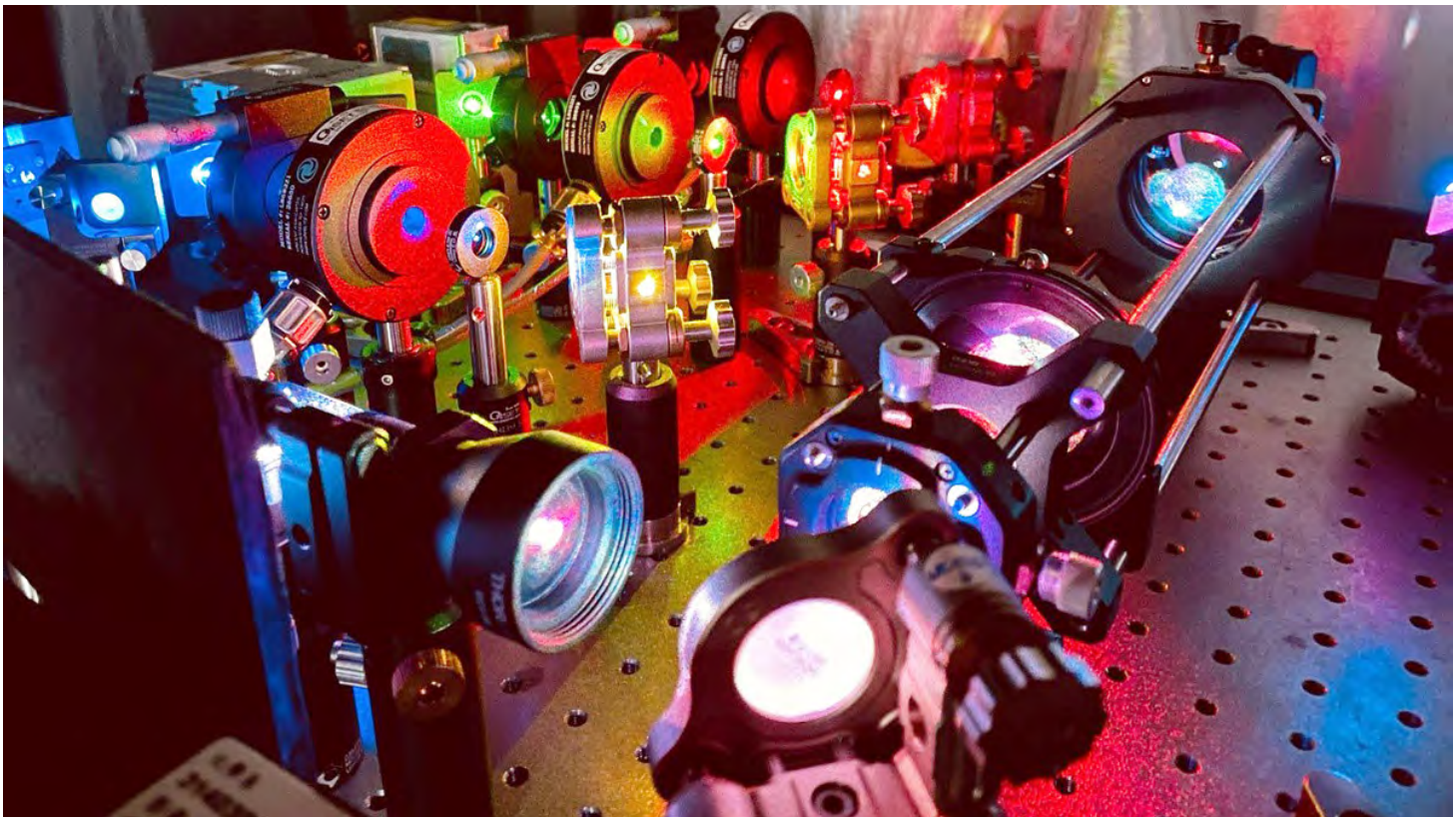
ACHIEVEMENTS

Interdisciplinary Collaboration Unveils Key Mechanistic Insights into DNA Recombination



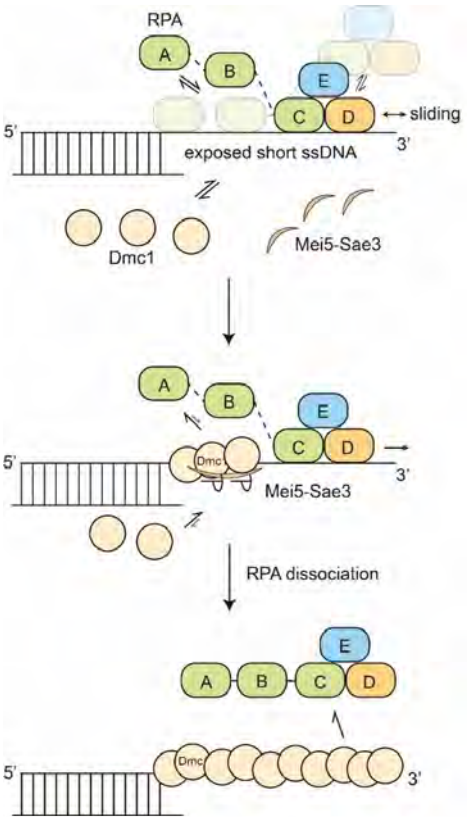
Key Technology: The single-molecule fluorescence microscope used in this study, demonstrates the crucial role of advanced technology in unraveling the complexities of DNA recombination.

Meiotic recombination is crucial for generating genetic diversity and ensuring proper chromosomal segregation during reproduction. This complex process requires recombinases to assemble on single-stranded (ss) DNAs, forming nucleoprotein filaments that facilitate homology search and strand exchange between homologous DNAs. However, ssDNAs are typically bound by abundant, high-affinity ssDNA-binding proteins (RPA), which protect these ssDNAs from degradation. The Mei5-Sae3 protein complex plays an essential role in assembling recombinases onto RPA-coated ssDNA, though the exact mechanism behind this has remained unclear—until now.

An interdisciplinary research team with members from NTU's Department of Chemistry, Institute of Biochemical Sciences, as well as from Osaka University, has employed advanced technologies, including single-molecule FRET and Colocalization Single-Molecule Spectroscopy (CoSMoS), to capture the intricate dynamics of this complex process. By using these cutting-edge technologies and proteins of high purity, the team observed the interactions between Dmc1 recombinase and Mei5-Sae3 on individual DNA molecules with exceptional time resolution, leading to mechanistic insights that traditional ensemble-based approaches could not provide.

The study revealed that the Mei5-Sae3 complex stabilizes Dmc1 nucleating clusters on DNA by preferentially reducing Dmc1 dissociation, ultimately promoting the dissociation of RPA from ssDNA. By using GFP-labeled RPA, the team observed the formation of an intermediate complex containing both Dmc1 and RPA on the ssDNA before RPA dissociation. This groundbreaking discovery unveils the first molecular model of how a mediator-recombinase interaction stimulates recombinase assembly and regulates the recombination process.

The study's co-first authors include NTU undergraduate Chemistry student Chin-Dian Wei, highlighting NTU's commitment to engaging students in cutting-edge research. Other contributing authors are Hao-Yen Chang, Chia-Hua Lu, Chih-Chun Chang, Asako Furukohri, and Stephen Mwaniki, with senior authors Peter Chi (NTU IBS), Hung-Wen Li (NTU Chemistry), and Akira Shinohara (Osaka University) leading the collaborative effort. This research was supported by the National Science and Technology Council (NSTC), NTU, and Osaka University.



Model: The Mei5-Sae3 protein complex stimulates Dmc1 assembly on RPA-coated DNA, shedding light on the intricate mechanisms of DNA recombination.

Group photo of the project research team.

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