Nanosensors for Reactive Oxygen Species: Reactive oxygen species (ROS) has been implicated as an important underlying cause in cancer and many neurodegenerative diseases. However, the molecular mechanisms that connect ROS to carcinogenesis and these pathological conditions remain insufficiently understood. This is mainly because most of our current understanding of the effects of ROS has come from indirect endpoint measurements such as DNA, protein damage and lipid peroxidation. These measurements only assess the cumulative effects of ROS and provide limited information on the molecular mechanisms of such effects. We proposed the development of novel fluorescence-based photonic nanosensors capable of direct and selective detection of ROS. We will use the proposed nanosensors to monitor changes in intracellular ROS concentration and distribution directly during carcinogenesis. By correlating these changes to the regulation of key cancer biomarker from parallel bioassays, we hope to further elucidate the differential roles of individual ROS in carcinogenesis and the molecular mechanisms of such roles. To achieve these goals, we have synthesized several potential ROS probes by introducing various benzenesulfonyl groups onto the fluorescein molecule. Unlike traditional ROS probes, these benzenesulfonyl-fluorescein derivatives detect ROS based on non-oxidative mechanisms, rendering selectivity toward different ROS. By varying the type and position of the substituent on the benzenesulfonyl group, the reactivity of the fluorescein derivative can be tuned. The selectivity of these probes toward different ROS is the topic of an on-going study. The outcome of this study will be used in further assisting the design of ROS probes with improved specificity toward individual ROS. We have also prepared amine-modified silica nanoparticles as the nano-platform for the ROS probes. Several parameters were varied in an effort to reduce the size of the nanoparticles and produce nanoparticles with more uniform size. In a proof-of-concept experiment, we successfully incorporated fluorescein isothiocyanate (FITC) onto the amine-modified silica nanoparticles. The feasibility of obtaining functional nanosensors through covalent attachment of benzenesulfonyl-fluorescein-based ROS probes was demonstrated. We plan to use these preliminary results to guide our synthesis of additional ROS probes and conduct more extensive selectivity study. We also plan to evaluate the performance of the nanosensors using a model cell system in the near future.

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