Technology Offer

Caging-group-free photoactivatable fluorescent dyes

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The invention introduces a groundbreaking technology comprising of caging-group-free photoactivatable fluorescent dyes. This innovative approach eliminates the need for conventional caging groups, offering small (500–600 Da), live-cell permeable and non-toxic markers, readily photoactivatable to bright and photostable fluorescent dyes suitable for a variety of applications, including conventional and super-resolution imaging methods, with a detection sensitivity down to a single molecule.

Advantages

- **Caging-group-free activation:** Reduces molecular complexity, simplifies chemical synthesis, and improves solubility and cell permeability.
- **Rapid and efficient photoactivation:** Quantitative conversion to the fluorescent state with low UV (one photon) or NIR (two photon) light doses compatible with the complex cellular environment.
- **Enhanced photostability:** Reduced photobleaching enables longer observation times and single-molecule-level sensitivity.
- **Live-cell labeling:** Cell membrane permeability allows for rapid labeling with state- of the art technologies such as HaloTag, SNAP-tag, and bioorthogonal click chemistry.
- **No toxic or reactive byproducts:** Ensures cell viability and integrity during long-term imaging processes.
- **Compatible with all microscopes:** Suitable for a variety of conventional (confocal, wide-field) and super-resolution microscopy techniques, including PALM/STORM, STED and MINFLUX.
- **Additive-free imaging:** No dedicated media/buffers enables detailed observation of cellular processes without compromising cell health.
- **Broad color options:** Combinable yellow-green, orange, and red emission options with a single dedicated photoactivation wavelength.
- **Large Stokes shift option:** Expands color-channel selection, facilitates multiplexing, and reduces spectral overlap.

Potential applications

- **Fluorescence microcopy and nanoscopy:** Photoactivatable bright and photostable labels for live-cell labeling with protein tags, as organelle specific markers, and immunostaining, in conventional and super-resolution methods.
- **Biomedical research:** Studying cellular processes, such as organelle or protein dynamics, and protein–protein interactions.
- **Pharmaceutical development:** High-throughput imaging screening for drug discovery, target validation and pathway analysis.
- **Clinical diagnostic:** Enhanced labelling for diagnostic probe and sensor development research.
- **Material science:** Tracing and mapping of materials, surfaces and interfaces at the nanoscale, flow and diffusion studies.
- **Neuroscience:** Observation of neuronal structure and activity with high precision.

Max-Planck-Innovation GmbH
Arnulfstr. 58
80335 München
www.max-planck-innovation.de

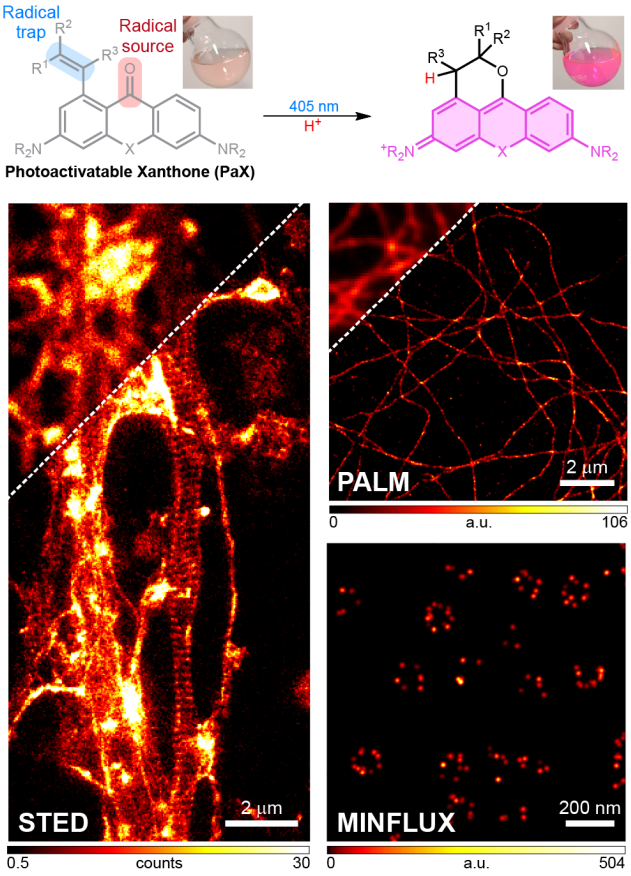

Fig. 1: Photoactivatable xanthones (PaX) enable fluorescence imaging with several conventional and super-resolution microscopy techniques.

Background

Traditional photoactivatable dyes rely on caging groups that add to the molecular mass of the fluorescent label, decrease solubility and can release toxic photoproducts. These new caging-group-free fluorescent labels have been designed with live-cell applications in mind. These labels provide an optimized tool for researchers, with significant improvements over prior art in terms of biocompatibility, efficiency, and imaging quality.

Technology

The technology leverages a novel photoactivation mechanism for a new class of photoactivatable xanthone-based dyes that can be precisely controlled by light without the need for traditional caging groups nor media additives. Upon irradiation, these dyes transition from a non-fluorescent to a bright and photostable fluorescent state, enabling high-resolution imaging of live cells. The dyes cover a wide spectrum of wavelengths and they are compatible with various labeling techniques and state of the art super-resolution microscopy methods.

Patent Information

PCT application (WO 2023284968 A1), entered the national phase in the USA and Europe

Publications

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Arnulfstr. 58
80335 München
www.max-planck-innovation.de

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Contact

Dr. Bernd Ctortecka Senior Patent- & License Manager, Physicist
Phone: +49 (0)89 / 29 09 19 – 20
eMail: ctortecka@max-planck-innovation.de

Max-Planck-Innovation GmbH
Arnulfstr. 58
80335 München
www.max-planck-innovation.de