Glycobiology is poised to be the next revolution in biology and medicine; however, technical difficulties in detecting and characterizing glycans have prevented many biologists from entering this field, thus hampering new discoveries and innovations. This research program aims at developing a conceptually novel technology that will allow straightforward identification of specific glycosylation patterns in biofluids and in live cells. Distinct glycosylation states will be differentiated by developing “artificial noses” the size of a single molecule, whereas selectivity toward specific glycoproteins can be obtained by attaching them to specific protein binders. To achieve high sensitivity and accuracy, several innovations in molecular recognition and fluorescence signaling have been integrated into the design of these unconventional molecular analytical devices.

Over the last years, we have validated the two main concepts underlying this proposal, namely, the ability to sense surfaces of specific proteins (1-7) and the ability to discriminate among a vast number of different analytes by using unimolecular, pattern-generating fluorescent molecular probes. (8,10) We have also shown how these two principles be integrated to afford a unimolecular fluorescent probe that can identify specific populations of protein biomarkers in biofluids and can discriminate among isoforms in living cells (11). The His-tag binders (1) protein surface receptors (1,4), and ‘turn-on’ fluorescent probes,(3) which were suggested in our proposal, have been successfully developed. Based on these achievements, a functional glycosylation sensor that can analyze the glycosylation pattern of the Human chorionic gonadotropin (hCG) protein has already been developed and used to discriminate among glycoform mixtures (12). In addition to tracking glycosylation, the unique technologies that emerged from this research program have yielded new ideas and design principles that are relevant to various areas in chemistry. Developing pattern-generating molecular probes and devices, (8,10) targeted, protein surface receptors, (1-7) and biomimetics of signaling proteins (4-6) are some of the original research directions that emerged from this study and that are being independently pursued.


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