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Selective fluorescent probes for molecular imaging of ROS/RNS: Challenges and opportunities

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An ever expanding array of biological processes such as development, aging, inflammation, immunity, cancer and neurodegeneration is dynamically sculpted by chemical mediators – reactive oxygen/nitrogen species (ROS/RNS) including superoxide anion radical ($O_2^{\bullet-}$), hydrogen peroxide (H_2O_2), hydroxyl radical ($^{\bullet}OH$), hypochlorous acid (HOCl) and peroxynitrite ($ONOO^-$). The formation, metabolism and detoxification of ROS/RNS contribute to human health and disease in complex ways, while heterogeneity in chemical behavior of ROS/RNS in cells renders selective detection of single ROS/RNS extremely challenging. With their intrinsic advantages such as high sensitivity, practical handling, inexpensive instrumentation, and ease of functional modifications, small-molecule fluorescent probes represent an ideal biorthogonal approach to ROS/RNS detection. Here we report novel sensing strategies and development of the **HKGreen**,[1-4] **HKSOX**,[5] **HKOCl**,[6,7] and **HKOH** series of fluorescent probes for the detection and molecular imaging of $ONOO^-$, $O_2^{\bullet-}$, HOCl, and $^{\bullet}OH$, respectively, featuring excellent selectivity and sensitivity toward the target species. In several platforms including live cell confocal imaging, microplate assay, flow cytometry, tissue staining and *in vivo* zebrafish imaging, the applicability of the probes has been thoroughly validated. Overall, these probes offer exciting opportunities for selective detection and molecular imaging of single ROS/RNS with greater depth, resolution and confidence.

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