Biocompatible probes for imaging of cellular structures

The ideal fluorescent probe for bioimaging is bright, absorbs at long wavelengths (> 600 nm) and can be flexibly implemented in living cells and in vivo. Typically, such probe consists of a fluorophore connected via a linker to a targeting moiety. Availability of targeting ligands is assured by a large number of studies aiming at development of inhibitors for a wide range of biomolecules. However, the design of synthetic, highly biocompatible fluorophores has proven to be extremely difficult and is lagging behind. Silicon-rhodamine was identified as a far red dye that can be specifically coupled to proteins, lipids and nucleic acids using different techniques. Importantly, its high permeability and fluorogenic character permit imaging of proteins in living cells and tissues, while its brightness and photostability make it ideally suited for live-cell super-resolution microscopy. Further investigation resulted in identification of the cell-permeable fluorophores spanning the whole visible spectrum. Despite these developments, generation of small molecule fluorescent probes still remains challenging. A major concern is that the use of an inhibitor as a targeting moiety often makes the staining detrimental to the function of a biomolecule. A promising way to solve this problem is the use of cleavable linkers which allow specific covalent labelling of a large biomolecule of interest with a fluorophore, while targeting moiety is cleaved and can be washed away. These probes would minimally disturb the imaged system and would be applicable for fluorescence microscopy and nanoscopy of a wide range of organisms and tissues. As an example, I will highlight the strategy to develop such probes targeting cytoskeleton and chromatin.

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