



## Literature Report VII



Cite This: *J. Am. Chem. Soc.* 2017, 139, 16273-16281

Article

[pubs.acs.org/JACS](https://pubs.acs.org/JACS)

### Mitochondria Alkylation and Cellular Trafficking Mapped with a Lipophilic BODIPY–Acrolein Fluorogenic Probe

Reporter: Wenchao Jiang

Date: 2020-07-02

# Contents

---

- ① Introduction
- ② Probe Design and Characterization
- ③ Super-resolution Mapping of AcroB Adduct Formation
- ④ Trafficking Visualized via Colocalization Imaging
- ⑤ Summary

# CV of Dr. Gonzalo Cosa

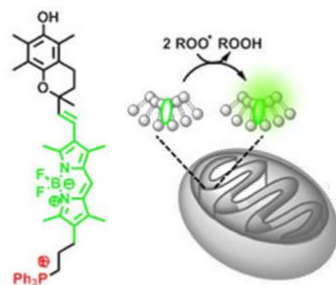


Professor in the Department of Chemistry at McGill University

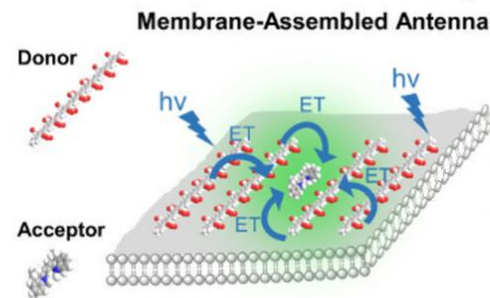
Ph.D. : Physical Organic and Photochemistry involved mechanistic studies on drug photodegradation

postdoctoral fellow in Paul Barbara's research group :  
Single Molecule Fluorescence

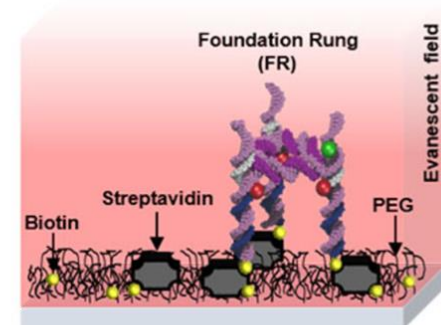
**current research centers** :designing, preparing and utilizing smart fluorescent probes for cell-imaging and applying single-molecule fluorescence methodologies to study protein/DNA/lipid interactions.



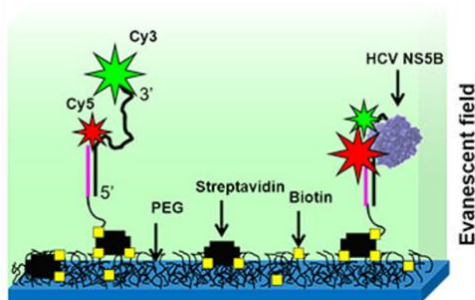
Imaging Redox Reactions With Newly  
Developed Fluorogenic Probes



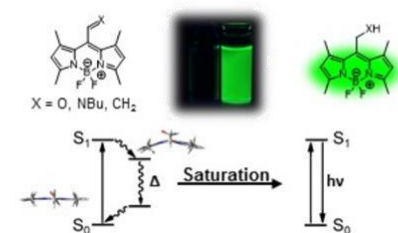
Exciton Transport in Lipid-Conjugated  
Polyelectrolyte Complexes



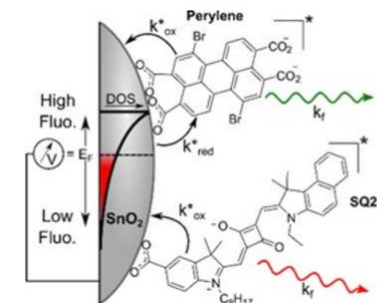
Synthesis and Single Molecule  
Visualization of Biomaterials



Single Molecule Biophysical Studies  
on Polymerase activity

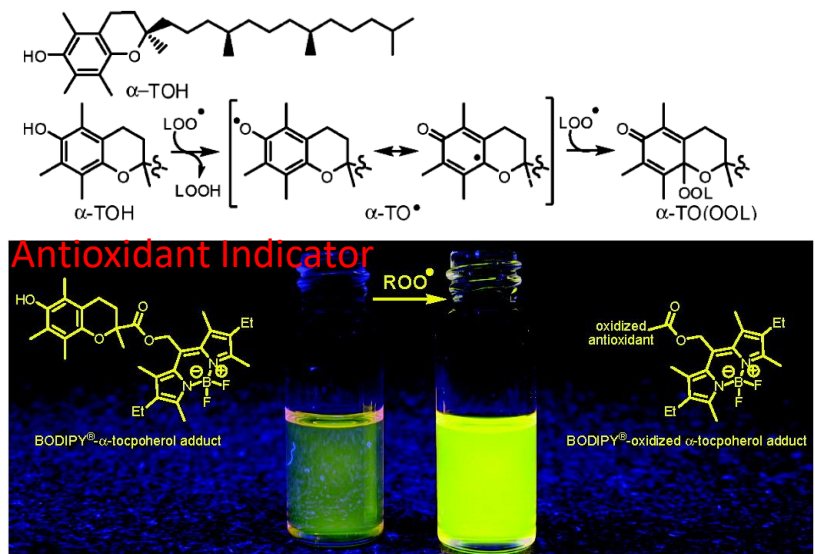


Photophysical and Photochemical  
Properties of Fluorescent Dyes

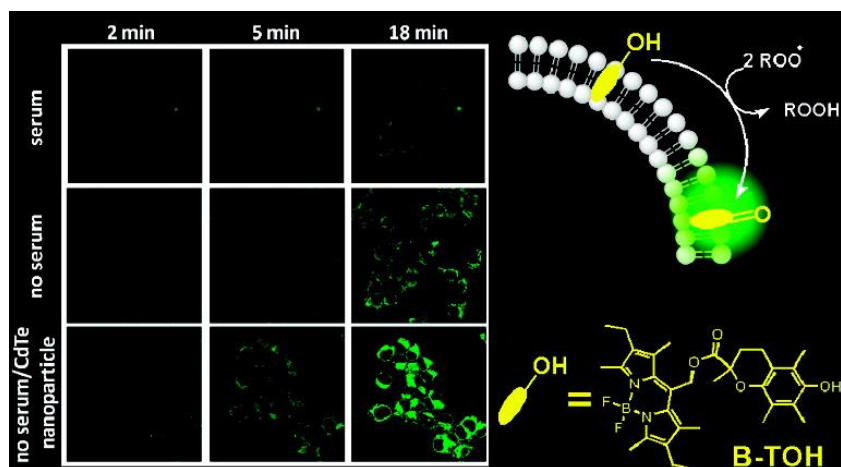


Single Molecule  
Spectroelectrochemistry Studies

# Research related to Redox Reactions

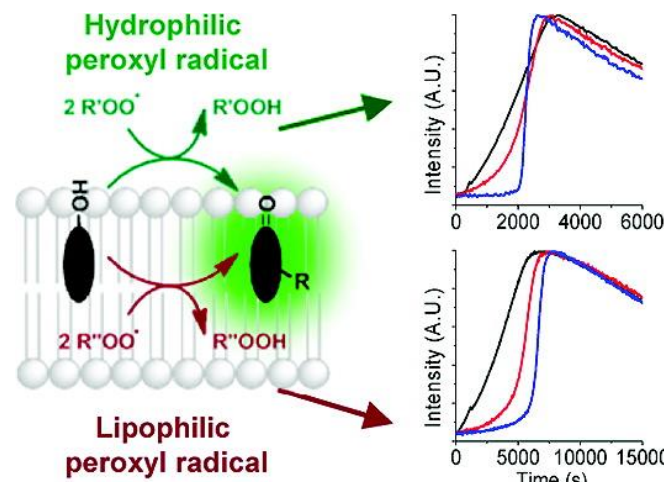


*J. Am. Chem. Soc.* 2007, 129, 7, 1842–1843

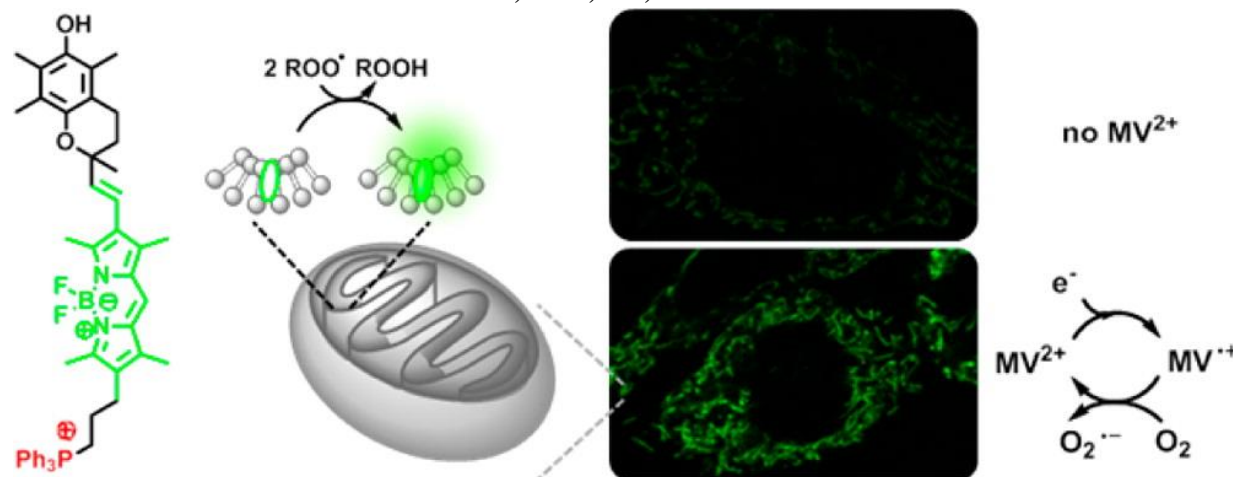
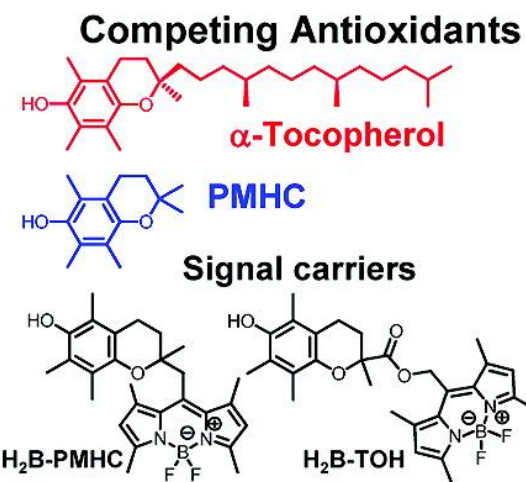


*Biochemistry* 2009, 48, 24, 5658–5668

Molecular Imaging of Lipid Peroxyl Radicals



*J. Am. Chem. Soc.* 2012, 134, 24, 10102–10113



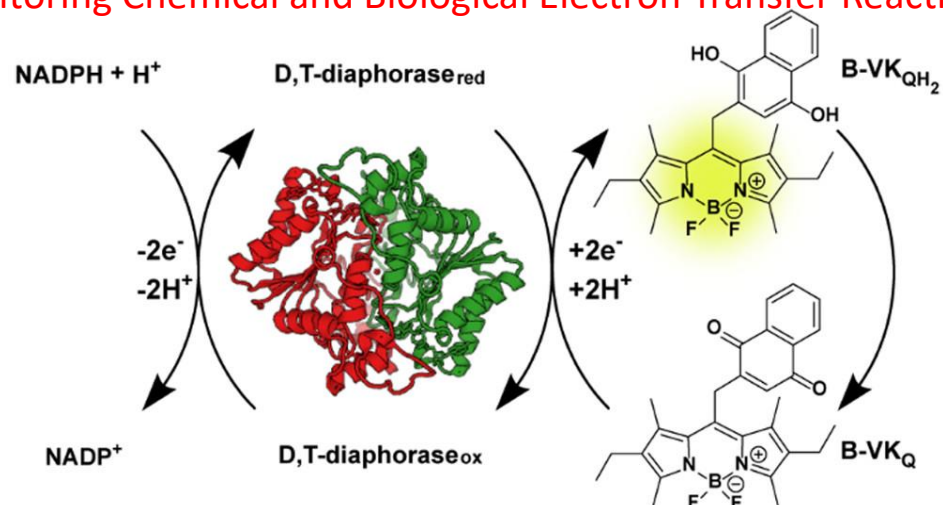
*J. Am. Chem. Soc.* 2013, 135, 45, 17135–17143

Monitoring the Antioxidant Status within the Inner Mitochondrial Membrane

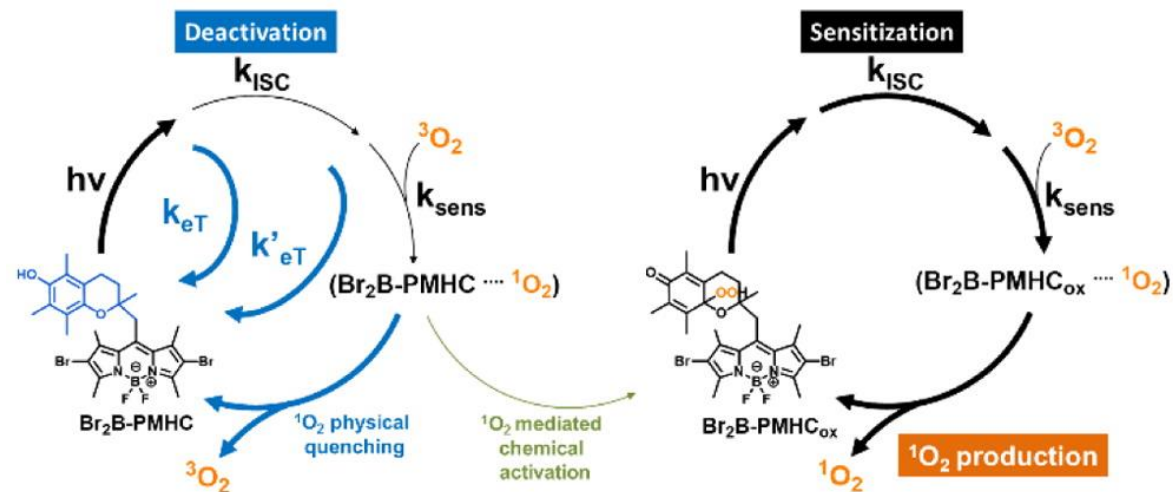


# Research related to Redox Reactions

## Monitoring Chemical and Biological Electron Transfer Reactions



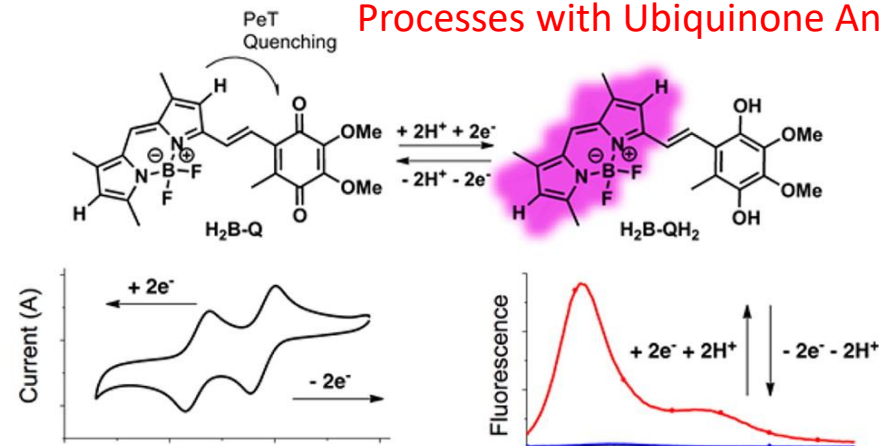
*J. Am. Chem. Soc.* 2016, 138, 50, 16388–16397



*J. Am. Chem. Soc.* 2016, 138, 4, 1215–1225

Reactive Oxygen Species Mediated Activation of a Dormant Singlet Oxygen Photosensitizer

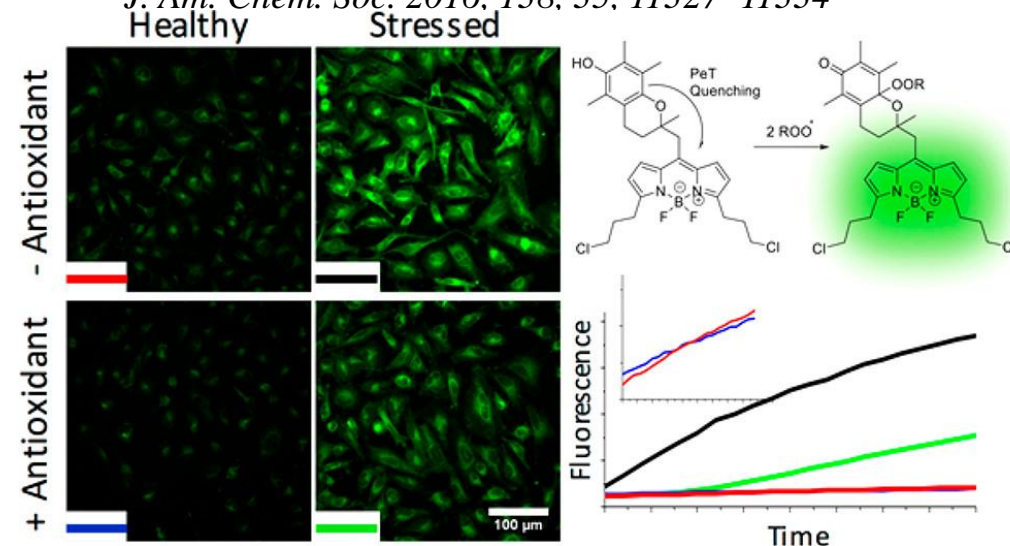
## Monitoring Chemical and Biological Redox Processes with Ubiquinone Analogue



Redox Reversibility

Fluorogenicity

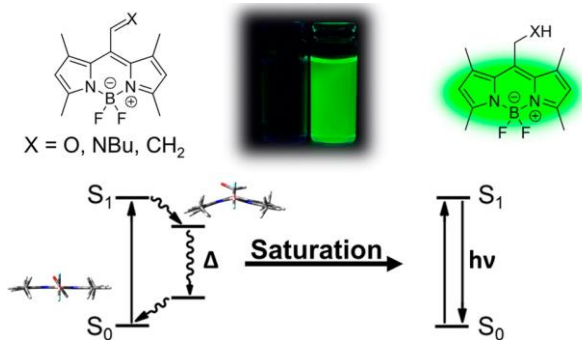
*J. Am. Chem. Soc.* 2016, 138, 35, 11327–11334



*J. Am. Chem. Soc.* 2017, 139, 44, 15801–15811

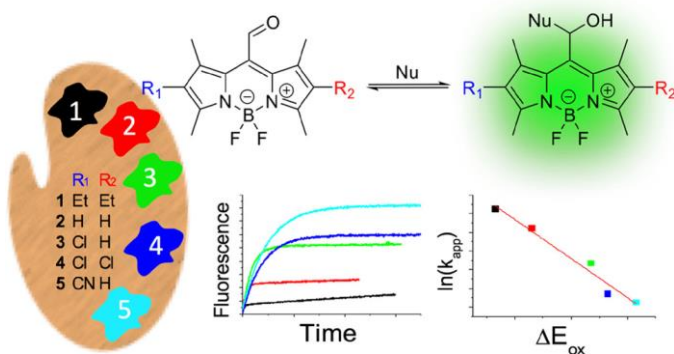
Rate of Lipid Peroxyl Radical Production during Cellular Homeostasis

# Introduction



*J. Phys. Chem. B* 2015, 119, 13, 4758–4765

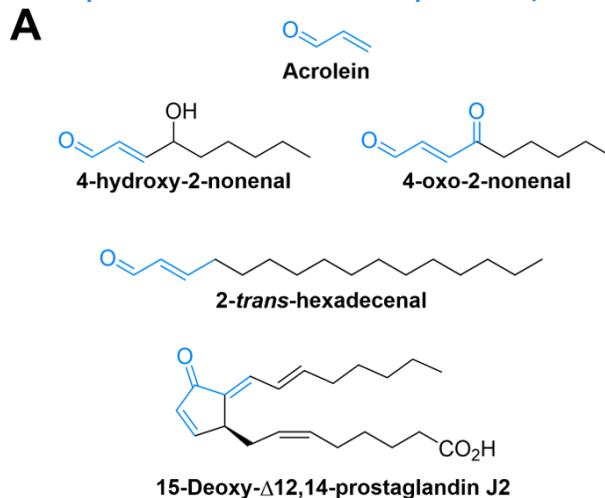
the Mechanism and Scope of Nonemissive meso-Unsaturated BODIPY



*ACS Omega* 2017, 2, 12, 8618–8624

Nucleophilic Addition Reactions Based on meso-Formyl BODIPY

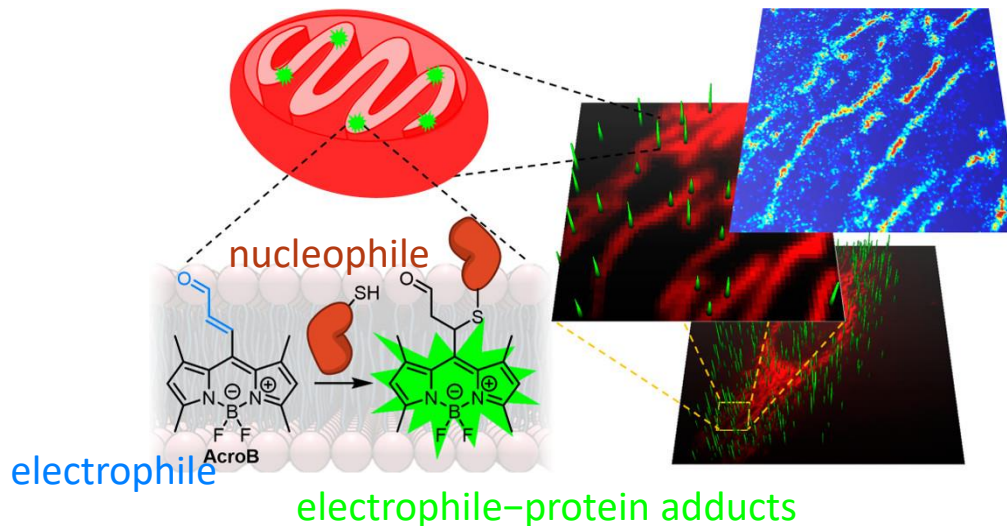
## Lipid-derived electrophiles (LDE)



在细胞膜内由多不饱和脂肪酸的酶促氧化或氧化应激条件下的催化自氧化产生的副产物

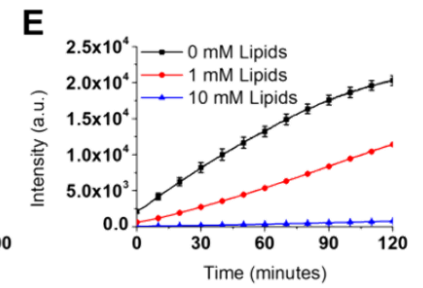
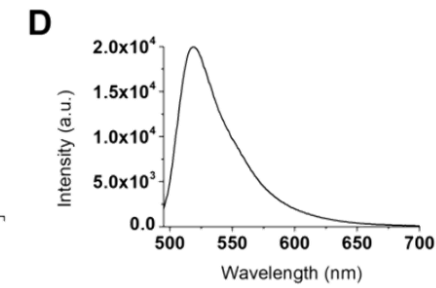
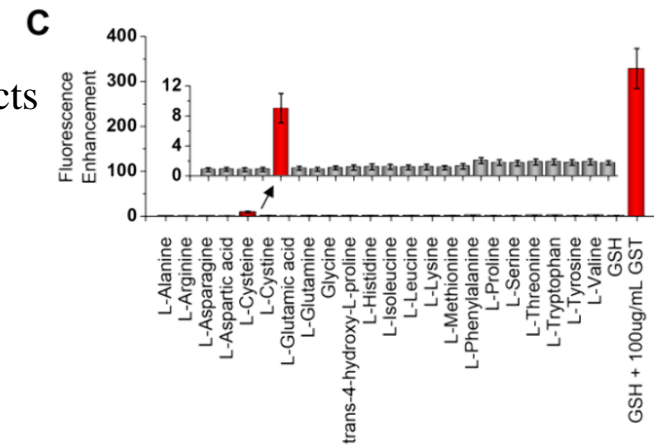
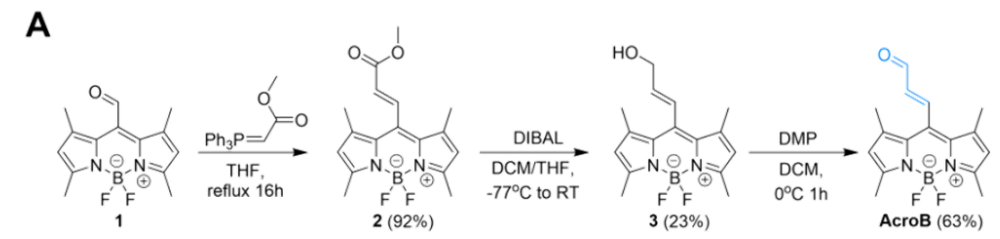
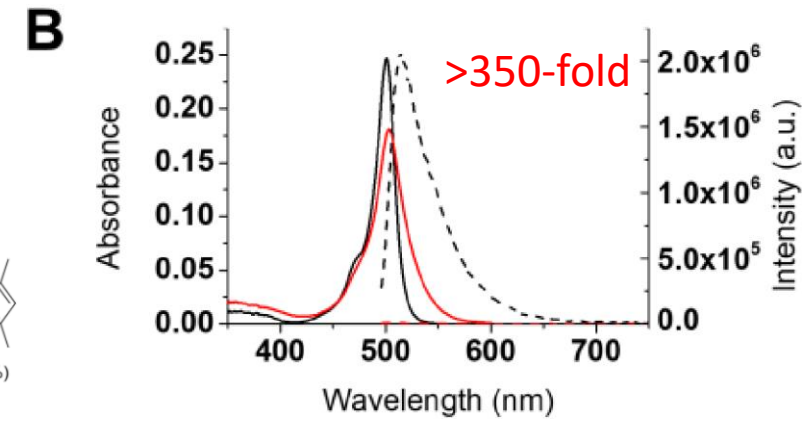
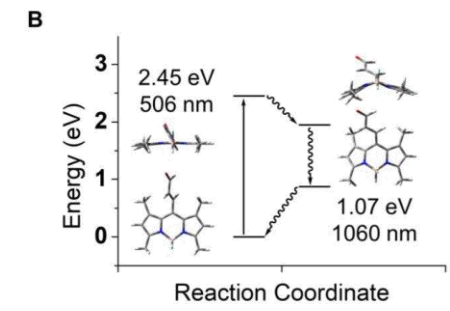
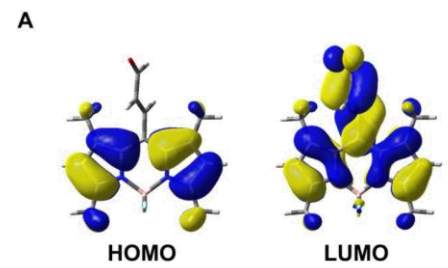
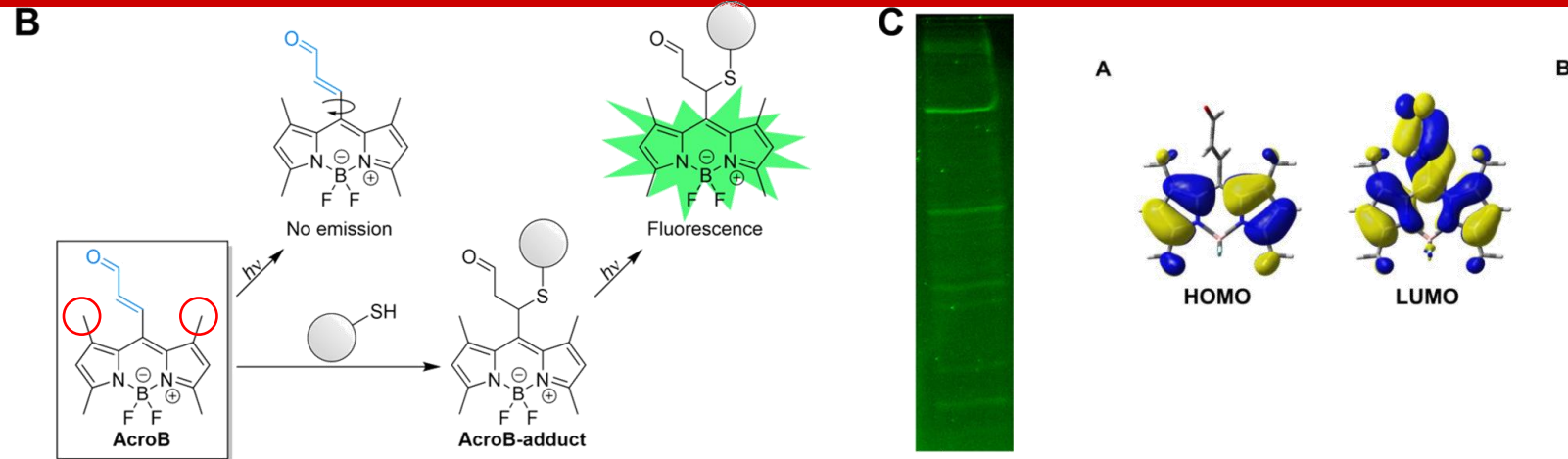
Cysteine  
Histidine/ lysine

## 实时可视化细胞环境对亲电试剂的时空响应



- where electrophile–protein adducts **form**
- how long they **reside**
- where they **accumulate**
- how they are **sorted**
- which **key organelles** are involved in their processing
- what are the **trafficking dynamics**

# Probe Design and Characterization



在脂质囊泡存在下荧光响应消失

L-cysteine: 9 fold

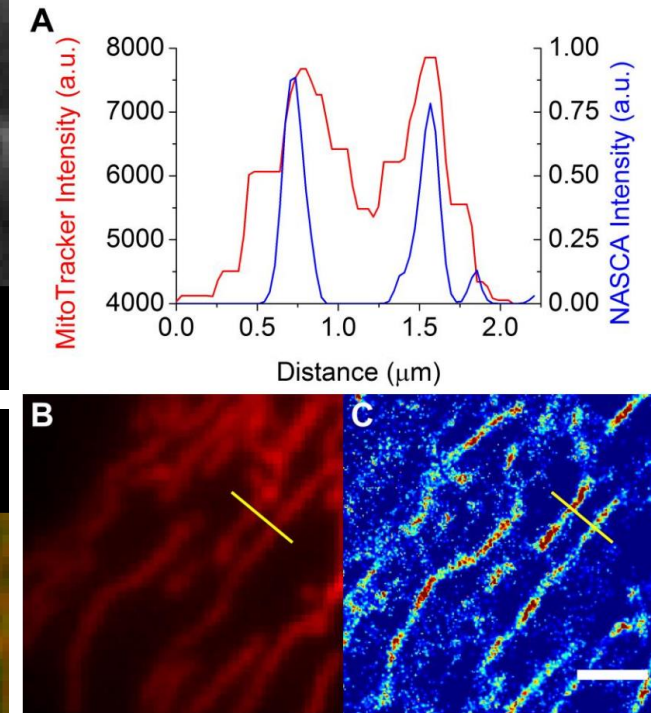
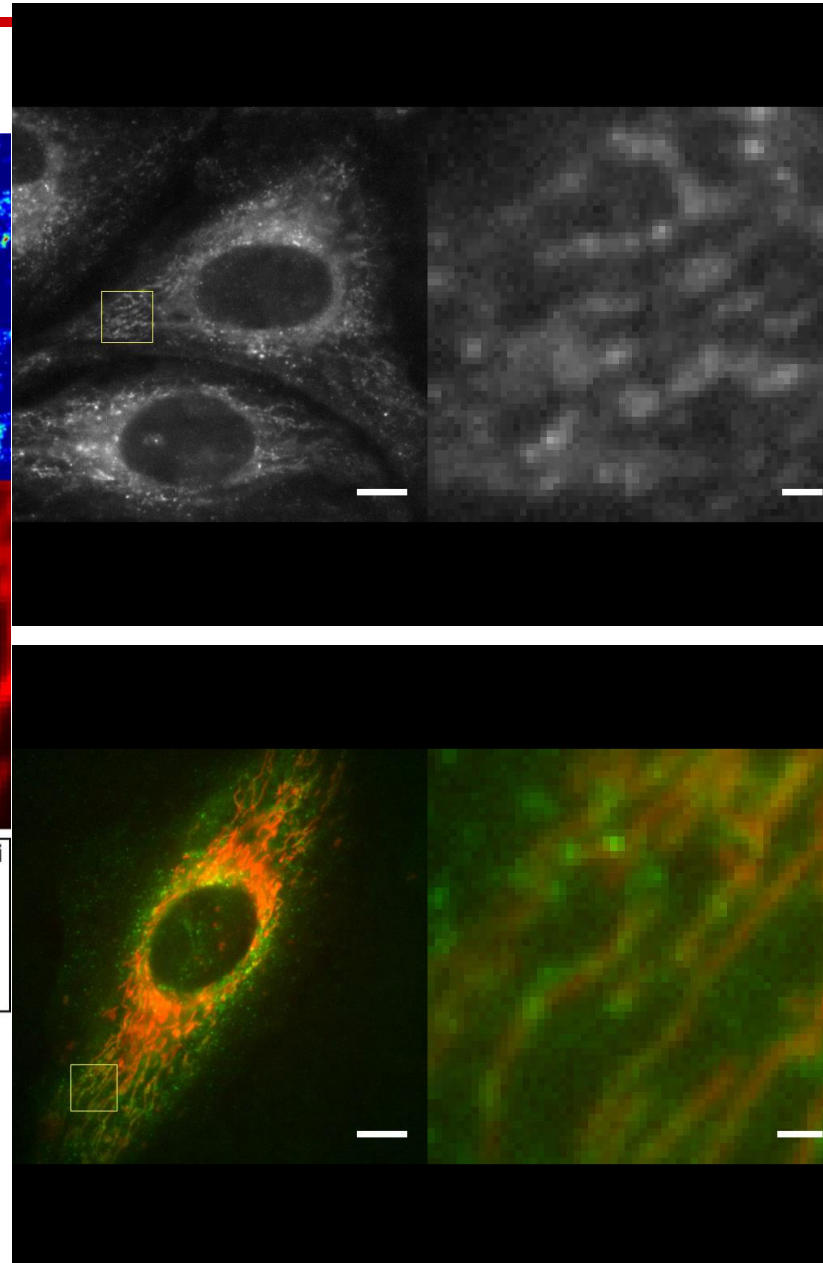
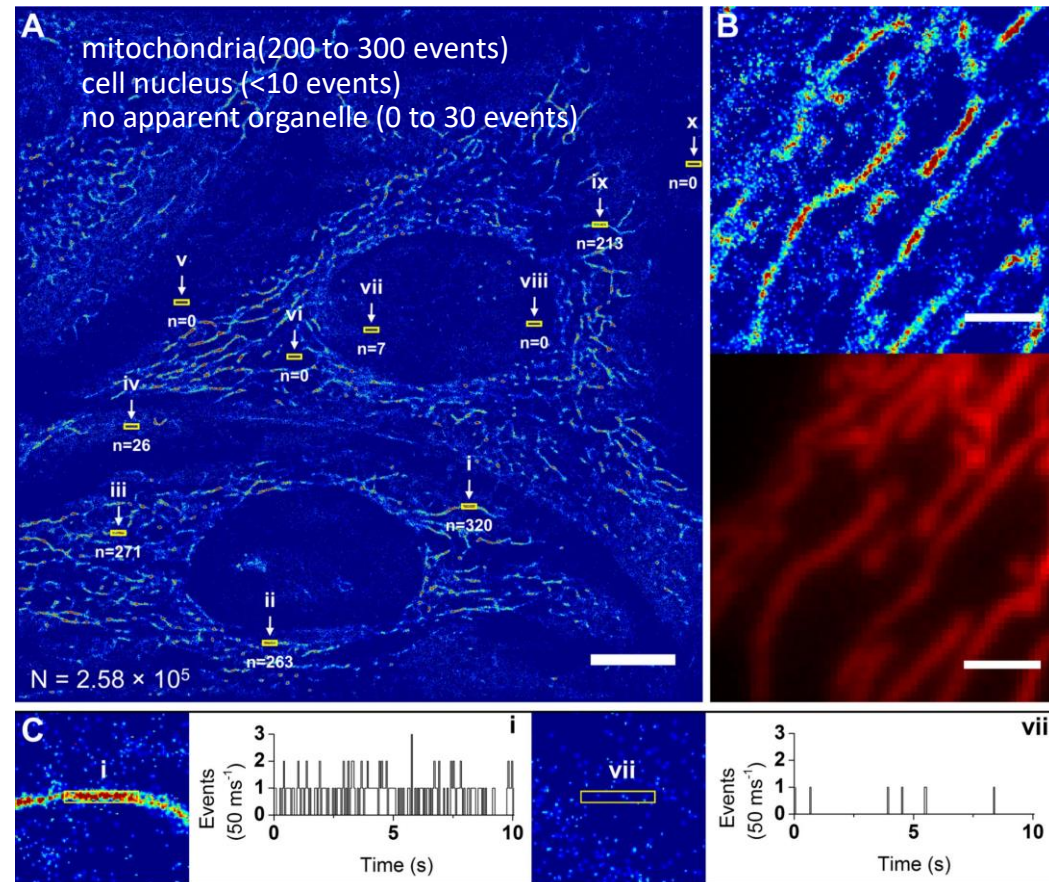
L-Lysine/L-histidine : Schiff base adducts

GSH+GST: ~350 fold



# Super-resolution Mapping of AcroB Adduct Formation

## Imaging alkylation of membrane proteins

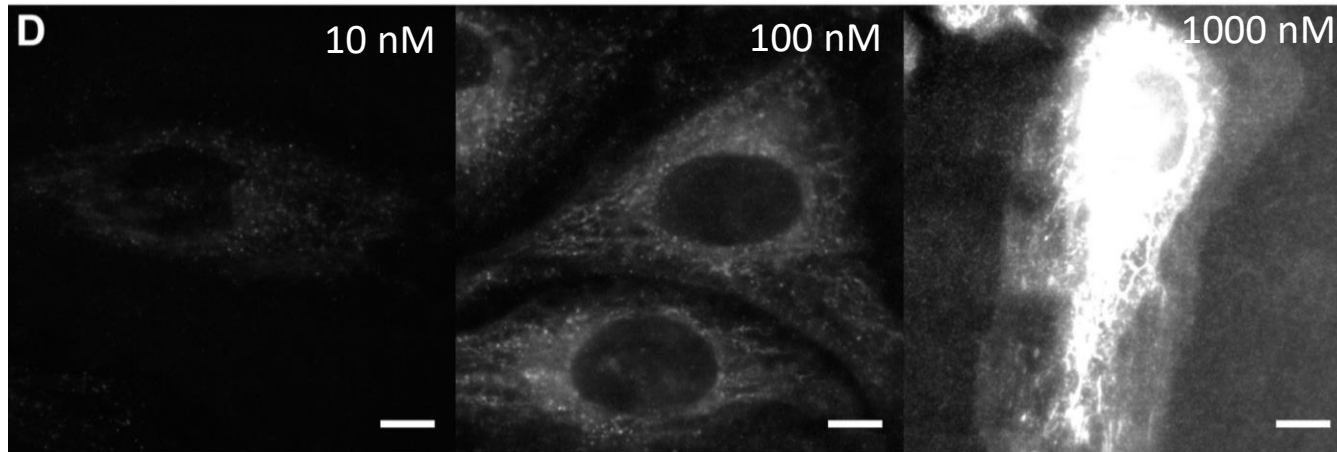


Reactions are occurring within the inner leaflet of the inner mitochondrial membrane

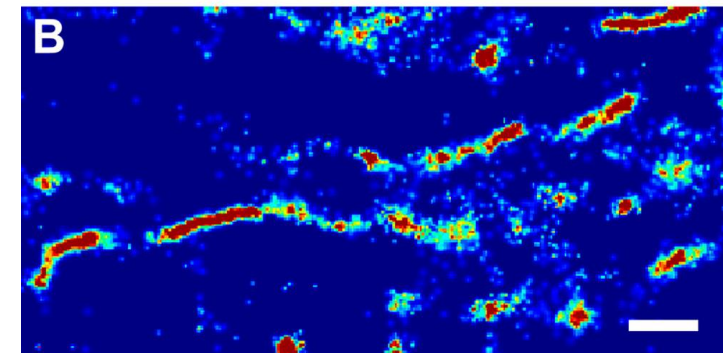
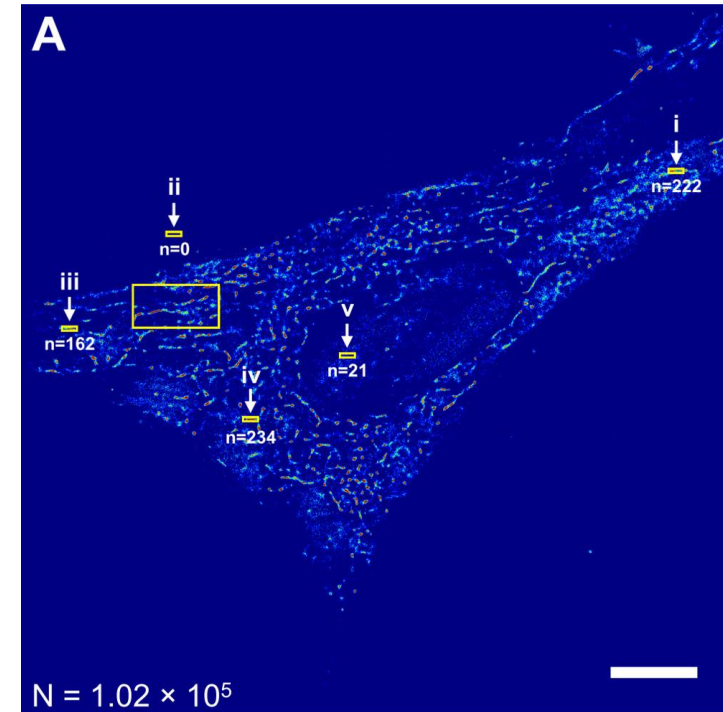
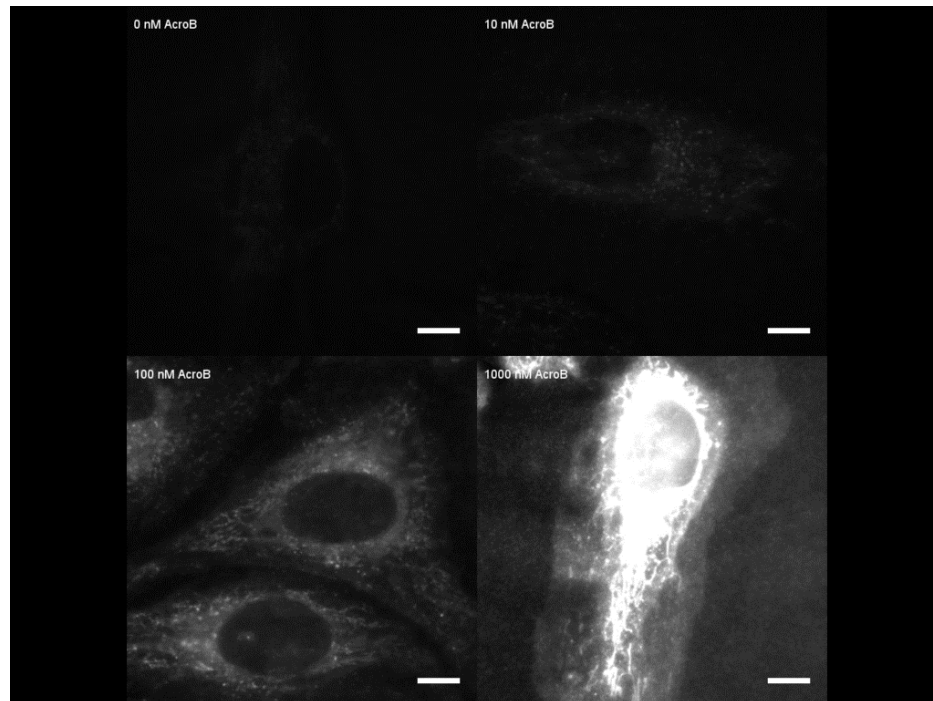
- Imaging protein posttranslational modification (PTM) by **AcroB**
- Colocalization of chemical events with mitochondria



# Super-resolution Mapping of AcroB Adduct Formation

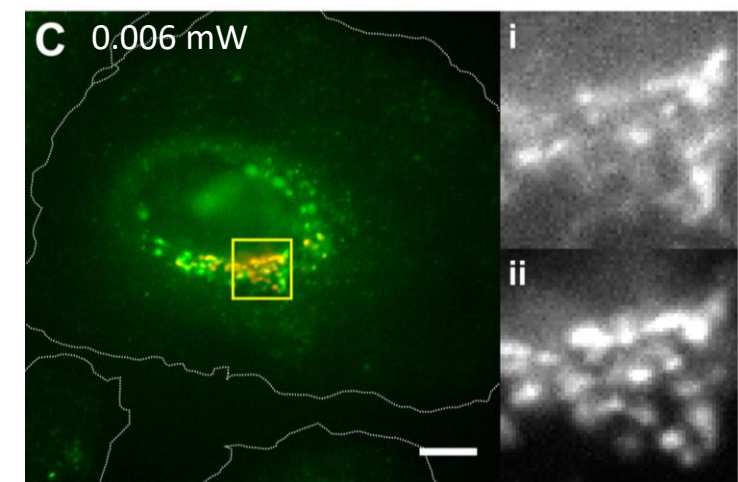
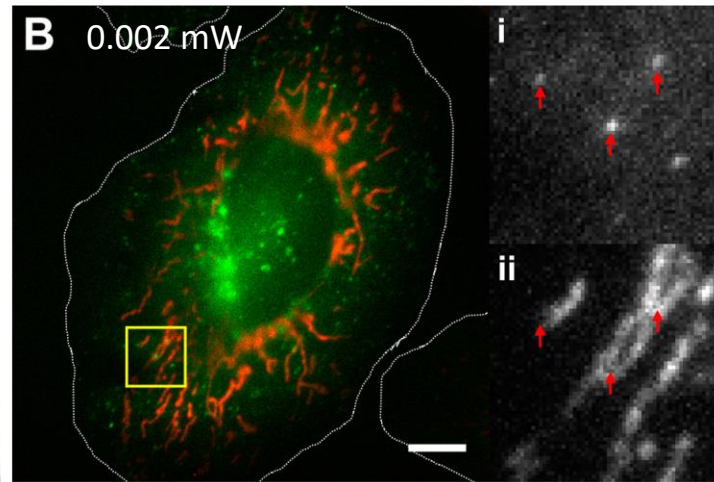
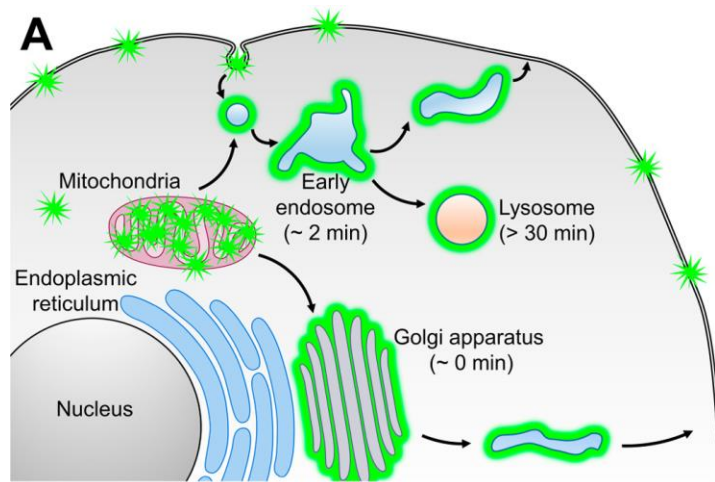


Concentration dependence of **AcroB**-adduct formation



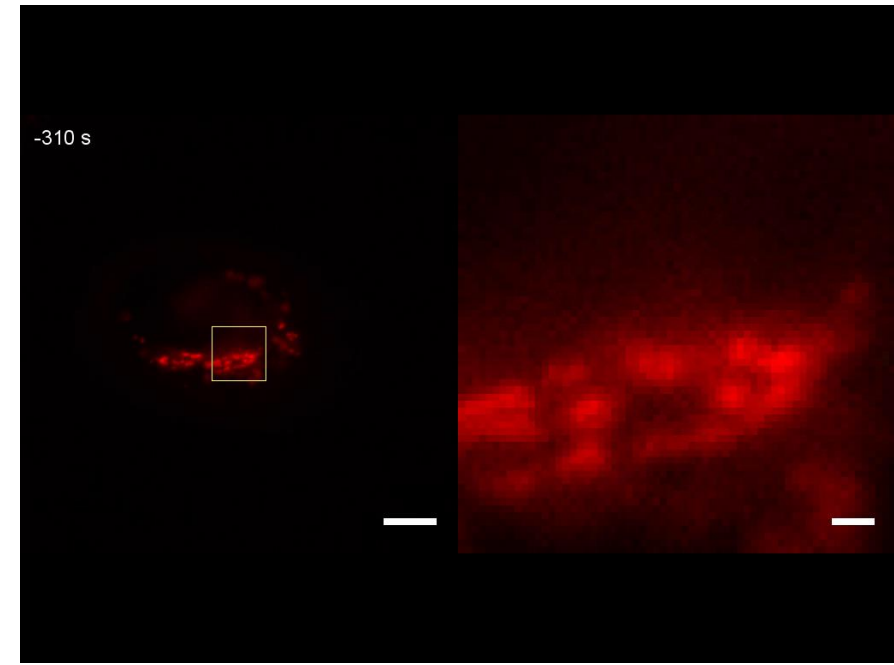
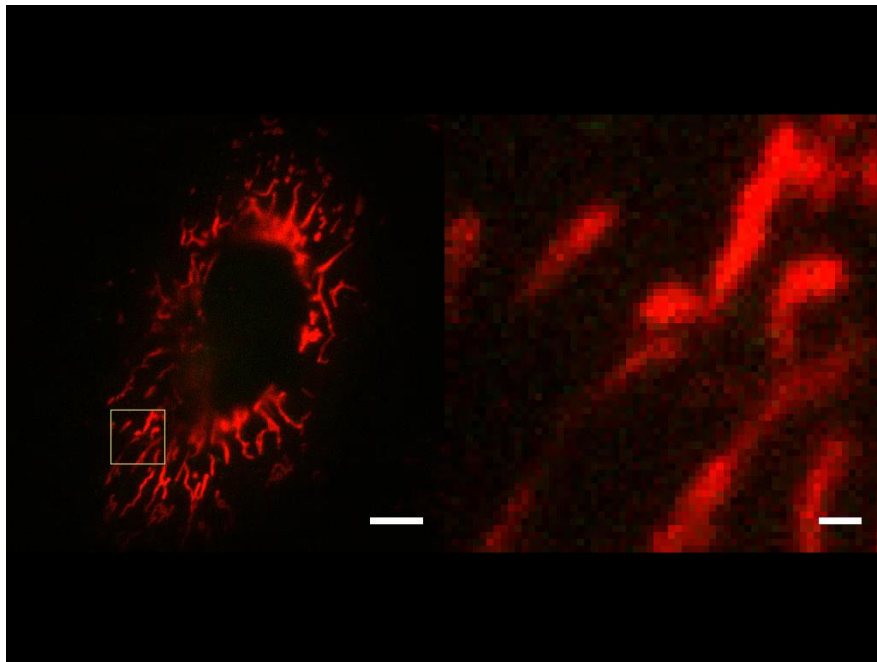
MRC5 (ATCC CCL-171) lung fibroblast cells

# Trafficking Visualized via Colocalization Imaging



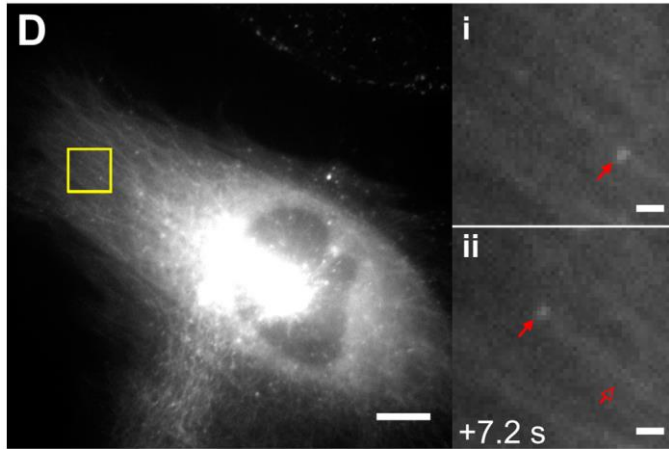
Accumulation of **AcroB**-adducts **outside of mitochondria**

Accumulation of **AcroB**-adducts within **the Golgi apparatus**

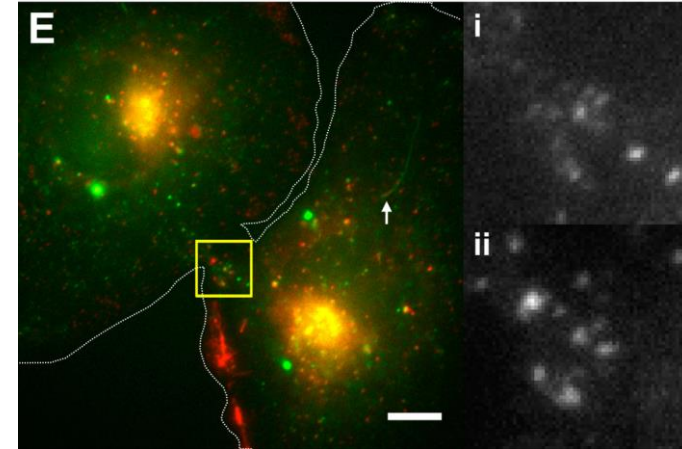




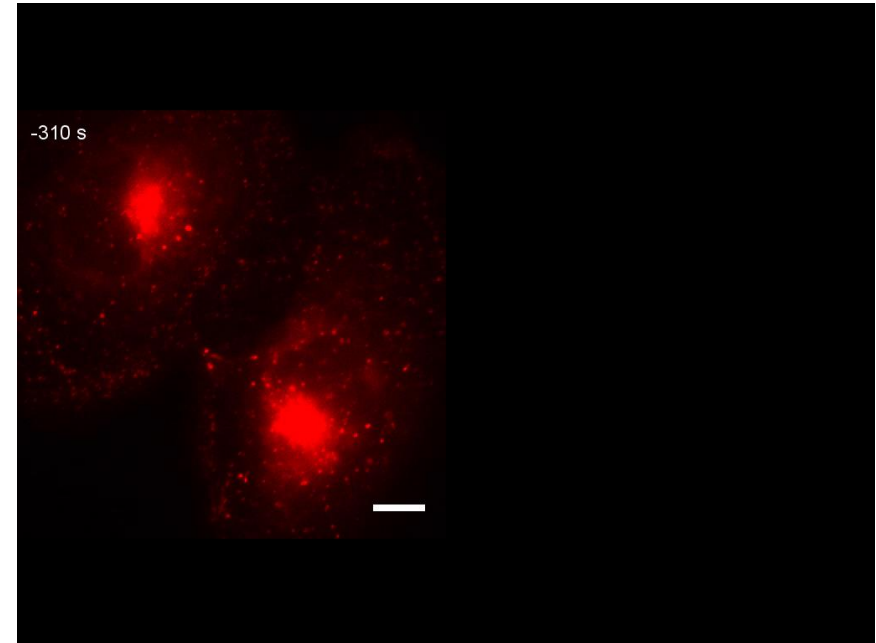
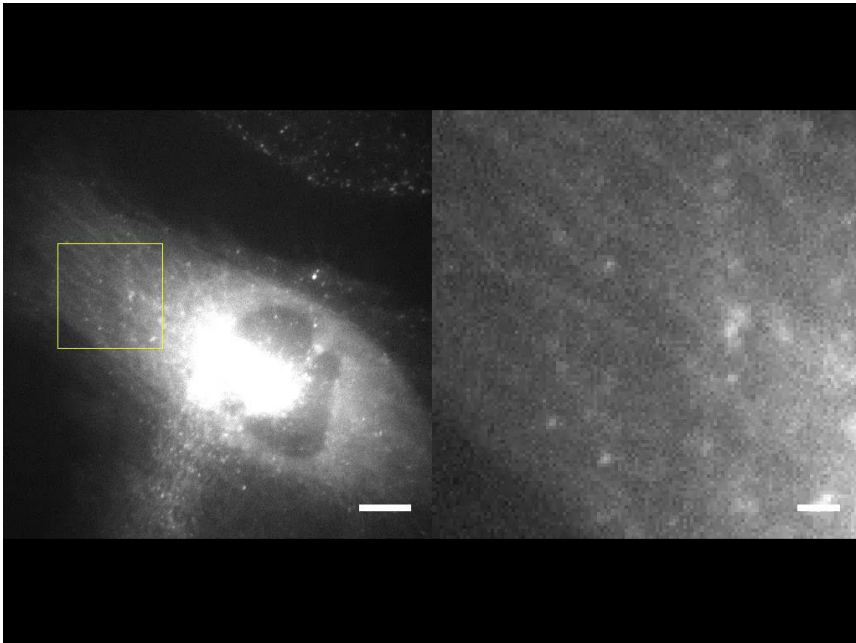
# Trafficking Visualized via Colocalization Imaging



Vesicle transport along **microtubules**

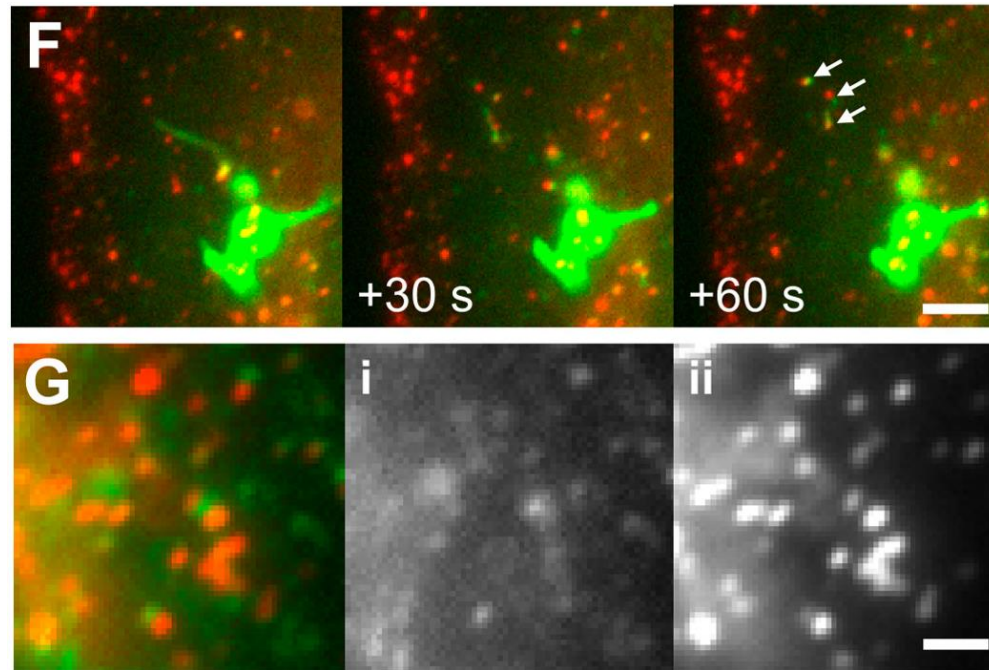


Accumulation of **AcroB**-adducts within **early endosomes**

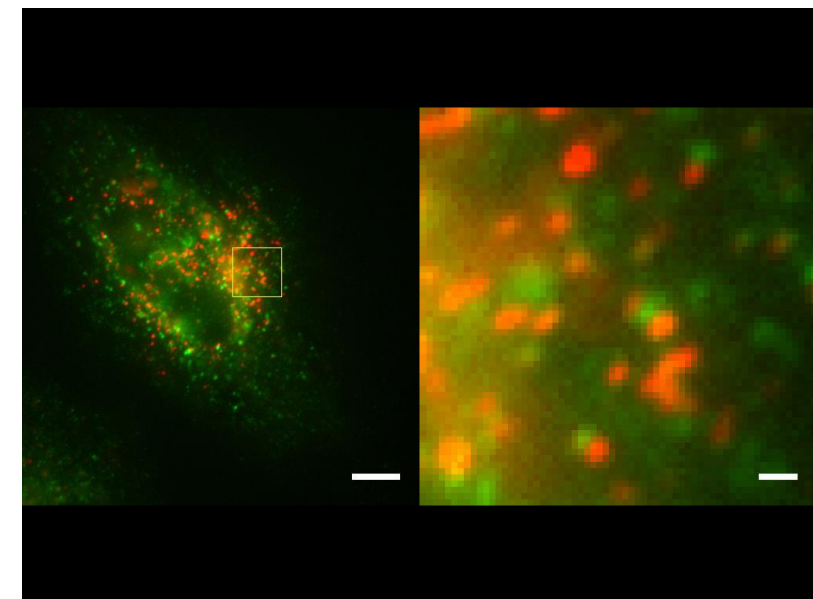
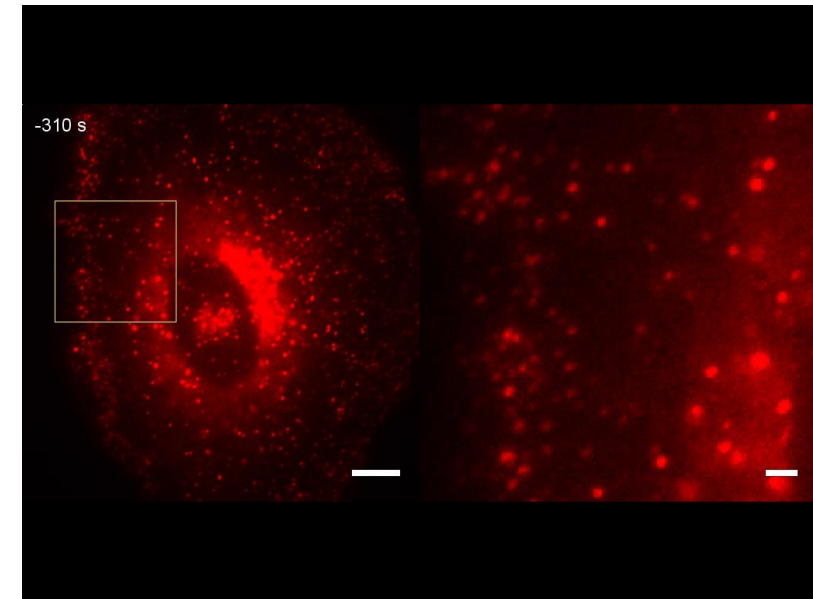




# Trafficking Visualized via Colocalization Imaging

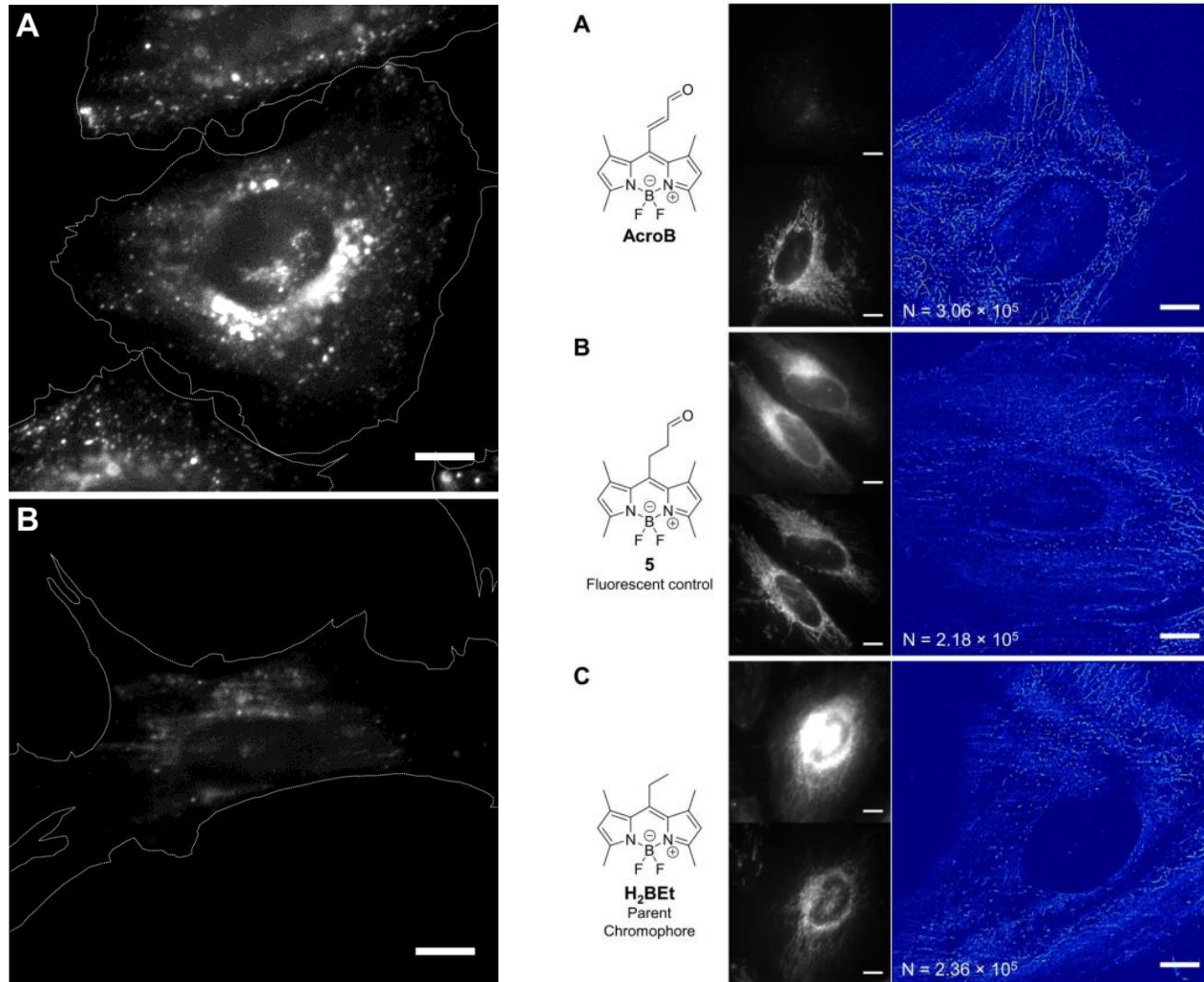


- Sorting of **AcroB**-adducts into **early endosomes**
- Accumulation of **AcroB**-adducts with **lysosomes**

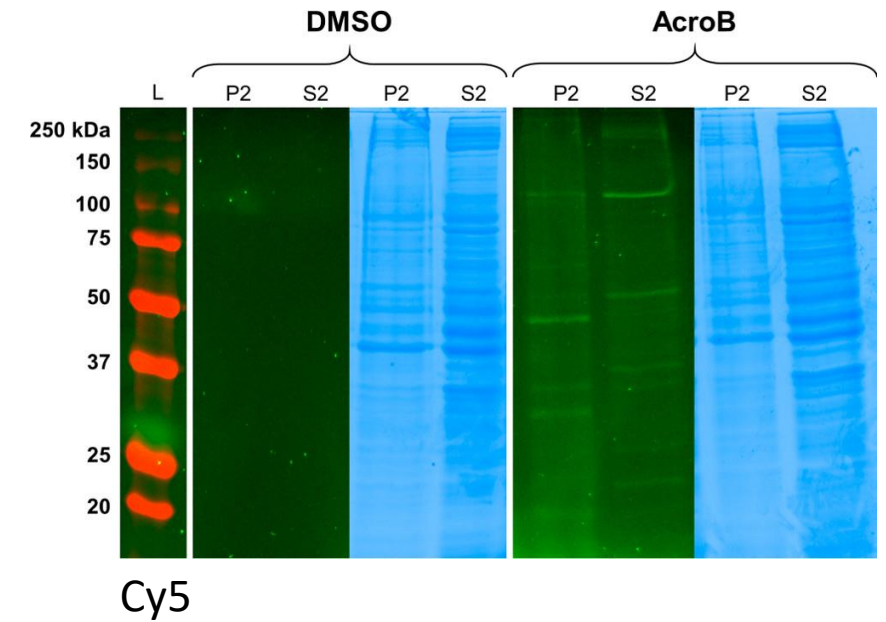


# Trafficking Visualized via Colocalization Imaging

the distribution of BODIPY



P2 (mitochondria, endosomes)  
S2 (cytosolic proteins)



# Summary

---

An approach to study the effects of electrophile alkylation on living cells has been developed

The fluorogenic probe AcroB maps chemical reactions within the cell lipid milieu and reveals the complex system of recycling mechanisms ,sorting and processing electrophile adducts

The new methodology for probing the spatiotemporal response of the cell milieu to electrophiles will be important in understanding neurodegenerative diseases and other pathologies related to LDE