- SIM microscopy reveals 3D Genome Repair Dynamics and Organization in Response to Double-Strand Breaks
- Cohesin, 3D Genome Reorganization, and DNA Repair: Insights from vfCRISPR and SIM Microscopy
- Elucidating the Higher-Order Molecular Assembly of Cohesin in DNA repair

Spatiotemporal Regulation of Cohesin-Mediated, Double-Strand Break Response Revealed by Super-Resolution Imaging and very fast CRISPR

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Abstract

How the three-dimensional (3D) genome organizes in response to DNA double-strand breaks (DSB) is a critical, yet not fully understood aspect of genome maintenance. The cohesin complex has been implicated in DNA repair, and defects in this complex can lead to erroneous genomic rearrangements during DNA damage, resulting in genome abnormalities and cancer. Recent research highlights the essential role of genome topology and chromatin spatial organization in DNA damage response and repair mechanisms. However, prior studies have been limited by their lack of spatiotemporal resolution and control over the genomic regions targeted for DSB repair. The Ha lab developed a light-activating CRISPR technology, termed very fast CRISPR (vfCRISPR), that offers the necessary temporal resolution, specificity, and precision for inducing DSBs in living cells. In this project, I employ vfCRISPR in combination with structured illumination microscopy (SIM) to investigate the nanoscale architectures of 53BP1 and cohesin subunits and examine their spatial coordination in 3D. Furthermore, I evaluate the spatiotemporal recruitment of cohesin at DNA damage sites and reveal the changes in 3D organization arrangements over time. By comprehending the organization of cohesin at a higher resolution in cells, this study provides valuable insights into its molecular functions in DNA repair and potential implications in various diseases.