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Membrane-targeted Molecule for Cell Optostimulation

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Light-driven modulation of cellular activity with both high spatial and temporal resolution is becoming of great interest in science. Existing approaches, such as optogenetics, have shown promising results and, as an alternative, we envision the use of light-sensitive molecules that act as photo-actuators avoiding genetic manipulation.

We present a comprehensive characterization of a newly synthesized conjugate molecule, named BV-1, which spontaneously and efficiently partitions into the lipid bilayers owing to its amphiphilicity.

We performed steady-state and time-resolved spectroscopic measurements revealing the presence of a charge-transfer state upon visible light irradiation as highlighted by its strong solvatochromism. Furthermore, BV-1 can undergo intersystem-crossing towards a triplet state, which can transfer energy to molecular oxygen. Thus BV-1 can be considered as a singlet-oxygen photosensitizer. All the data are supported by quantum chemistry calculations, with good agreement.

In vitro experiments point out that BV-1 shows relatively low toxicity in dark conditions, while the illumination with visible light induces membrane poration and permeabilization, which in turn leads to a robust and persistent depolarization in HEK cells and a phototoxic effect in *E.coli* cultures.

Taken together, our data suggest the occurrence of two independent and likely synergic light-driven mechanisms responsible for the increase of the membrane permeabilization and the formation of pore-like structures: i) the lipid peroxidation due to the presence of singlet oxygen within the cell membrane and ii) the conformational reorganization of BV-1 that alters the integrity of the membrane.