

Cross-linking histones and DNA to prevent transient site exposure

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Research Experiences for Undergraduates

Exposure to radical oxygen species, UV light, or toxins causes DNA damage. If left uncorrected, damaged bases may pair with incorrect base pairs, introducing permanent errors into the DNA sequence. DNA repair enzymes excise damaged bases to prevent mutagenesis.

Although DNA repair is well-characterized in free DNA, it is unknown how DNA repair

enzymes gain access to DNA densely packed in chromatin. The basic unit of chromatin is the nucleosome core particle: 146 base pairs of DNA wrapped around a protein “spool” of eight histones. DNA repair enzymes may access to DNA when it spontaneously unwraps from the histone octamer.

Undergraduate student Janina Moretti (HMC) hopes to investigate this model by creating nucleosome core particles with DNA covalently bonded to the histone octamer. By introducing cysteine residues into histones at sites that come in contact with DNA, disulfide bonds can be formed between the histone and DNA bases with modified thiol linkers. This summer Janina identified five potential cross-linking sites. She purified recombinant wild-type and mutant histones and refolded individual histones into the octamer.

