David G Churchill, J Alzheimers Dis Parkinsonism 2016, 6:5(Suppl)
http://dx.doi.org/10.4172/2161-0460.C1.021

Chalcogen-richorganic molecular probes for intended neurodegenerative disease purposes

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In the pursuit of advances in neurodegenerative disease research, our laboratory is currently working on chemical synthesis along three directions: protein phosphorylation and phosphate/phosphonylation detection, aromatic organoselenium-based chemistry, and MRI contrast agent technologies are all active areas in our chemical laboratory. In our organoselenium work, we are interested in making next-generation small molecular probes for the detection of reactive oxygen species. We are pursuing reversibility, as well as improved selectivity and sensitivity. This is undertaken in the context of also studying biothiols. Sulfur, selenium, or tellurium canbe placed within a ring, and within a π-delocalized manifold for chemical oxidation, or also as a substituent on the aromatic ring. This oxidation, as observed previously by M. Detty et al. (1990), imparts a significant electronic effect on the π-delocalized system and is enough to dramatically alter photophysical properties ("turn-on" fluorescence). The chemical oxidation of an "in-ring" selenium or tellurium also brings with it a possible concomitant sterical contribution that is also important. We have taken to functionalizing BODIPY systems–an extension of research from seeking new corrole chemistry. Recently, we have opened up to using other fluorophores; two general design parameters that are often exploited are (i) the aryl rotational group and (ii) the donor-acceptor photoinduced electron transfer (PET) mechanism. Based on previous results, we saw that profound differences can be imparted by substituting a thiophene for a phenyl group. Further, substituting Se in place of S, or adding gearing groups help alter the PET mechanism–a strategy that can be combined with chalcogen chemical oxidation/reduction. We often conduct many interference studies and cuvette assays, but also consider the probe when taken up into living cells, especially those of relevance to neurological diseases. Also, some of our work has ties with Fenton chemistry. New π-delocalized skeletons that we discover can be further exploited within the topic of molecular sensing. As always, synthesis is central to our work and emergent utility of these materials is being pursued.

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