Imaging the genome with CRISPR

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Award: New Innovator Award
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The spatial architecture and temporal dynamics of the genome play critical roles in regulating its function. However, visualizing endogenous DNA sequences in living cells remain challenging due to the lack of imaging tools. We developed such a tool by repurposing the bacterial CRISPR system, previously engineered for RNA-guided gene editing and regulation. We utilized an EGFP-tagged endonuclease-deficient Cas9 protein and a structurally-optimized small guide (sg) RNA to enable robust imaging of both repetitive and non-repetitive DNA sequences in the nucleus. The target flexibility of the CRISPR system allows us to simultaneously track multiple genomic loci, helping to elucidate chromosome structure change during the cell cycle. Our study defines a new class of genome imaging tool and highlights its potential to exploit genomic organization and dynamics in living cells.