Regulated protein degradation in eukaryotes is performed by the proteasome, which contains a 20S catalytic core particle (CP) capped at either end by a 19S regulatory particle (RP). Substrates for the proteasome are typically marked by post-translational addition of ubiquitin chain(s). The proteasome captures such substrates through receptors located in the RP that bind directly to ubiquitin or to shuttle factors that bind the proteasome with UBL domains and ubiquitin with UBA domains. Together with our collaborators, we have found that the RP houses three major receptors for ubiquitinated substrates, Rpn1, Rpn10 and Rpn13. We have used NMR to define how Rpn13 is assembled into the proteasome and to find how each of these receptors bind to ubiquitinated substrates. In Rpn1, tandem recognition sites for the ubiquitin fold exist within a toroid structure that provides at one location an interaction surface for ubiquitin or the UBL-UBA shuttle factor Rad23 and at the other, a binding site for deubiquitinating enzyme Ubp6/Usp14. We have determined the structure of the Rpn1 ubiquitin recognition site with K48 linked ubiquitin chains or with the Rad23 UBL domain. This study provides mechanistic understanding of how the proteasome captures its ubiquitinated substrates.

Bio

Dr. Walters is Acting Chief and a Senior Investigator in the Structural Biophysics Laboratory of the Center for Cancer Research in the National Cancer Institute (NCI). Her team members use a variety of research techniques, especially NMR spectroscopy, to study how the proteasome recognizes and processes its ubiquitinated substrates. She received her Ph.D. in Biophysics from Harvard University, where she worked in Dr. Gerhard Wagner’s group. She was a postdoctoral fellow at Harvard Medical School in Dr. Peter Howley’s lab before joining the University of Minnesota as an Assistant Professor, where she was an American Cancer Society Research Scholar. Dr. Walters joined the NCI in 2013 as a Senior Investigator.