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Bio-macromolecular detection: new organic vital dyes

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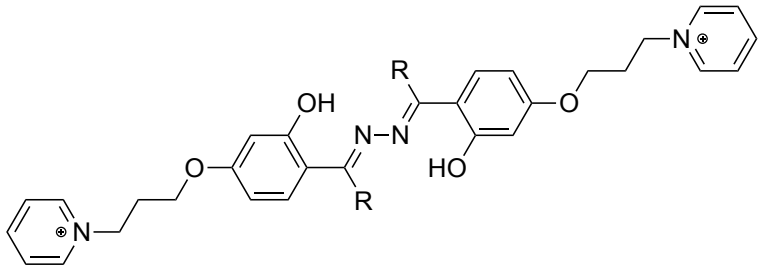
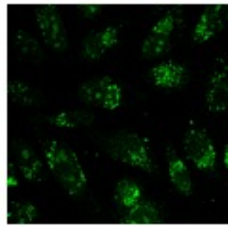
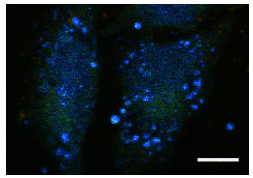
Bio-macromolecular detection: new organic vital dyes

Graphical Abstract





protein aggregates



lipid droplets

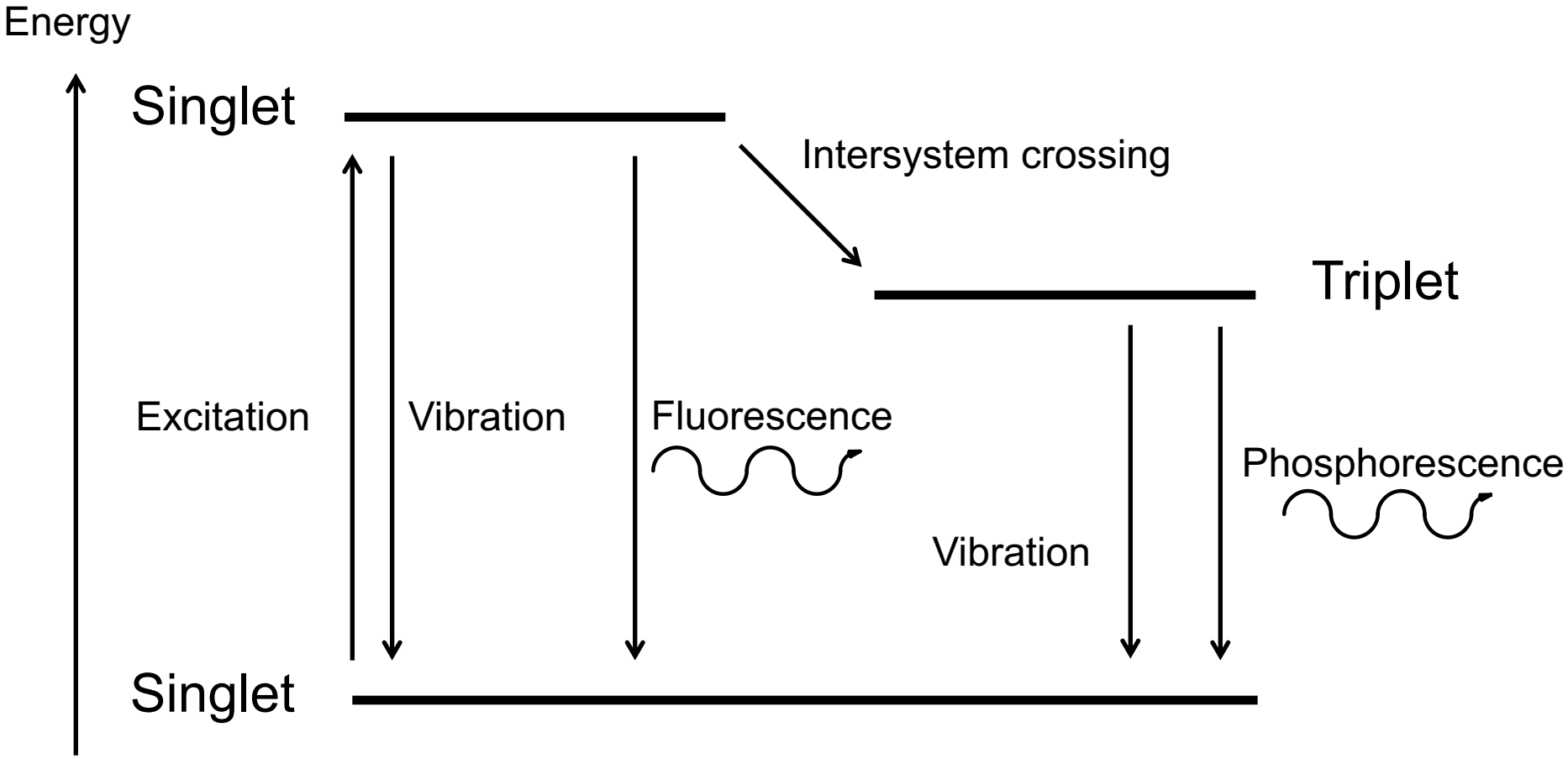
Abstract:

Aggregates of lipids or proteins are associated with high incidence diseases. The detection of these bio-macromolecules is a key issue in both fundamental research studies and in medical diagnostics. Push-pull chromophores and luminogenic materials with aggregation-induced emission (AIE) properties have gained importance as dyes in biological studies and diagnostics.

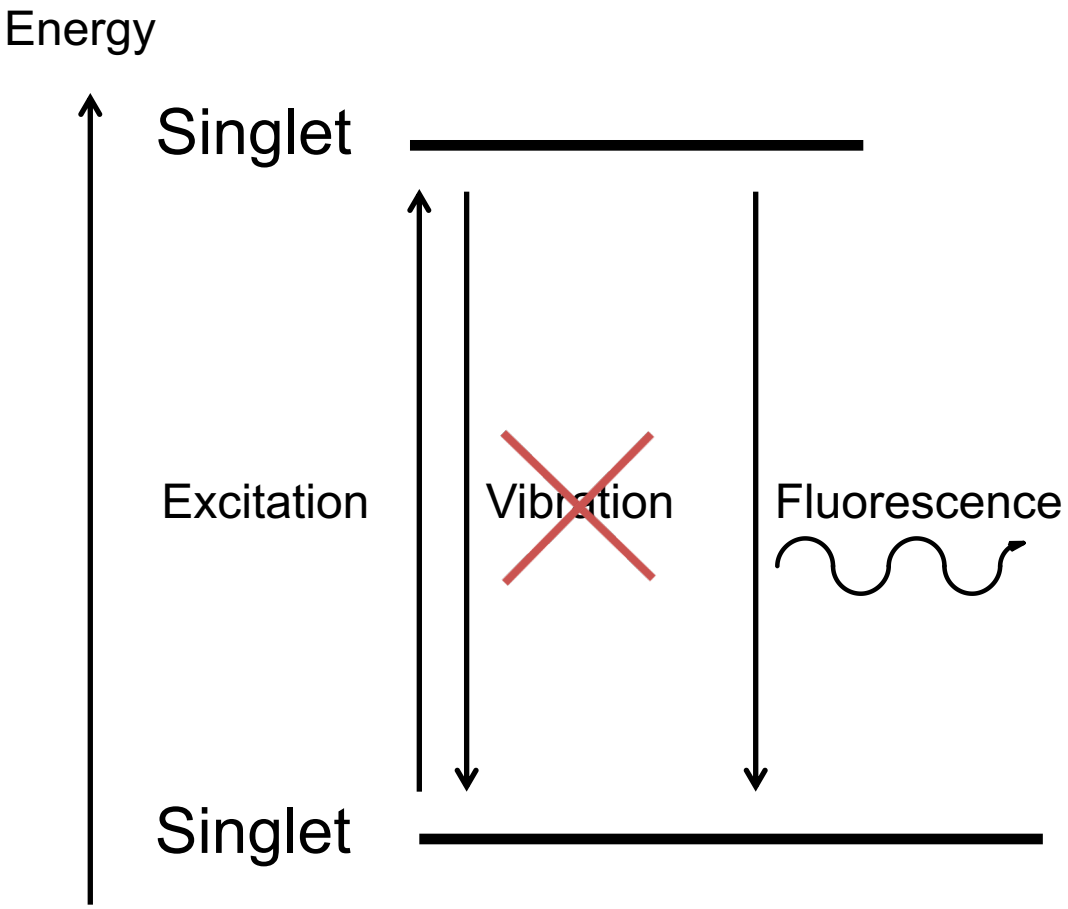
Here, we will describe our recent work on the synthesis and characterization of a group of **fluorescent probes with affinity for lipid or protein aggregates**. Optoelectronic properties and biological evaluation of the fluorophores will also be presented. As lipid aggregates are concerned, one of the tested dyes showed good fluorescence intensity in cells, lipid vesicles, zebrafish embryos and presented altered emission spectra depending on the polarity of the medium, due to its push-pull character. This fluorophore demonstrated to be suitable for high-content screens for the diagnosis of Farber's disease, a lysosomal storage disease. Furthermore, a new protein aggregate AIEgen was used as a biological vital dye and proved to be a promising fluorescent probe for the selective staining of protein aggregates, allowing imaging by fluorescence confocal microscopy, with a selectivity comparable to a commercial dye, and for detection of protein aggregates in routine diagnosis.

Keywords: aggregation-induced emission, fluorophores, macromolecular aggregation, solvatochromism

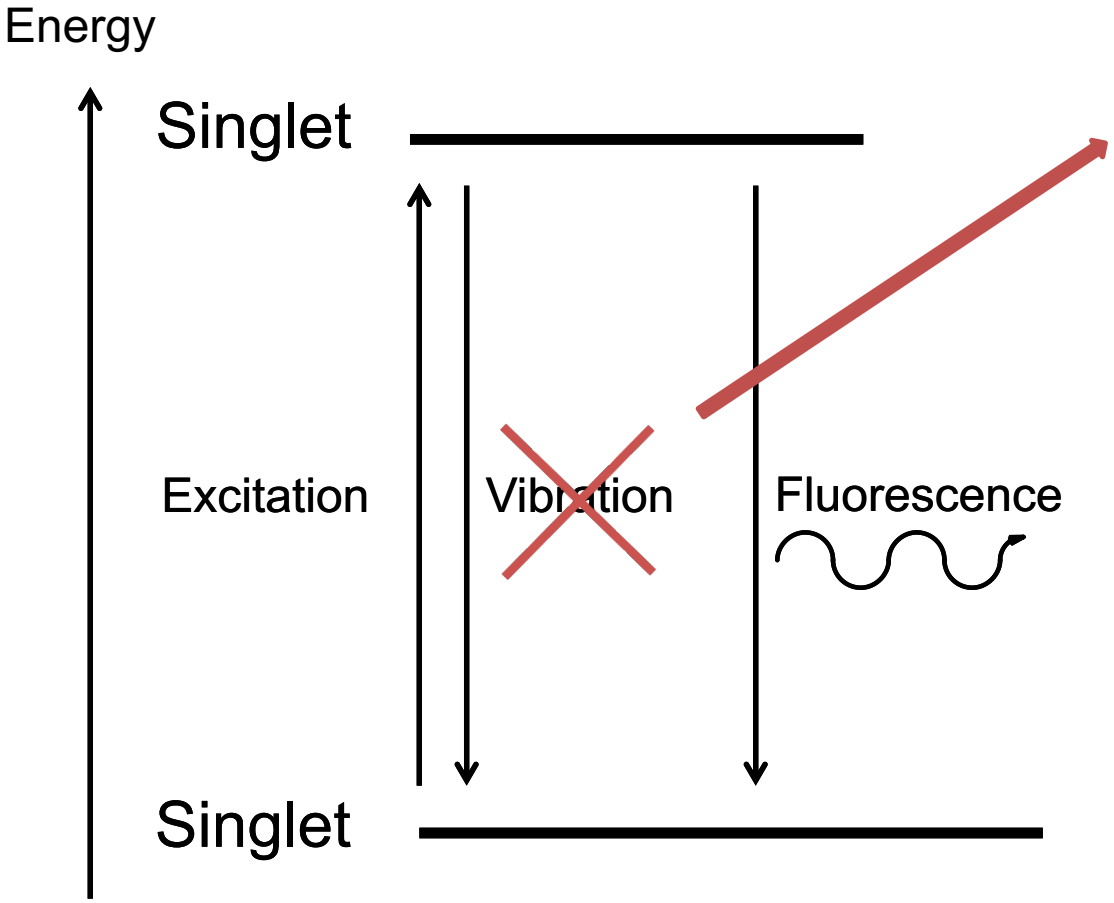
Protein aggregates sensors: Rationale



Protein aggregates sensors: Rationale



Protein aggregates sensors: Rationale



Crystallization

Aggregation

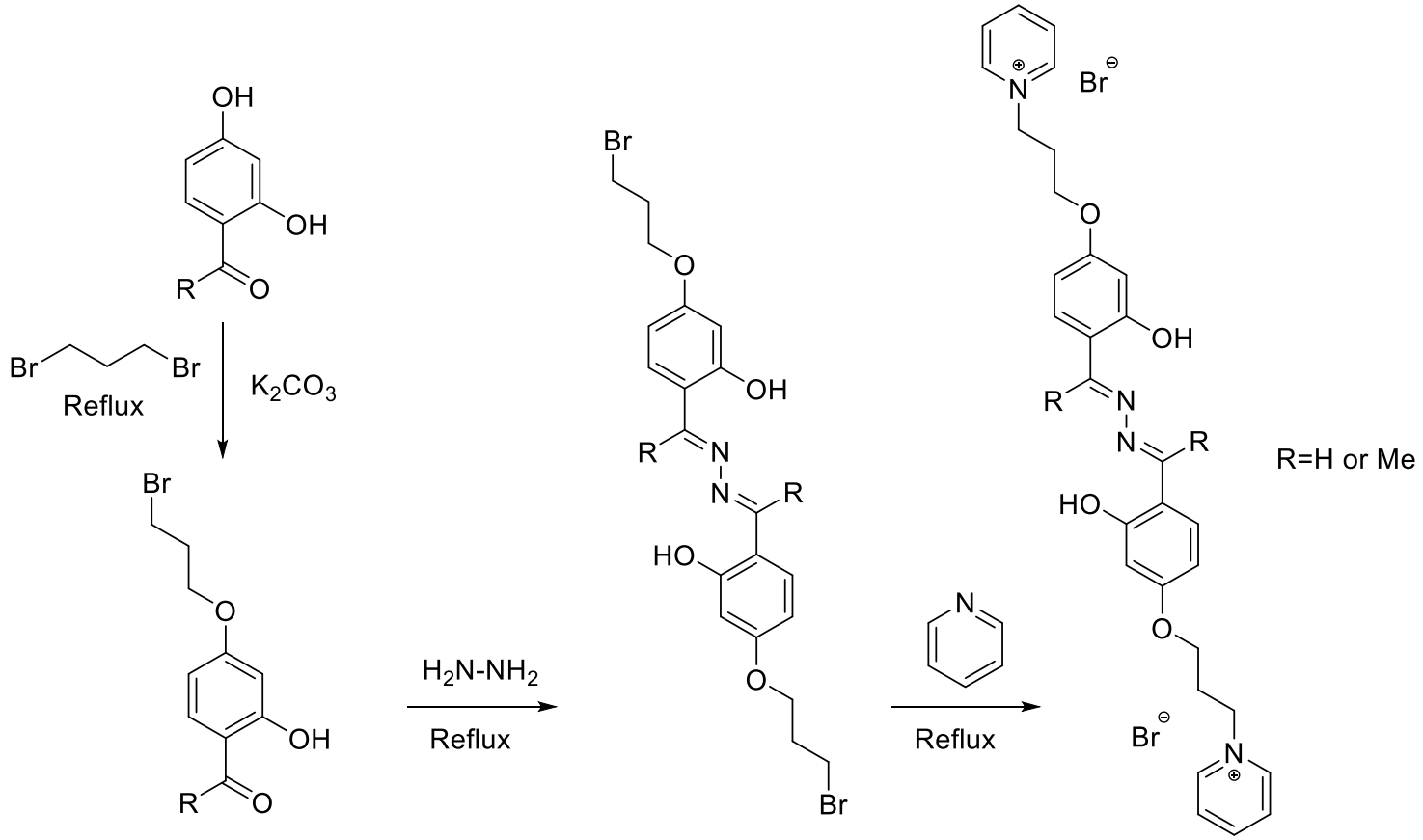
Solid matrix

Low temperature

Chemical modification

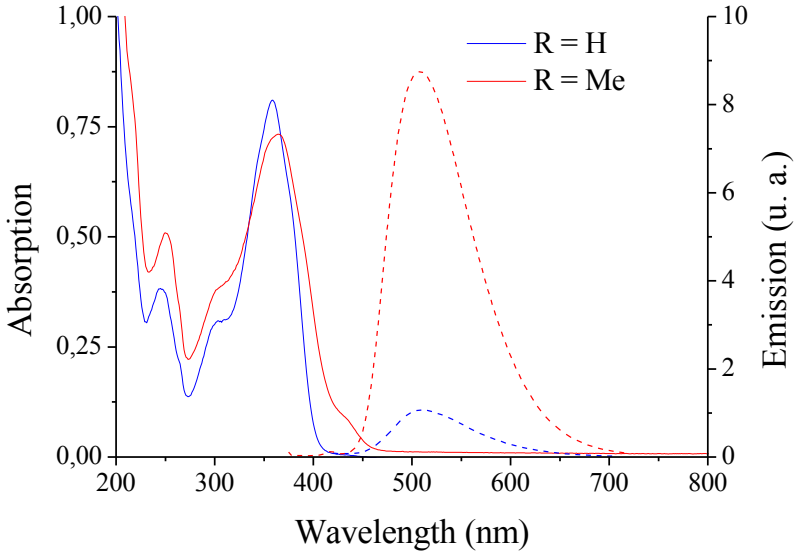
Encapsulation

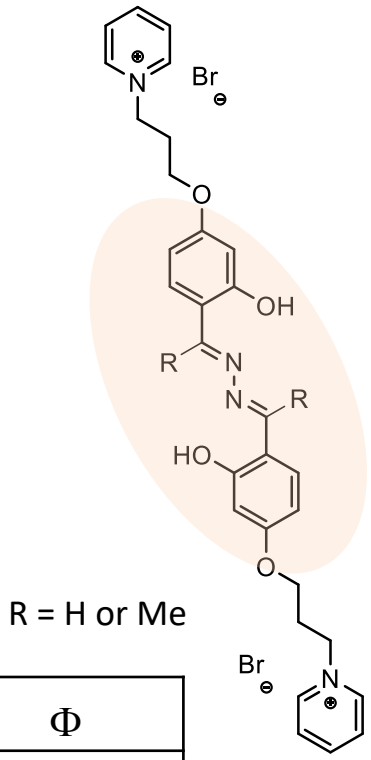
Protein aggregates sensors: Design, synthesis and characterization



Nunes da Silva R., *et al. Chem. Asian J.* **2019**, 14, 859.

Protein aggregates sensors: Design, synthesis and characterization



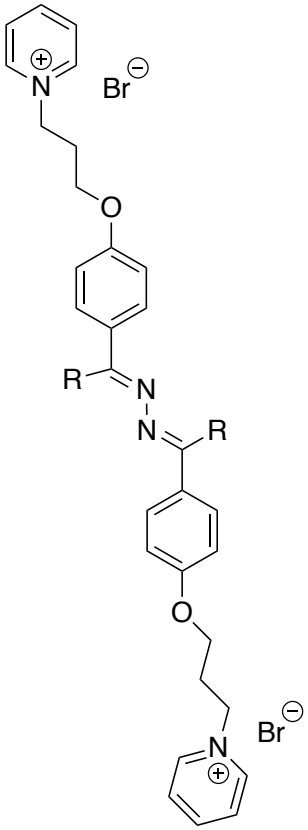


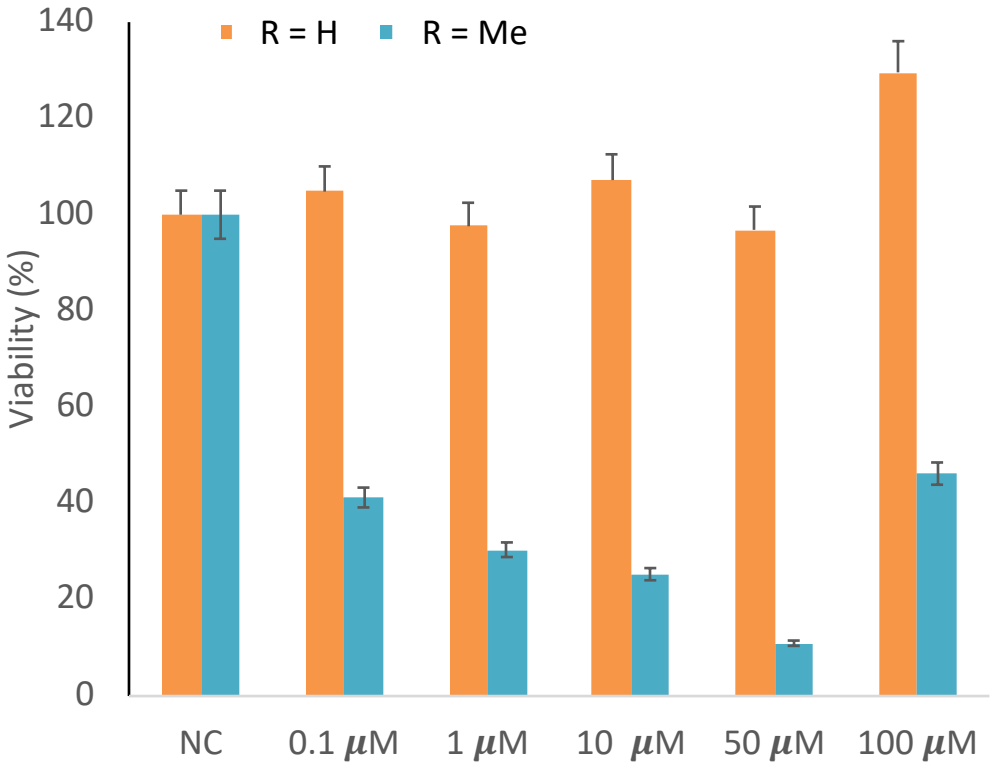
R = H or Me

R	λ_{max} Abs (nm)	ε ($M^{-1}cm^{-1}$)	λ_{max} Em (nm)	Φ
H	360	38700	510	$1x10^{-5}$
Me	365	31500	510	$5x10^{-5}$

Nunes da Silva R., *et al. Chem. Asian J.* **2019**, 14, 859.

Protein aggregates sensors: cytotoxicity





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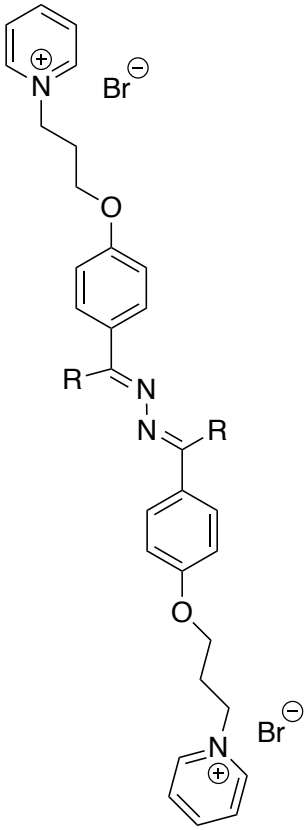
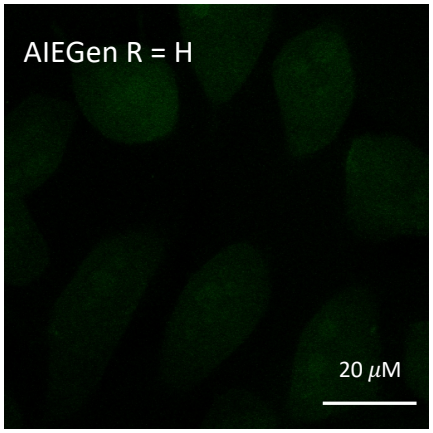
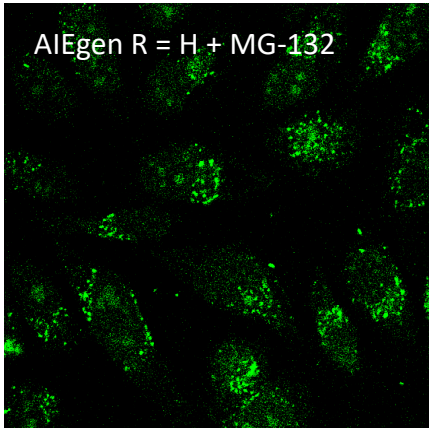
Protein aggregates sensors: detection



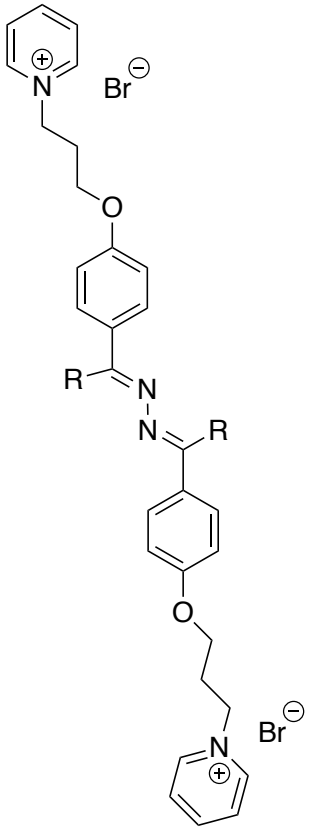




ProProH

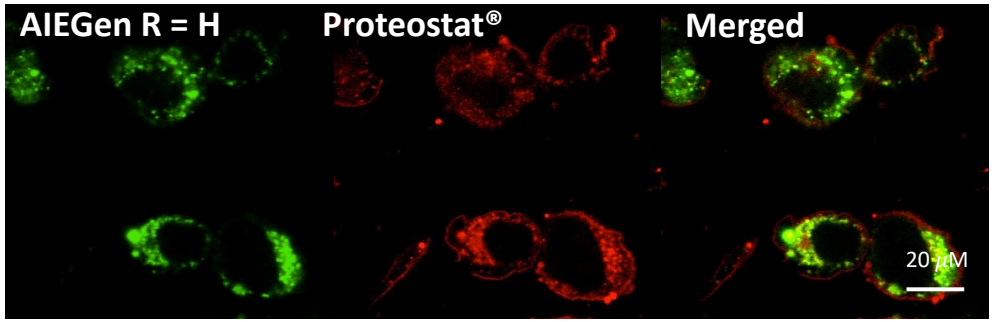
Nunes da Silva R., *et al. Chem. Asian J.* **2019**, 14, 859.

Protein aggregates sensors: detection



ProProH

MG-132 condition: with protein aggregates



Nunes da Silva R., *et al. Chem. Asian J.* **2019**, 14, 859.

Lipid droplets sensors: Rationale

Solvatochromism ⟹ Reversible change of the absorption or emission spectrum of a material that is induced by the action of solvents or surrounding media.

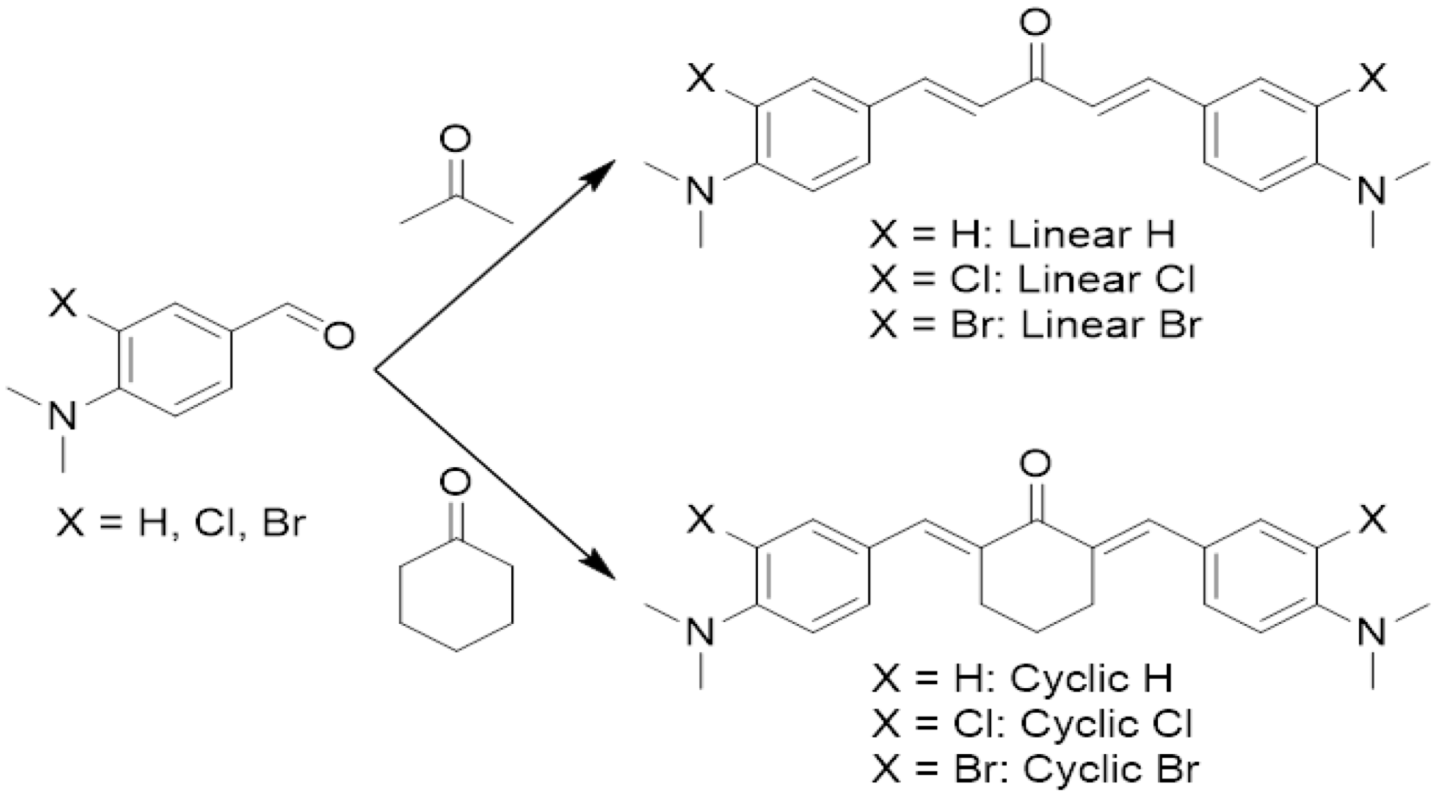
⇓

The color change is the consequence of the absorption maximum shift, which occurs due to differences between the solvation energy of the initial and excited state in various solvents.

Push-Pull-Push fluorophores

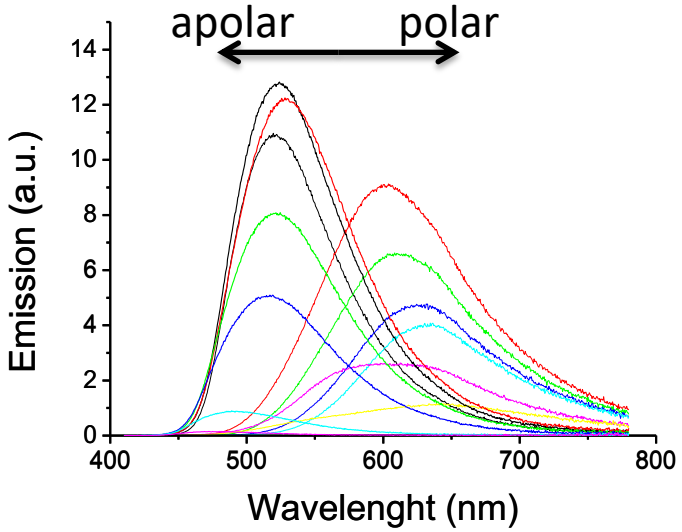
Stokes' shift is large, and their emission maximum is greatly influenced by the surrounding media.

Lipids droplets sensors: Design, synthesis and characterization



Patent WO/2017/182945 A1 for “Fluorescent cell markers with large Stroke’s shift”.

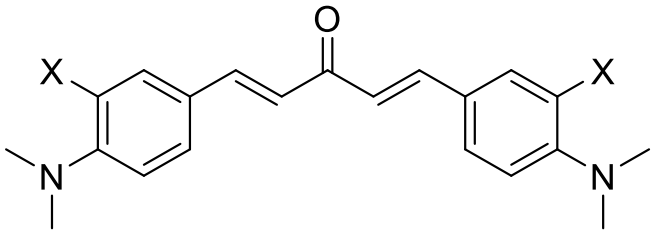
Lipids droplets sensors: Design, synthesis and characterization

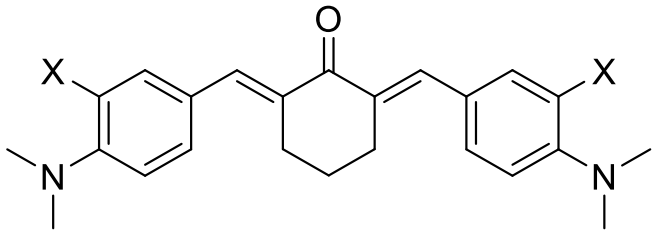


Compound	Absorption maximum[a] (nm)	ε (M^{-1} cm^{-1})[a]	Emission maximum (nm)[b]	Quantum yield[c]	Stokes' shift (nm)
linear-H	442	41 000	552	0.14	110
linear-Cl	390	14 000	560	0.10	170
linear-Br	370	7 500	562	0.05	192
cyclic-H	433	20 000	550	0.01	117
cyclic-Cl	381	20 500	578	0.01	197
cyclic-Br	378	24 500	572	0.01	194

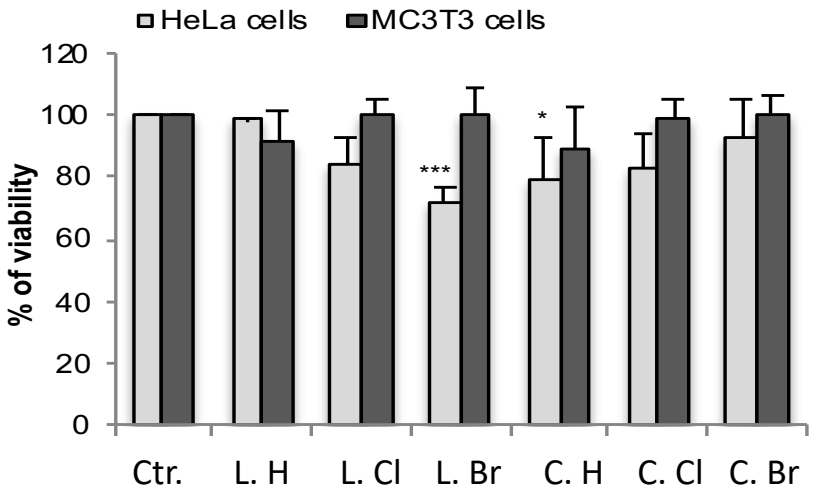
Patent WO/2017/182945 A1 for "Fluorescent cell markers with large Stroke's shift".

Lipids droplets sensors: cytotoxicity





X = H, Cl, Br



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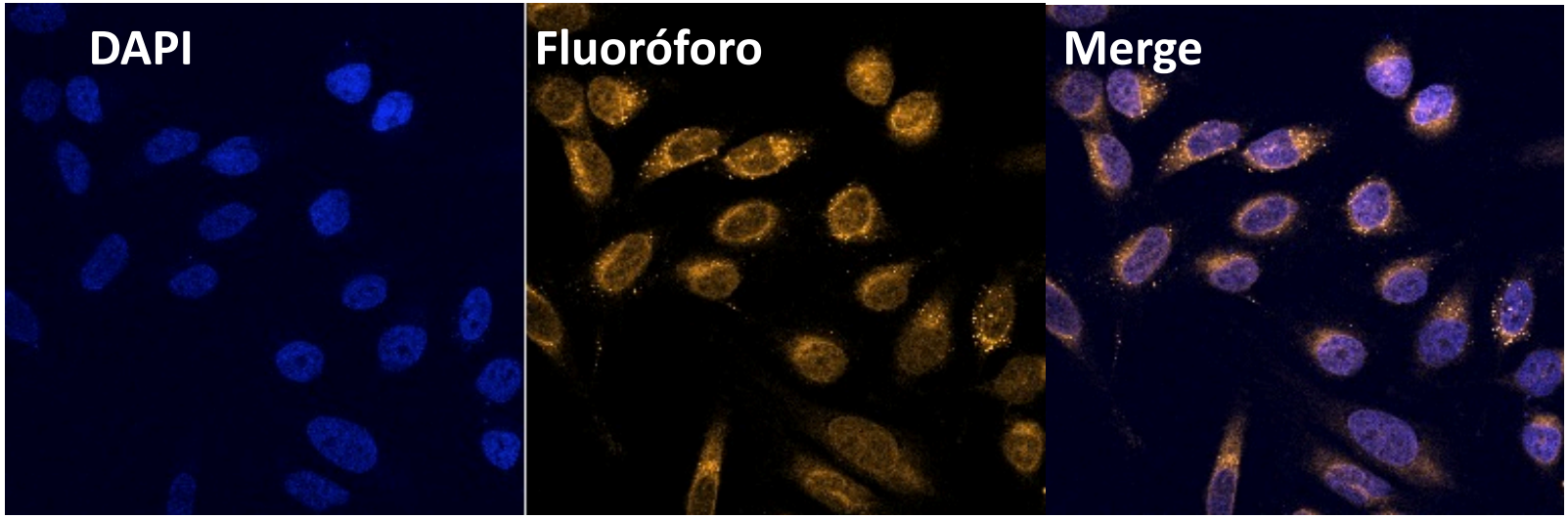
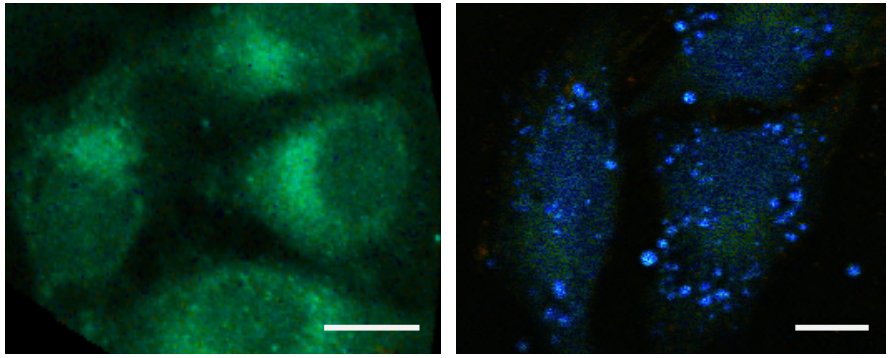
Lipids droplets sensors: detection



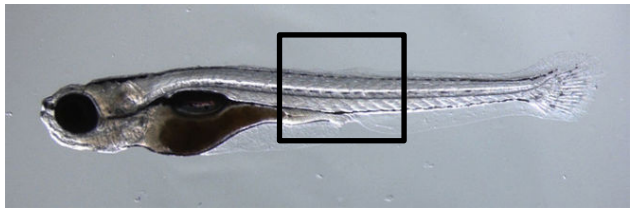


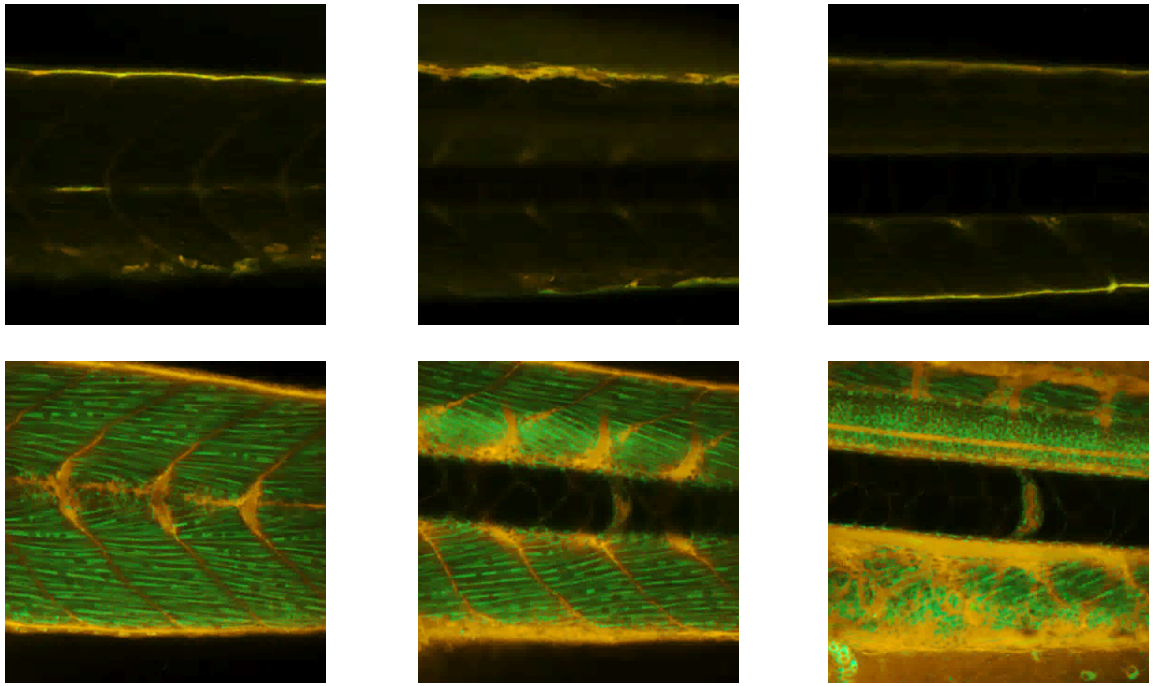
C. Cl --> liprobe

Patent WO/2017/182945 A1 for “Fluorescent cell markers with large Stroke’s shift”.

Lipids droplets sensors: detection

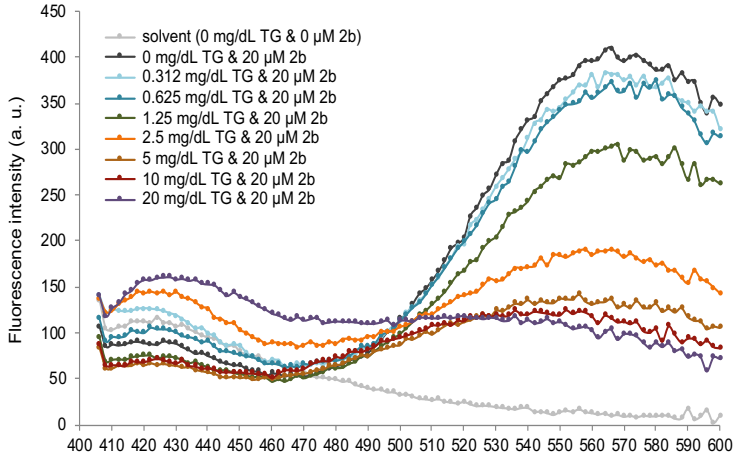
Zebra fish

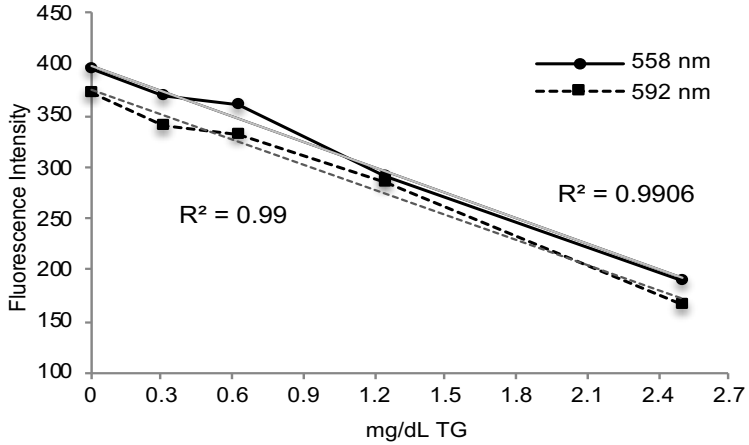


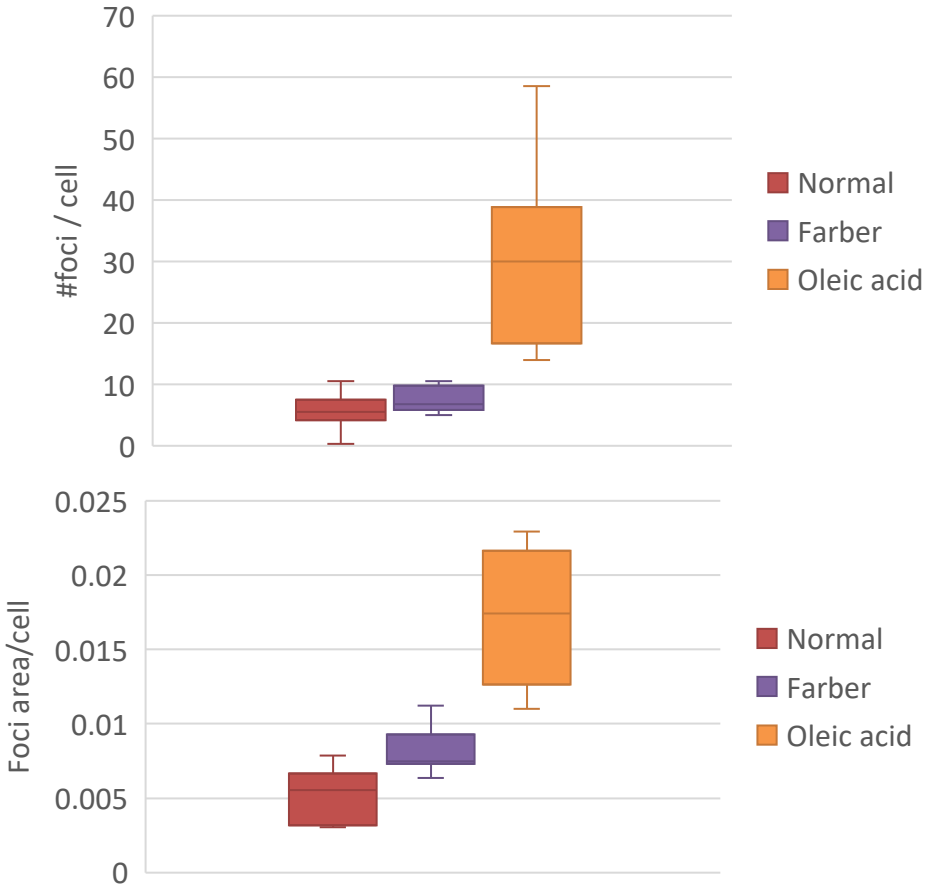


Patent WO/2017/182945 A1 for “Fluorescent cell markers with large Stroke’s shift”.

Lipids droplets sensors: diagnosis







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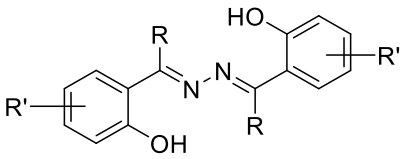
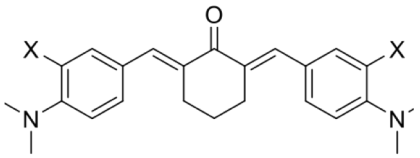
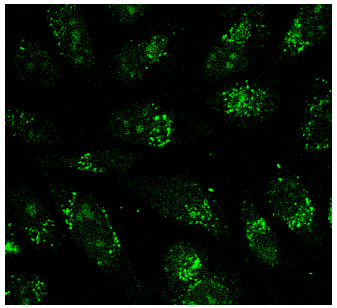
Conclusions



protein aggregates

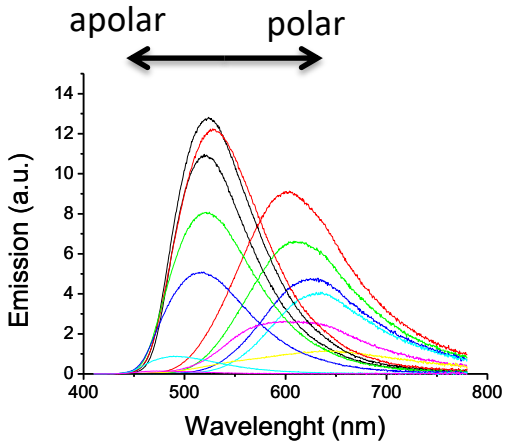


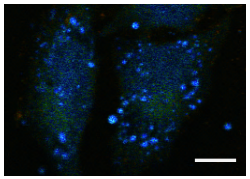
lipid droplets

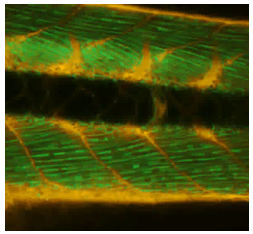


Promising fluorescent probe for the selective staining of protein aggregates, allowing imaging by fluorescence confocal microscopy, with a selectivity comparable to Proteostat.

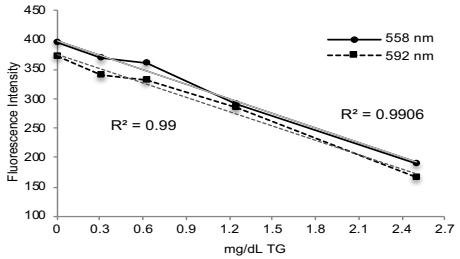
Dye

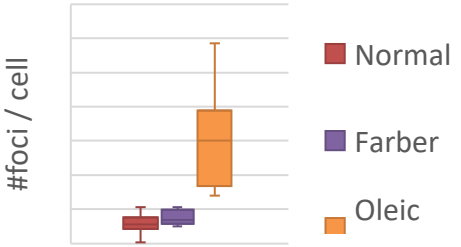






Diagnosis





Acknowledgments

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