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CRISPR-associated transposons (CASTS) enable programmable DNA insertion, yet there is a limited understanding of how they recognize specific DNA sequences and activate DNA insertion. Dr. Jeffery Swan will conduct structural and kinetic studies of CASTs in Dr. Elizabeth Kellogg's lab at Cornell University. Dr. Swan will investigate the AAA+ (ATPases Associated with diverse cellular Activities) regulator TnsC which influences both ATP hydrolysis and DNA deformation. He will use cryo-electron microscopy to structurally characterize the fully assembled integration complex, and single-molecule and ensemble kinetic experiments to better understand transpososome assembly and activation. Swan anticipates that these studies will guide future attempts to rationally engineer CASTs for gene-editing and therapeutic applications.

As a Ph.D. student in Dr. Carrie Partch's lab at the University of California at Santa Cruz, Swan investigated the role of the KaiC, an AAA+ protein that effectuates circadian timing. Dr. Swan demonstrated that the ATPase activity in KaiC imparts cooperativity to the transition between autophosphorylation and autodephosphorylation, which is an important feature of the circadian clock. With his expertise in AAA+ proteins, Dr. Swan is ready to investigate how TnsC enables the programmable DNA insertion of CASTs.

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