Hide and seek: How do DNA glycosylases locate oxidatively damaged DNA bases amidst a sea of undamaged bases?

Dr. Suzan Wallace, University of Vermont

The first step of the base excision repair (BER) pathway responsible for removing oxidative DNA damage utilizes DNA glycosylases to find and remove the damaged DNA base. Although much is known about the biochemistry of DNA glycosylases, how glycosylases find the damaged base amidst a sea of undamaged bases using only thermal energy has long been a question in the BER field. Single molecule total internal reflection fluorescence microscopy (SM TIRFM) with tightropes of lambda DNA molecules suspended on silica beads, have allowed for an exciting look into this search mechanism and has shown that DNA glycosylases scan around the DNA backbone in a bidirectional and random fashion. By comparing the search behavior of bacterial glycosylases from different structural families and with varying substrate specificities, we found that glycosylases search for damage by periodically inserting a wedge residue into the DNA stack as they redundantly search tracks of DNA that are 450-600 base pairs in length. Similar results have been found for the mammalian glycosylases OGG1 and MUTYH. However, APE1, the second enzyme in the BER pathway, travels much faster exhibiting one dimensional diffusive behavior. We are now working with tightropes of plasmid DNA containing site-specifically placed lesions. Taken together, these studies open up a wealth of possibilities for further study in real time of the interactions between DNA glycosylases and the downstream BER enzymes with various DNA substrates.

Date: Friday, December 1, 2017
Time: 11:00 a.m. to 12:00 p.m.
Location: AHC3– 205, MMC (Live)
Marine Sciences Building Room 105 (MSB-105) – BBC (via Polycom)