Docket #: S11-281

ChiRP - RNA interactome analysis

ChiRP (“Chromatin Isolation through RNA Purification”) is a patented RNA “interactomics” technique developed in Prof. Howard Chang's laboratory to capture and identify DNA, RNA or protein molecules that interact with any RNA of interest in a cell. This method includes a single, unbiased, high throughput protocol for isolating all macromolecules associated with an RNA molecule. This is followed by downstream assays for identification and quantitation. The technology also includes a computational pipeline to both design oligonucleotide probes and analyze results (click thumbnail image below to view illustration of work flow).

Thousands of non-coding RNA molecules are now known to have a variety of functional roles - such as regulating chromatin remodeling, gene expression, cancer, aging and many other important biological processes. Just as ChIP-seq has opened the door for genome-wide DNA-protein interactions, ChIRP-seq studies of the “RNA interactome” may reveal many new kinds of biology.

Stage of Research
The inventors have demonstrated the sensitivity and specificity of ChIRP on known interactions with roX2 (FDR = 0). They have also used the technique to reveal new principles of noncoding RNA biology with two human long noncoding RNAs (lncRNAs TERC and HOTAIR).

Applications

- **RNA Research** to characterize the entire space of molecules that interact with any given RNA:
    - DNA (ChIRP-seq)
    - RNA (ChIRP-RNAseq)
    - proteins (ChIRP-protein-mass spectrometry)

Advantages

- **High throughput** - designed for genome wide assays (compared to prior techniques that analyze one locus at a time)
- **Comprehensive and unbiased:**
  - general protocol allows concurrent identification of proteins, DNA, and RNA, saving time from optimization of separate purification processes
  - applicable to any RNA of interest without prior knowledge of the structure or functional domain of the RNA
- **Specific:**
  - for ChIRP-DNA-sequencing, extensive controls are in place to ensure specificity (FDR = 0 in positive control experiments)
  - for ChIRP-protein-mass spectrometry, stringent protocol measures the RNA capture profile in a quantitative manner and demonstrate a typical 1:1000 fold enrichment of target RNA, yielding highly specific proteome data
- **RNA capture** - this is the first method developed that can identify RNA interactions with other RNA molecules

Publications

- Ci Chu, Kun Qu, Franklin L. Zhong, Steven E. Artandi, Howard Y. Chang, Genomic Maps of Long Noncoding RNA Occupancy Reveal Principles of RNA-Chromatin Interactions, *Molecular Cell* Nov. 18, 2011, published online Sept. 29, 2011 (doi:10.1016/j.molcel.2011.08.027)
- Mary Muers, RNA: Genome-wide views of long non-coding RNAs Nature Review Genetics 12, 742-743 (November 2011).

Patents

- Published Application: 20130123123
- Issued: 8,748,354 (USA)

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