BIOORTHOGONAL CHEMICAL IMAGING FOR BIOMEDICINE

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Innovations in light microscopy have tremendously revolutionized the way researchers study biological systems with subcellular resolution. Although fluorescence microscopy is currently the method of choice for cellular imaging, it faces fundamental limitations for studying the vast number of small biomolecules. This is because relatively bulky fluorescent labels could introduce considerable perturbation to or even completely alter the native functions of vital small biomolecules. Hence, despite their immense functional importance, these small biomolecules remain largely undetectable by fluorescence microscopy. To address this challenge, we have developed a bioorthogonal chemical imaging platform. By coupling stimulated Raman scattering (SRS) microscopy, an emerging nonlinear Raman microscopy technique, with tiny and Raman-active vibrational probes (e.g., alkynes, nitriles and stable isotopes including 2H and 13C), bioorthogonal chemical imaging exhibits superb sensitivity, specificity, multiplicity and biocompatibility for imaging small biomolecules in live systems including tissues and organisms. Exciting biomedical applications such as imaging fatty acid metabolism related to lipotoxicity, glucose uptake and metabolism, drug trafficking, protein synthesis, DNA replication, protein degradation, RNA synthesis and tumor metabolism will be presented. This bioorthogonal chemical imaging platform is compatible with live-cell biology, thus allowing real-time imaging of small-molecule dynamics. Moreover, further chemical and spectroscopic strategies allow for multicolor bioorthogonal chemical imaging, a valuable technique in the era of "omics". We envision that the coupling of SRS microscopy with vibrational probes would do for small biomolecules what fluorescence microscopy of fluorophores has done for larger molecular species, bringing small molecules under the illumination of modern light microscopy.