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Novel Method of Using Modified and Optimized Bacterial-derived Genetic CRISPR System for Imaging, Regulating and Editing Mammalian Genomic Elements

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OTHER INFORMATION

KEYWORDS

CRISPR, Genome editing, small guide RNA, Genome imaging, Cas9

CATEGORIZED AS

- ▶ **Imaging**
- ▶ Medical
- ▶ Molecular
- ▶ **Medical**
- ▶ Diagnostics
- ▶ Gene Therapy
- ▶ Research Tools
- ▶ **Research Tools**
- ▶ Nucleic Acids/DNA/RNA

RELATED CASES

2014-045-0

INVENTION NOVELTY

This invention is a novel method using optimized small guide RNAs (sgRNAs) to enable dynamic imaging, editing and regulation of specific genomic elements in living mammalian cells via the CRISPR system.

VALUE PROPOSITION

The best current technology for imaging specific DNA sequences in living cells has relied on fluorescently tagged DNA-binding proteins, an approach that is restricted to imaging artificial repetitive sequences inserted into the genome or specialized genomic elements. While fluorescence in situ hybridization (FISH) enables target sequence flexibility through base pairing of the nucleic acid probes, it is incompatible with live imaging due to sample fixation and DNA denaturation. A genome-imaging technique that combines the flexibility of nucleic acid probes and the live imaging capability of DNA-binding proteins would thus be a major advancement in enabling the study of genomic conformation and dynamics in living cells.

This novel invention provides the following advantages:

- Non-invasive live cell imaging of specific genomic elements (i.e., telomeres, centromeres, single genes) in mammalian cells.
- Detects spatiotemporal organization and dynamics of native chromatin structure.
- Enhanced efficiency and specificity (>50% increase) of genomic imaging, regulation and editing.
- Robust, flexible, highly sensitive and high resolution platform.
- High-throughput detection of multiple genomic events and disease-associated elements (i.e., aberrations in gene copy numbers, deletion, duplication & rearrangement).
- Modified and optimized sgRNA structure with increased stability, improved expression level and Cas9 assembly, and thus enhanced targeting efficiency.

TECHNOLOGY DESCRIPTION

Scientists at the University of California, San Francisco have developed a novel method for imaging chromosome, chromatin structure and specific genes in living mammalian cells. By rationally designing and optimizing structures of sgRNAs, inventors have enabled the dynamic imaging, editing and regulation of specific genomic elements via the CRISPR system.

The imaging system consists of an EGFP-tagged, endonuclease-deactivated dCas9 protein and a custom designed sgRNA. The structure of the sgRNA has been intensively modified to enhance its expression level, stability, target specificity and molecular assembly with the dCas9 protein in mammalian cells. The optimized sgRNA sequence and structure has proprietary advantages over original sgRNAs that are used for all genome editing and gene editing and regulation applications. The sgRNA also contains a designable 20-30 nt

base pairing region that is complementary to any chromosome site of interest.

The method is highly sensitive with high resolution, and can be used for chromosome or gene copy detection and dynamic analyses in the living cells. This optimized CRISPR system notonly enables dynamic tracking of repetitive elements such as telomeres andcentromeres, it also enables visualization of non-repetitive genomic sequences in thehuman genome. Investigators are currently working on the direct delivery of RNAs forcellular imaging, multi-color imaging, and using this method to detect and diagnose genetic disorders.

APPLICATION

- ▶ Optimized sgRNAs with enhanced efficacy (50% increase) for genome editing, transcription, epigenetic regulation or genome imaging
- ▶ High resolution, non-invasive genome imaging in living cells
- ▶ Detection of highly repetitive and complex genome sequence and structure
- ▶ Large-scale diagnostics of diseases and genetic disorders related to genome deletion, duplication and rearrangement
- ▶ Multiplexed genome imaging and diagnostics for complex diseases
- ▶ Diagnose diseases with unknown causes (e.g., resulting from misorganized genome structures).
- ▶ Enhancing FISH labeling efficacy
- ▶ Disease-specific genetic assays

LOOKING FOR PARTNERS

To develop this technology into a molecular kit for genome editing, a reagent for genome imaging or a diagnostics kit for disease specific genetic assays.

STAGE OF DEVELOPMENT

pre-clinical

RELATED MATERIALS

- ▶ [Chen B. et al Dynamic Imaging of Genomic Loci in Living Human Cells by an Optimized CRISPR/Cas System. Cell 2013](#)

DATA AVAILABILITY

under CDA/NDA

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	10,822,606	11/03/2020	2014-045
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