Nature Reviews Genetics | AOP, published online 9 July 2013; doi:10.1038/nrg3534

NON-CODING RNA

Ribosomes, but no translation, for lincRNAs

> this study provides an approach that should be more widely applicable to determining what proportion of the transcriptome is translated

Long intergenic non-coding RNAs (lincRNAs) are emerging as a class of important regulatory molecules. Although several lines of evidence indicate that the functions of most lincRNAs do not involve the translation of a protein, the finding that many of these transcripts are occupied by ribosomes has challenged this. A new study describes a more accurate means of distinguishing between coding and non-coding transcripts than by simply looking at ribosome occupancy; this supports a non-coding view of lincRNA function.

Ribosome profiling is a recently developed method that involves digesting RNA and sequencing the portion that is bound by 80S ribosomes to give a profile of ribosome occupancy along transcripts. In 2011, Ingolia *et al.* used this method to show that a large set of mammalian lincRNAs are bound by ribosomes, raising the possibility that these transcripts encode small proteins.

Now, the same researchers and their collaborators have reassessed these findings. Guttman *et al.* showed that even in the case of transcripts for which a non-coding nature is firmly established — such as small nucleolar RNAs — ribosomal binding is seen using ribosome profiling. This finding led them to look for a better way of distinguishing between coding and non-coding RNAs.

It is well-documented that ribosomes that are engaged in translation are released from transcripts when they reach a stop codon. As a result, when ribosome profiling is applied to protein-coding transcripts, this is seen as an abrupt drop in ribosome occupancy in 3′ untranslated regions (UTRs). Guttman *et al.* reasoned that this translational termination should not occur for non-coding transcripts and developed a metric that they termed the ribosome release score (RRS) to distinguish between coding and non-coding transcripts on this basis.

Indeed, the authors showed that RRS discriminates well between known protein-coding RNAs and known non-coding RNAs. Importantly, RRS categorizes lincRNAs with the well-established non-coding RNAs, indicating that lincRNAs generally are not translated into proteins.

As well as its implications for lincRNA biology, this study provides an approach that should be more widely applicable to determining what proportion of the transcriptome is translated. It also raises questions about ribosome binding to non-coding transcripts — is this just noise, or does it serve a biological function?

Louisa Flintoft

ORIGINAL RESEARCH PAPER Guttman, M. *et al.* Ribosome profiling provides evidence that large noncoding RNAs do not encode proteins. *Cell* http://dx.doi.org/10.1016/j.cell.2013.06.009 (2013)

FURTHER READING Ingolia, N. T., Lareau, L. F. & Weissman, J. S. Ribosome profiling of mouse embryonic stem cells reveals the complexity and dynamics of mammalian proteomes. *Cell* **147**, 789–802 (2011)

Getty