Synopsis of Original Research Paper

Bioimaging of lipid peroxidation induced by cell damage or aging

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Oxidative stress due to cell damage or aging results in lipid peroxidation, which produces various lipid radicals and α, β-unsaturated aldehydes. The highly reactive aldehyde species readily modify specific or unspecific protein sites and maybe involved in many diseases such as atherosclerosis and cancer. Although many analytical methods have been developed for lipid peroxidation, imaging of the aldehydes in living cells is still challenging due to lack of appropriate chemical probes. Here, I designed, synthesized an investigated two aryl azide-based fluorescence probes to detect acrolein, the shortest α, β-unsaturated aldehydes with a three carbon unit, and an alkoxyamine-based probe targeting the reactive aldehydes. One of the aryl azide-based probes with a 7-nitrobenzoxadiazole scaffold yielded the corresponding formyl triazole product upon reaction with acrolein. The reaction product showed substantially red-shifted absorbance compared to the unreacted probe, however, instability of the azide group in the probes may limit their use for the imaging of acrolein in living cells. The other probe containing a rhodamine scaffold with an alkoxyamine substituent showed pH-dependent absorbance and fluorescence spectra, which are characteristic for many rhodamine derivatives due to the open and closed spirocyclic forms in equilibrium. When it was mixed with α, β-unsaturated aldehydes at pH 7, significant increase of absorbance and fluorescence was observed likely because the open form was stabilized for the reaction product. Thus, the probe was applied to HeLa cells. Confocal microscopy images showed fluorescence increase in some cellular compartments. Co-labeling the cells with a lysosome-targeted dye revealed that the probe turned to fluorescence in lysosome, where the local pH is known to be 4.5-5.0. Accumulation of the probe in lysosome may hamper the desired imaging of the reactive aldehyde species. Further investigation is in progress to determine where the probe distributes in the cells and if it can detect endogenous aldehydes under oxidative stress.