Methods for Global RNA-Chromatin Interactome Discovery

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BACKGROUND

Recent decades of genomic research reveal that mammalian genomes are more prevalently transcribed than previously anticipated. It is now quite clear that mammalian genomes express not only protein-coding RNAs but also a large repertoire of non-coding RNAs that have regulatory functions in different layers of gene expression. Many of those regulatory RNAs appear to directly act on chromatin, as exemplified by various long noncoding RNAs (lncRNAs). Some of those regulatory RNAs mediate genomic interactions only in cis, while others, such MALAT1 and NEAT1, are capable of acting in trans. These findings suggest an emerging paradigm in regulated gene expression via specific RNA-chromatin interactions. Various techniques have been developed to localize specific RNAs on chromatin. These methods, such as chromatin Isolation by RNA purification or comprehensive identification of RNA binding proteins (ChIRP), capture hybridization analysis of RNA targets (CHART), and RNA affinity purification (RAP), all rely on using complementary sequences to capture a specific RNA followed by deep sequencing to identify targets on chromatin. Importantly, all of these methods only allow analysis of one known RNA at a time, and up to date, a global view is lacking on all RNA-chromatin interactions, which is critical to address a wide range of functional genomics questions.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have developed a general protocol and methodology for systematic localization of all potential chromatin-interacting RNAs in an unbiased fashion. This approach involves mapping Global RNA Interactions with DNA by deep sequencing (GRID-seq) via using a bivalent linker to ligate RNA to DNA in situ and present a global picture on RNA-chromatin interactions, exposing distinct classes of cis- and trans-acting RNAs in both human and Drosophila genomes.

APPLICATIONS

This invention provides a method to detect chromatin interacting RNAs in any given state of a cell or tissue by examining global RNA interactions with DNA by deep sequencing. This invention further provides methods to generate a global view of the chromatin-RNA interactome by mapping the binding locations on the genome of each detected chromatin interacting RNA.

ADVANTAGES

This invention allows for systematic localization of all potential chromatin-interacting RNAs in an unbiased fashion.

STATE OF DEVELOPMENT

Utilization of this methodology revealed a large set of both coding and non-coding RNAs in both human and Drosophila genomes that are prevalently associated with enhancers, particularly super-enhancers, which enable us to infer enhancer-promoter connectivity in 3D genomes.

INTELLECTUAL PROPERTY INFO

This technology has a patent pending and is available for licensing.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	20180039729	02/08/2018	2016-341

CONTACT

University of California, San Diego
Office of Innovation and Commercialization
innovation@ucsd.edu
tel: 858.534.5815.



OTHER INFORMATION

KEYWORDS

RNA-chromatin, 3D Genomes, deep sequencing, noncoding RNA, chromatin-RNA interactome, enhancer-promoter

CATEGORIZED AS

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

RELATED CASES

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University of California, San Diego
Office of Innovation and Commercialization
9500 Gilman Drive, MC 0910, ,
La Jolla,CA 92093-0910

Tel: 858.534.5815
innovation@ucsd.edu
https://innovation.ucsd.edu
Fax: 858.534.7345

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