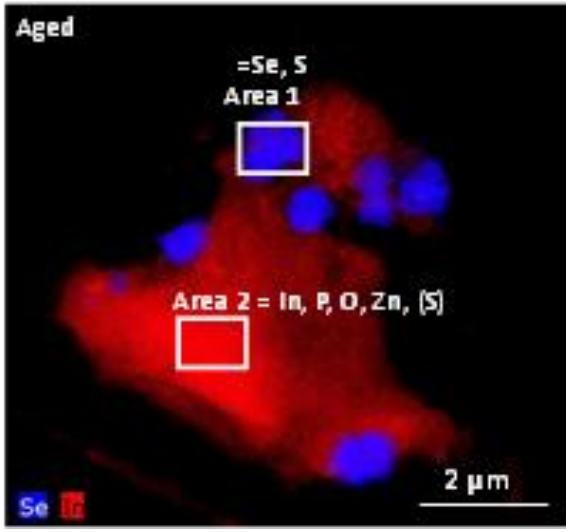
Assays or collecting

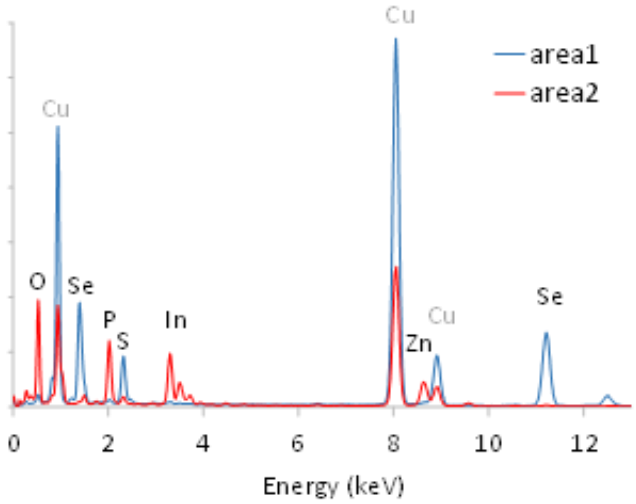
➡ **The most relevant target is the skin**

STEM-EDX ANALYSIS OF QDS





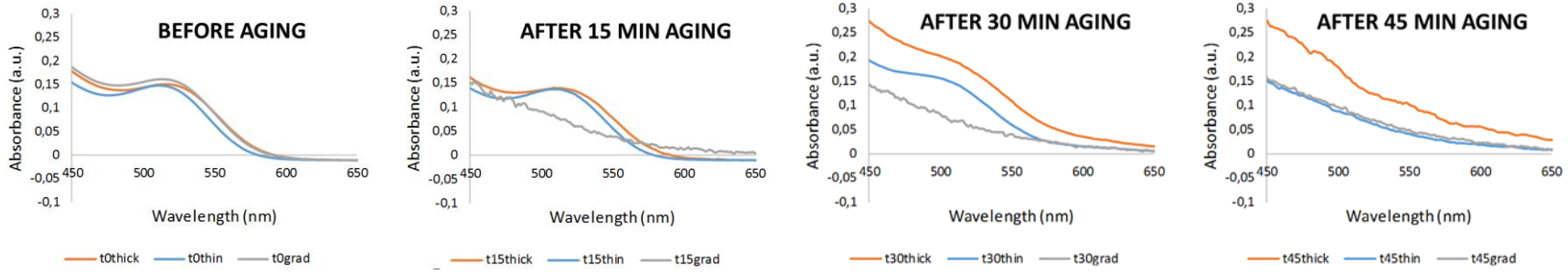




➡ **area1 = Se, S**
➡ **area2 = In, P, O, Zn**

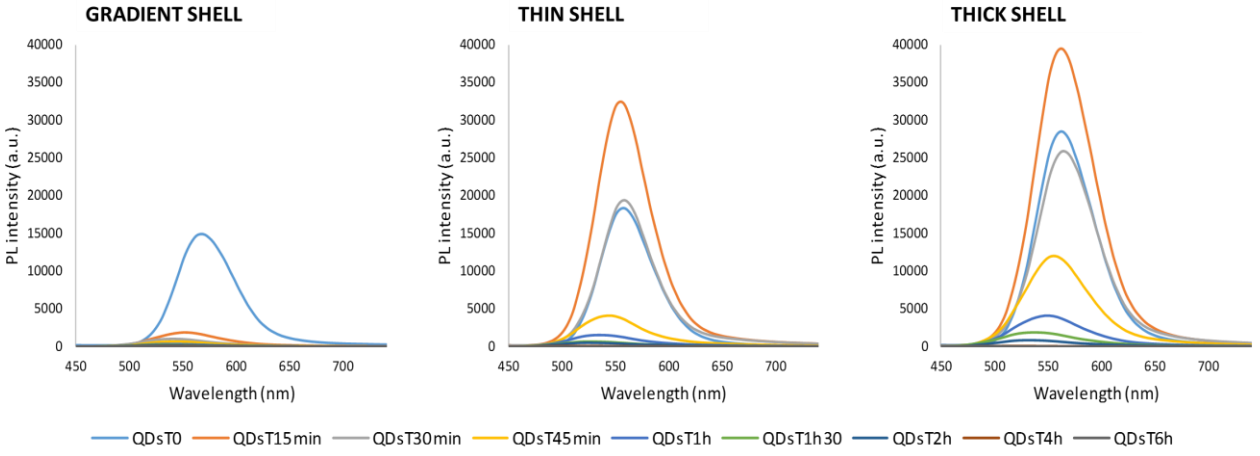
CHARACTERIZATION OF QDS

UV-visible measurement:



➡ **The sunlight induces the quick aging of QDs**

Photoluminescence measurement:



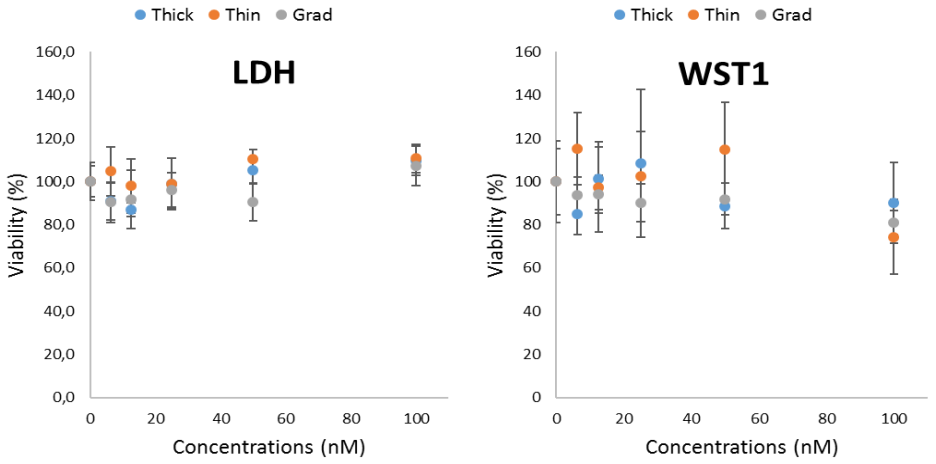
Photoluminescence of QD at 1 µM in PBS after an aging of 0, 15min, 30min, 45min, 1h, 1h30, 2h, 4h and 6h.

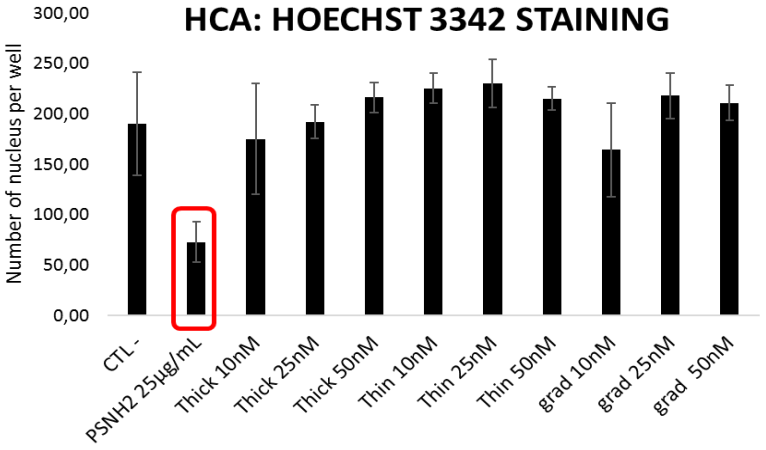
➡ **Double shell increases the fluorescence and resistance of QD to aging**

➡ **The thicker the shell, the greater the effect**

CYTOTOXICITY

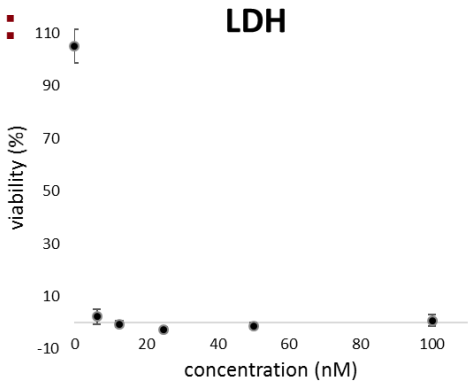
Before aging:

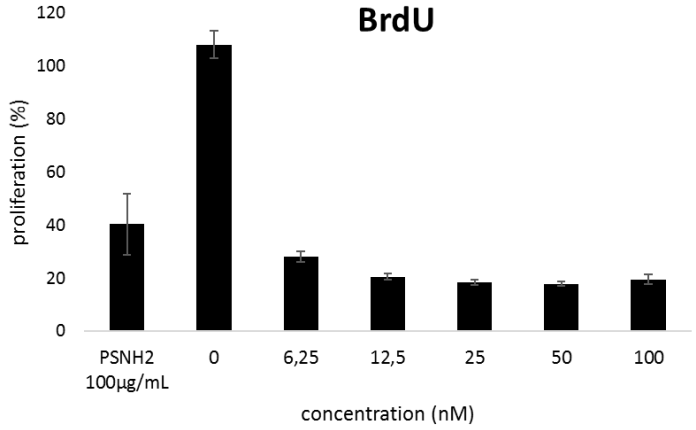




➡ **In their pristine form, QDs appear not to be cytotoxic**

After aging:





GRADIENT SHELL

➡ **After aging, the gradient shell QDs become very cytotoxic**

CONCLUSION & PERSPECTIVES

Conclusion:

- ❑ Physico-chemical transformation is very rapid
- ❑ Dissolution occurring during the first two hours of aging
- ❑ Pristine form QDs are not very cytotoxic
- ❑ Transformed QDs are much more toxic

Shell design of QDs:

- ➢ Reduces the toxicity
- ➢ Slows the degradation

But does not totally prevent from dissolving and releasing toxic In ions

Perspectives:

- ❑ Chemical transformation during aging (EXAFS)
- ❑ Cell accumulation (ICP-MS)
- ❑ intracellular distribution (MET-EDX)

THANK YOU FOR YOUR ATTENTION!

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STEM-EDX ANALYSIS OF QDS