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## PRESS RELEASE

### New study profiles the chromatin dissociation dynamics of newly transcribed RNA

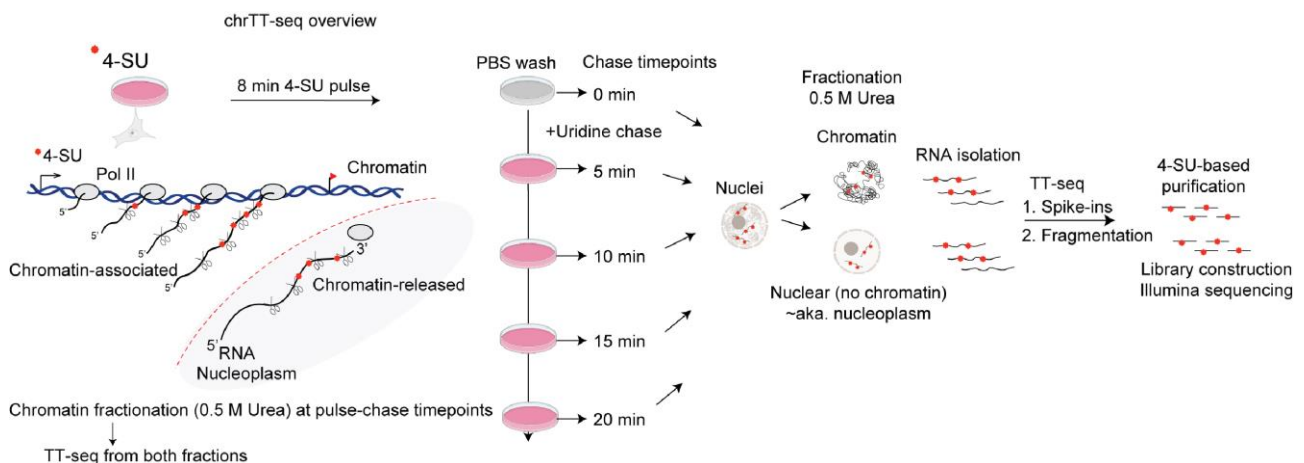
A new research study, product of a collaboration by researchers at IMBB FORTH and Helmholtz Center Munich, published yesterday in the peer reviewed scientific journal *Cell Systems*, describes how modeling the dynamics of chromatin dissociation of newly transcribed RNA can reveal more about the subnuclear localization, processing and functional potential of long non-coding RNAs.

The biggest portion of the human genome is transcribed into various non-coding RNA species, some of which with regulatory potential, while most with unexplored functions. Playing an important role in regulation of gene expression, enhancers are distal regulatory elements that produce such short and long non-coding RNAs (lncRNAs). lncRNAs transcribed from enhancers show high cell-type and cell-state specificity, which renders them promising therapeutic targets.

In order to understand features of enhancer transcription and uncover differential processing of enhancer-transcribed lncRNAs, Evgenia Ntini, group leader at IMBB FORTH, first and co-corresponding author of the study, established a new method (chrTT-seq) to follow nascent RNA transcripts from their transcription on chromatin to their release (Figure 1). This allows measuring their processing, and assessing chromatin dissociation dynamics of newly transcribed RNA.

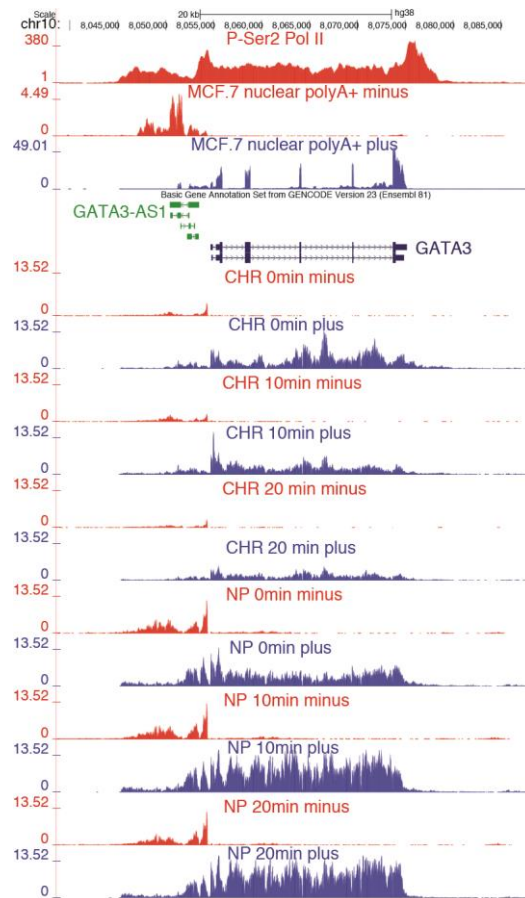
**Figure 1**

**a.**



Nikolaou Plastira 100  
Vassilika Vouton  
GR 700 13 Heraklion  
Crete, Greece  
Tel. +30 2810391700  
Fax +30 2810391101  
Email: imbb@imbb.forth.gr

b.



Legend: Method overview

- a. chrTT-seq combines pulse-chase metabolic labeling with chromatin fractionation and deep sequencing.
- b. Following chromatin dissociation dynamics at the GATA3 (protein coding gene, mRNA) - GATA3-AS1 (lncRNA, antisense) locus. UCSC tracks depict nascent RNA read coverage (blue, plus strand; red minus strand) at 0, 10, 20 min pulse-chase timepoints, from the chromatin-associated ('CHR') and chromatin-released (aka. nucleoplasmic, 'NP') fraction.

The experimental data were used to train machine-learning models to predict distinct degrees of chromatin dissociation and identify features that are either important for fast chromatin release, or associated with slow release and chromatin tethering. "We find a range of chromatin dissociation rates for newly transcribed RNAs", Ntini says, "and could identify features, like splicing and distinct binding probabilities for specific RNA binding proteins, that underlie these dynamics. Furthermore, lncRNAs transcribed from enhancers and the anchor points of chromosomal loops display fast chromatin release. Thus, calling them 'enhancer-associated' does not imply that they remain 'chromatin-tethered'".

Overall, understanding the processing and dynamics of subcellular and subnuclear localization of lncRNAs, along with their compartment-specific RNA-binding protein interactions, can help elucidate more about their functional potential in health and disease, and drive the design of effective RNA-based therapeutic strategies.



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**More info:**

Evgenia Ntini  
Principal Researcher, IMBB-FORTH  
eMail: [evgenia.ntini@imbb.forth.gr](mailto:evgenia.ntini@imbb.forth.gr) | Tel.: +30 2810391378

**Relevant links:**

<https://www.imbb.forth.gr/imbb-people/en/research-ntini>  
<https://doi.org/10.1016/j.cels.2023.09.005>