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Fluorogenic Chemical Probes for Wash-Free Imaging of Cell Membrane Damage in Ferroptosis, Necrosis, and Axon Injury
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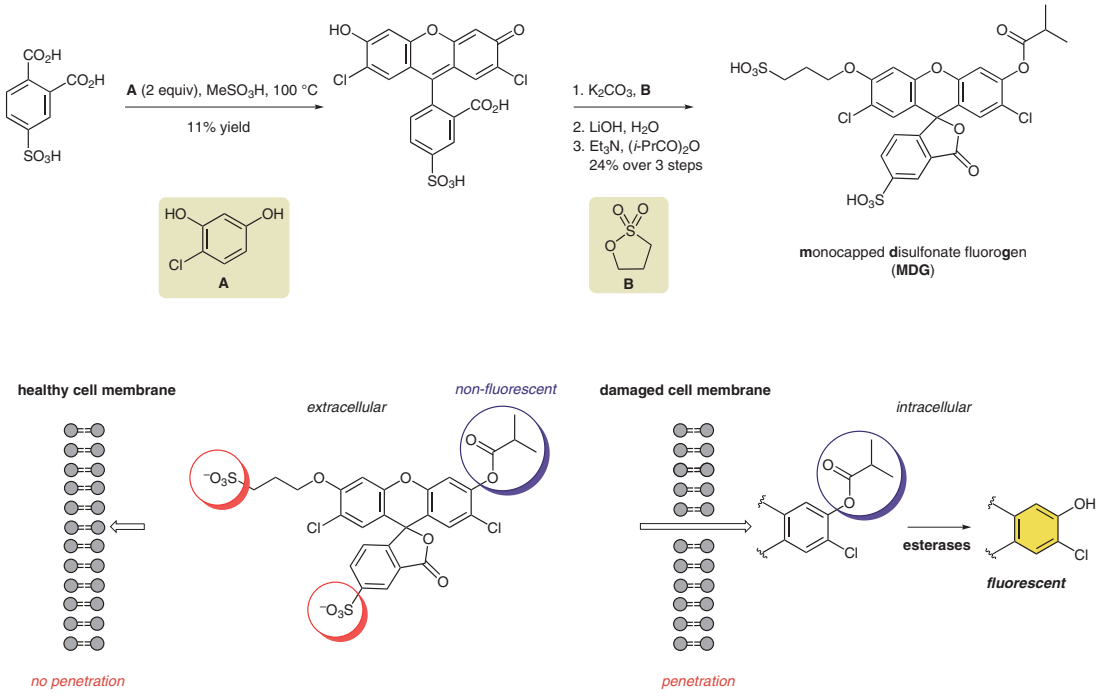
Mastering Cell Penetration: Wash-Free Fluorogenic Probes for Membrane Damage



Significance: Damage to cell membranes is a hallmark in many cellular processes including ferroptosis, necrosis, and axonal degeneration. Selectively labeling those cells that have suffered membrane damage is thus an important goal in biomedical research. Currently used labeling agents are permanently colored (trypan blue), need washing to remove non-penetrated dye to achieve a good image contrast or require potentially toxic DNA-binding for fluorescence (DAPI). The authors developed fluorophores that are virtually non-fluorescent in the extracellular space and can only penetrate damaged membranes. This allows for selective and wash-free imaging of cells that have sustained membrane damage.

Comment: Mauker, Beckmann, Thorn-Seshold, and co-workers designed fluoresceins that contain two permanently charged sulfonate groups and an isobutyrate ester. By virtue of the sulfonate groups, these **m**onocapped **d**isulfonate fluoro**g**ens (reasonably abbreviated as **MDG**) can only penetrate cells with damaged membranes. Inside the cells, esterases cleave the ester bond and thus lead to onset of fluorescence. Because fluorescence is limited to the intracellular space no washing is needed. They commence their synthesis of **MDG** by condensing 4-sulfophthalic acid and 4-chlororesorcinol (**A**). The resulting sulphofluorescein is then alkylated with 1,3-propane sultone (**B**). The concomitantly formed ester is hydrolyzed and the remaining phenol is converted to the isobutyrate ester (**MDG**).

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membrane damage

Synfact of the Month