Add-Seq: Quantitative Genome-Wide, Single-Molecule, And Long-Range Nucleosome Profiling

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BACKGROUND

In cells, DNA is organized by wrapping DNA strands around histone proteins, creating protein-DNA complexes called nucleosomes which comprise the basic unit of chromatin. Chromatin is associated with regions of low gene expression, as compacted DNA is inaccessible to proteins that would promote transcription. Conversely, regions in the DNA not bound by histones experience higher gene expression, as this DNA is readily available to be transcribed.

Nucleosomes are not uniformly positioned on a DNA molecule, and they change based on factors like which genes are expressed during different cellular processes. It is beneficial to understand where nucleosomes are positioned, as this can provide insight into how genes are regulated, or how factors like epigenetic modifications or chromatin structure affect this accessibility and can additionally illuminate gene expression patterns in disease for designing therapies.

Nucleosome profiling is a technique used to study the positions of nucleosomes along a DNA molecule. Typically, histones are crosslinked to DNA, then the DNA is fragmented and digested leaving only regions protected by nucleosomes left for short-read sequencing. However, this fragmentation only reveals nucleosome positioning at the resolution of a few hundred base pairs, leaving the larger genomic context of these nucleosome positions to be desired. To address this, researchers at UC Santa Cruz developed Add-SEQ, a pipeline using long-read nanopore sequencing to map nucleosomes across long stretches > 10 kb of single DNA molecules.

TECHNOLOGY DESCRIPTION

Add-SEQ was developed to address the need for a wider genomic context during nucleosome profiling. This technology uses angelicin crosslinking to hybridize histones to DNA. The angelicin-bound DNA is then sequenced with nanopore sequencing and analyzed with a computational pipeline to determine locations of previously bound nucleosomes on long DNA strands. This larger genomic context allows for nucleosomes to be called across an entire gene or even multiple genes, and affords the ability to map nucleosomes to highly repetitive regions.

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OTHER INFORMATION

KEYWORDS

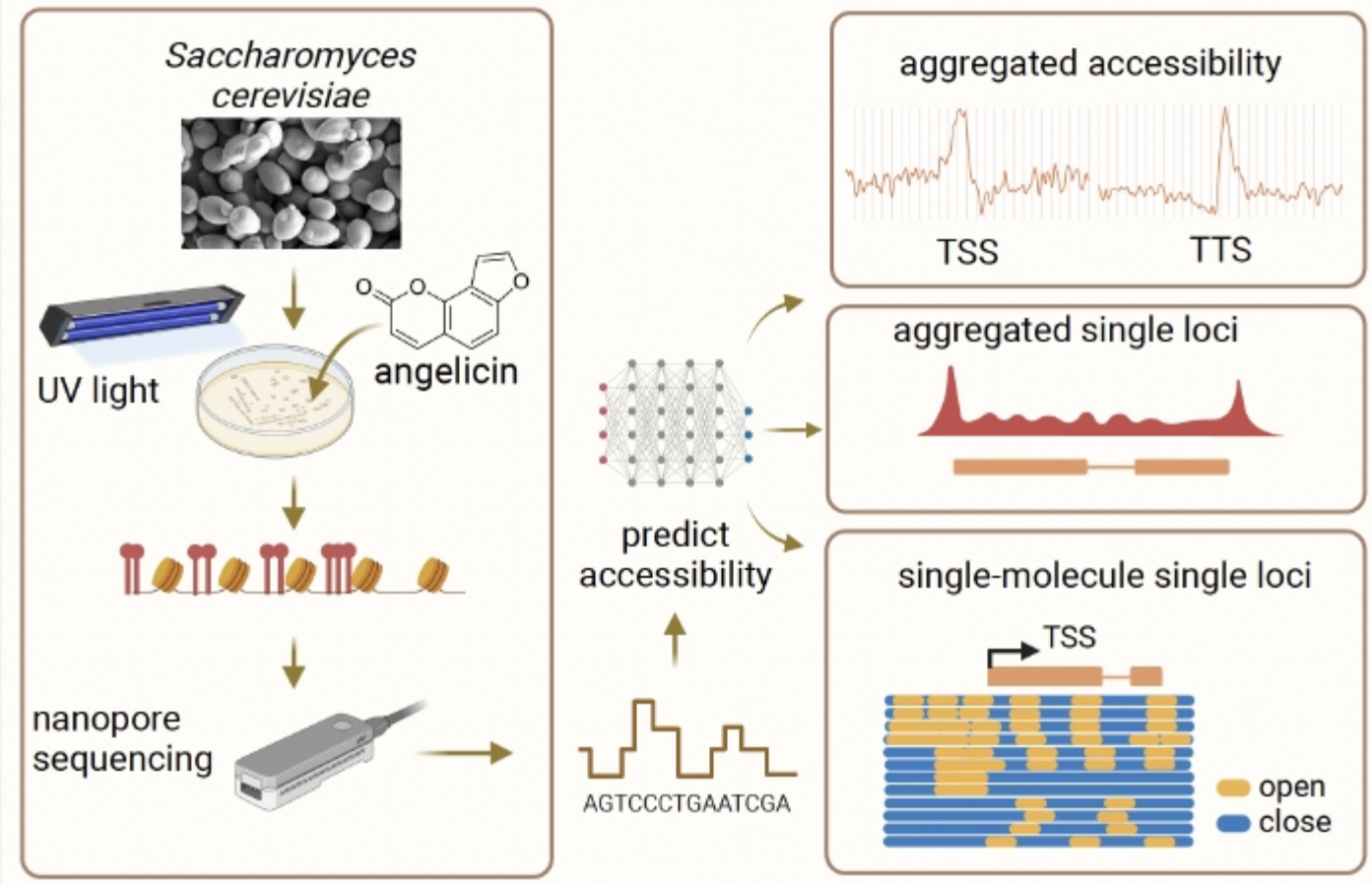
nucleosome profiling, nanopore, single molecule, long-read sequencing, chromatin, gene regulation, epigenetics, crosslinking

CATEGORIZED AS

- **Biotechnology**
  - Genomics
  - Other
- **Research Tools**
  - Nucleic Acids/DNA/RNA
  - Other

RELATED CASES

2018-393-0



APPLICATIONS

- gene expression and regulation
- multigene nucleosome profiling
- map epigenetic modifications
- chromatin dynamics
- disease mechanisms of gene expression

ADVANTAGES

- nucleosome profiling across long stretches of DNA

INTELLECTUAL PROPERTY INFORMATION

Country	Type	Number	Dated	Case
United States Of America	Published Application	20210054438	02/25/2021	2018-393

RELATED MATERIALS

- SMAdd-seq: probing chromatin accessibility with small molecule DNA intercalation and nanopore sequencing - 08/12/2025

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