Methods For Adding Polymers Of Modified Nucleotides To Natural RNAs

Tech ID: 33040 / UC Case 2019-503-0

BACKGROUND

When this invention was originally conceived, there were no systems available for sequencing the entire length of an RNA transcript. Next Generation Sequencing (exemplified by the Illumina® sequencing platform) only allows sequencing of short (70-150 base reads) and only cDNA templates.

Direct, long read RNA sequencing, (exemplified by nanopore sequences produced by Oxford Nanopore Technologies) can sequence an entire polyadenylated transcript (when a poly-T adapter is included), but not a non-polyadenylated transcript - it misses the last nucleic acids. It is also unable to accurately determine the length of the poly-A region of the polyadenylated transcript.

Researchers at UC Santa Cruz developed a system that solves this problem. The entire length of a natural RNA can now be sequenced, unlocking new insights into RNA expression and variability.

TECHNOLOGY DESCRIPTION

The addition of a short polymer of non-canonical (or modified) nucleotides (i.e. not found in natural RNA or DNA) results in a strong and unique signal in a nanopore sequencer that clearly indicates the junction between the added modified nucleotides and the natural nucleotides.

In one application, modified nucleotides can be added to the end of the poly-A tail of a eukaryotic mRNA and the length of the poly-A tail readily determined.

Sequences prior to the junction indicate the natural end of the original RNA. This further enables quantification of the numbers of RNAs in a sample with a given 3' end structure.

Non-canonical nucleotides are added by a polynucleotide-3' nucleotidyl transferase and can be any non-canonical nucleotide that elicits a strong signal in nanopore sequencing.

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OTHER INFORMATION

KEYWORDS

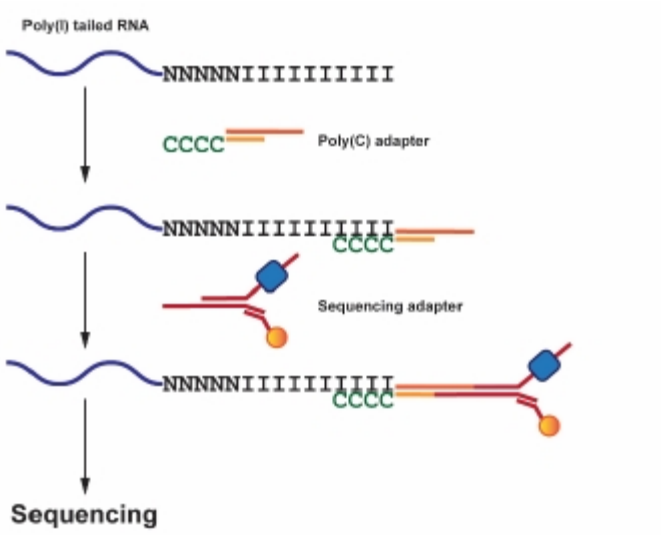
Nanopore sequencing, RNAseq, Full length RNA sequencing, Determining poly-A length, RNA sequencing

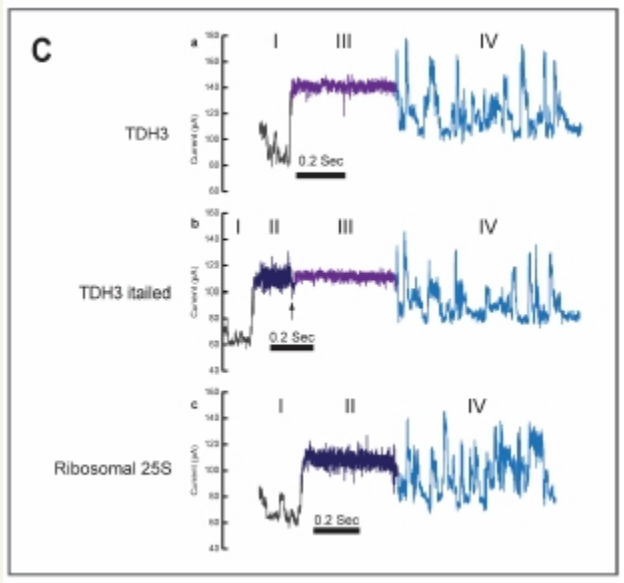
CATEGORIZED AS

- **Biotechnology**
  - Genomics

RELATED CASES

2019-503-0





APPLICATIONS

Sequencing the natural 3' ends of RNAs by nanopore sequencing

Determining the length of an RNA poly-A tail by nanopore sequencing

Measuring specific RNA concentration in a sample

ADVANTAGES

Only method that results in accurately identifying the natural sequence of the entire 3' end of an RNA - including the length of the poly-A tail in a eukaryotic mRNA.

Non-canonical nucleic acids clearly signal of the end of the natural sequence.

INTELLECTUAL PROPERTY INFORMATION

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	11,926,819	03/12/2024	2019-503
United States Of America	Published Application	20240247251	07/25/2024	2019-503

RELATED MATERIALS

- Synthesis of modified nucleotide polymers by the poly(U) polymerase Cid1: application to direct RNA sequencing on nanopores - 08/26/2021

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Methods for Determining Base Locations in a Polynucleotide
- Methods of Producing Size-Selected Nucleic Acid Libraries and Compositions and Kits for Practicing Same
- Reading The 5 Prime End Of Eukaryotic Poly(A) Rna Molecules

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