The nucleosome is the target of multiple chromatin enzymes and factors in the nucleus, but the molecular basis for how this multicomponent protein/DNA complex is recognized is largely unknown despite the crystal structure determination of the nucleosome 14 years ago. As part of our efforts to understand how the cell acts on its DNA genetic material packaged as chromatin, we are investigating how chromatin modification enzymes such as histone acetyltransferases (HATs) and chromatin factors such as RCC1 (regulator of chromosomal condensation) interact with the nucleosome.

RCC1's association with the nucleosome recruits and activates the small GTPase Ran protein, creating a concentration gradient of RanGTP (Ran in its GTP bound state) around the chromosomes. This RanGTP gradient is a key positioning signal within the cell required for mitosis, nucleocytoplastic transport and nuclear envelope dynamics. We have determined the molecular basis for how RCC1 interacts with the nucleosome through a combination of biochemical studies and the crystal structure of the 300 kDa RCC1/nucleosome core particle complex at 2.9 Å resolution. We find that RCC1's β-propeller domain recognizes the architecture of the nucleosome through a combination of both protein-protein and protein-DNA interactions. Our crystal structure also provides a first atomic view of the nucleosome core particle containing the Widom 601 DNA sequence. We find that the 601 DNA forms a 145 bp nucleosome core particle and is thus overwound compared to human alpha-satellite DNA.