

Extensive transcriptional heterogeneity revealed by isoform profiling

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Overview

- Transcript isoforms (TIF): RNAs that traverse the same region on genome, but have different start and end sequences
- Study was carried out in yeast
- Identify TIF variation and its functional relevance

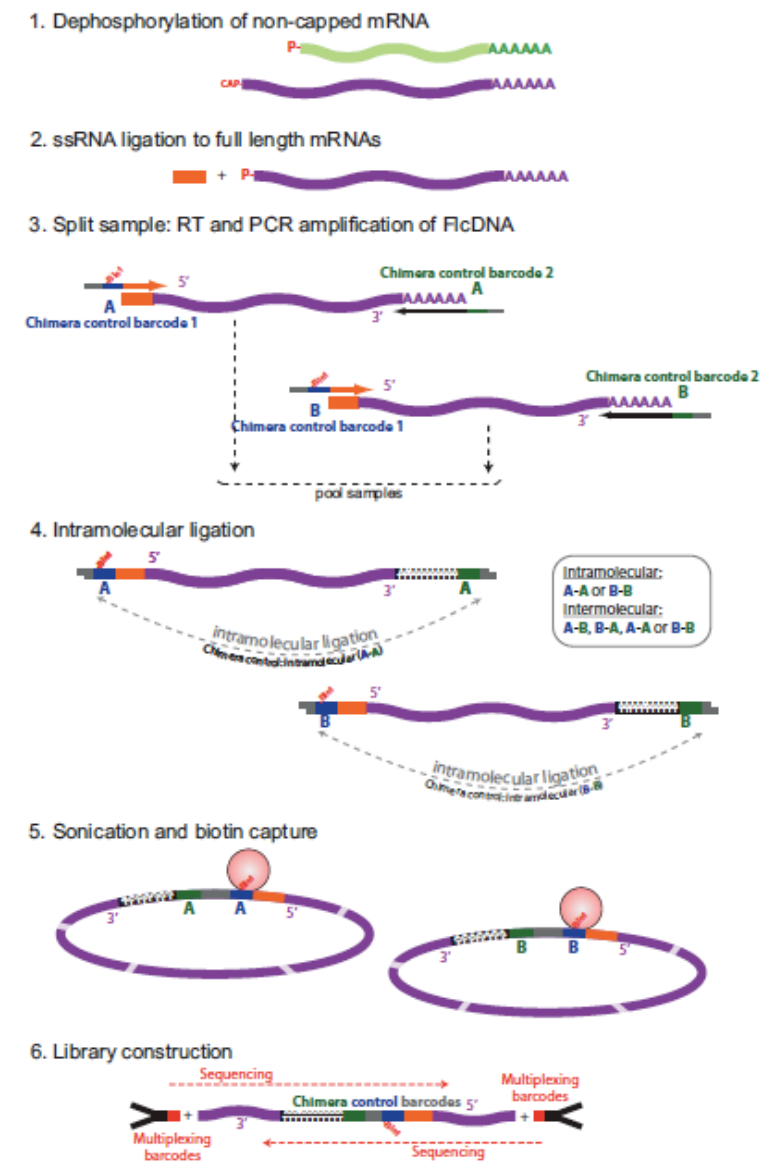
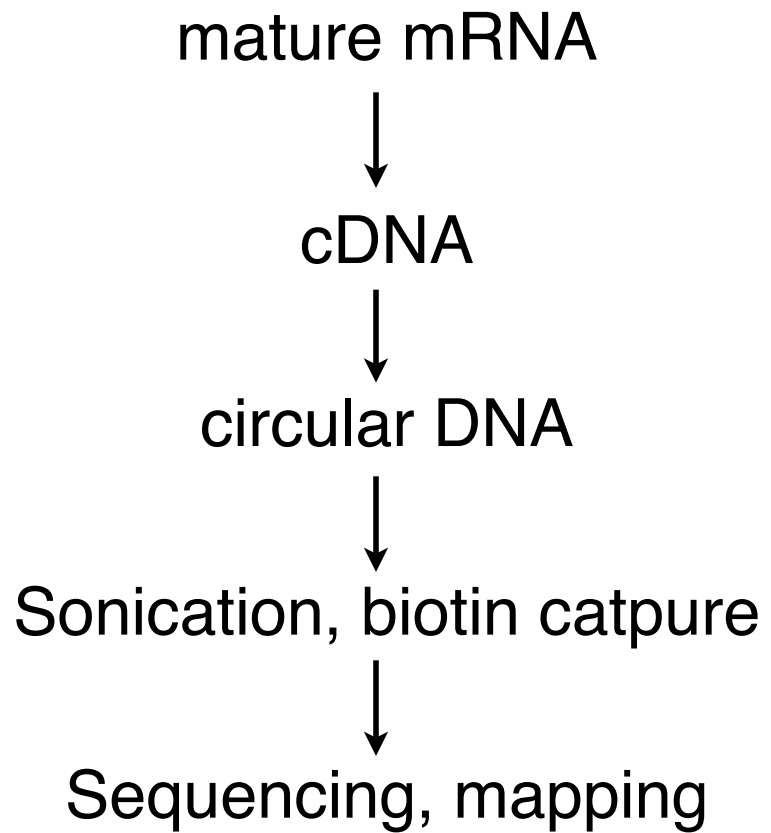
Outline

- Identify Transcript isoforms (TIFs) with TIF-Seq
- TIF variations and their categories
- Potential biological functions of TIFs

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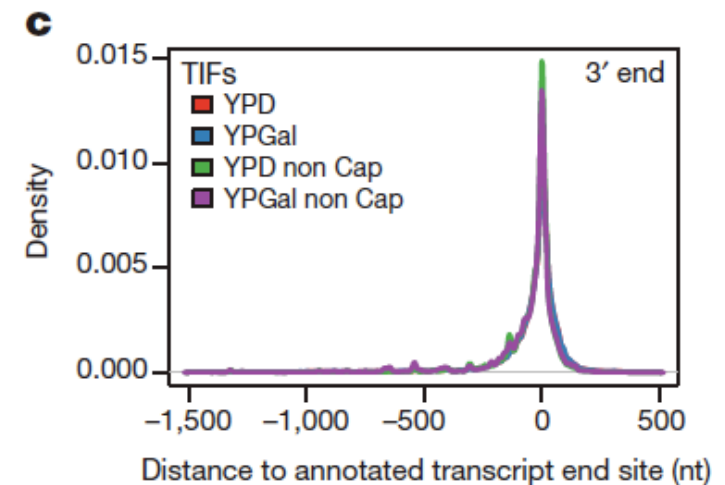
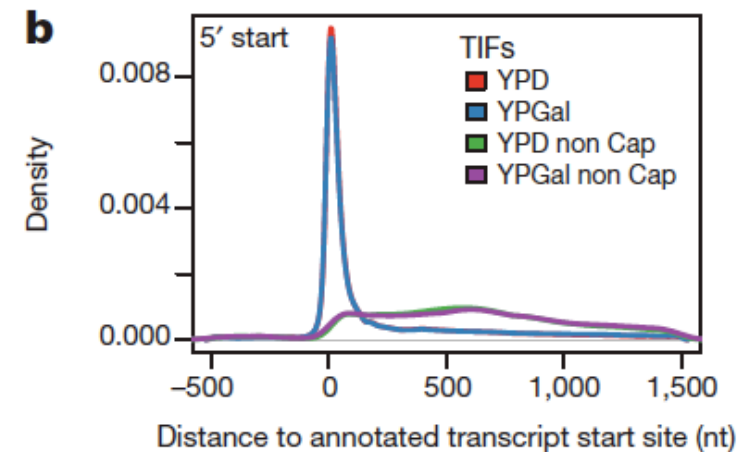
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TIF-Seq

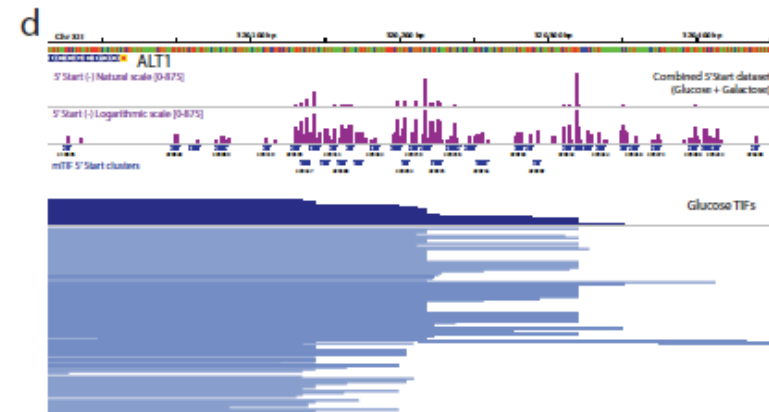
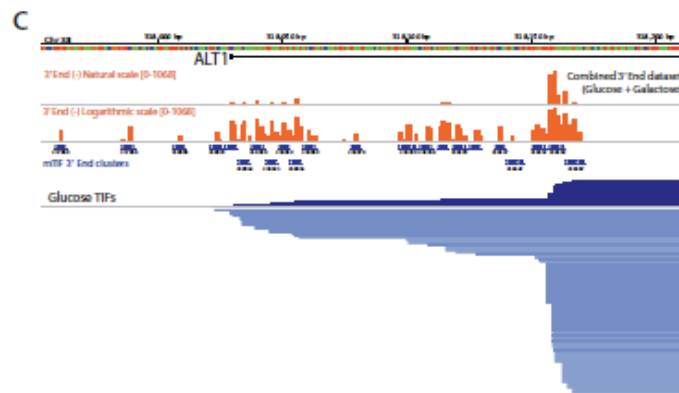
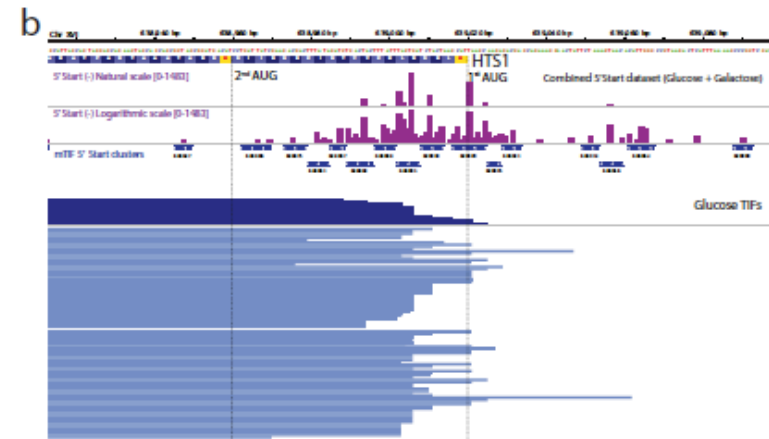
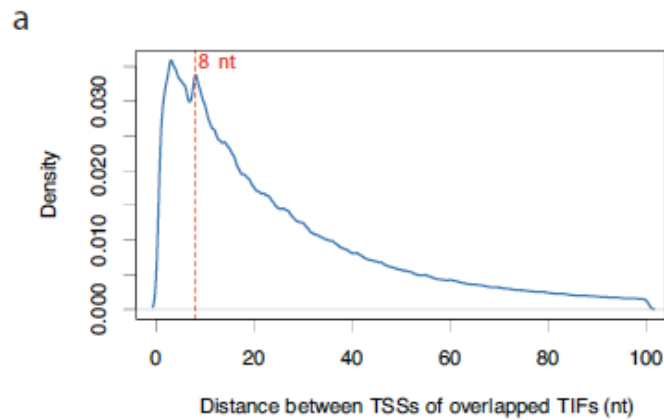


Transcript Isoform

- Compared yeast grown in two conditions: glucose and galactose
- Totally over 1.88 million unique TIFs found, over 776,000 supported by at least two reads
- Distribution of 5' and 3' ends of TIFs consistent with previous annotation



mTIF

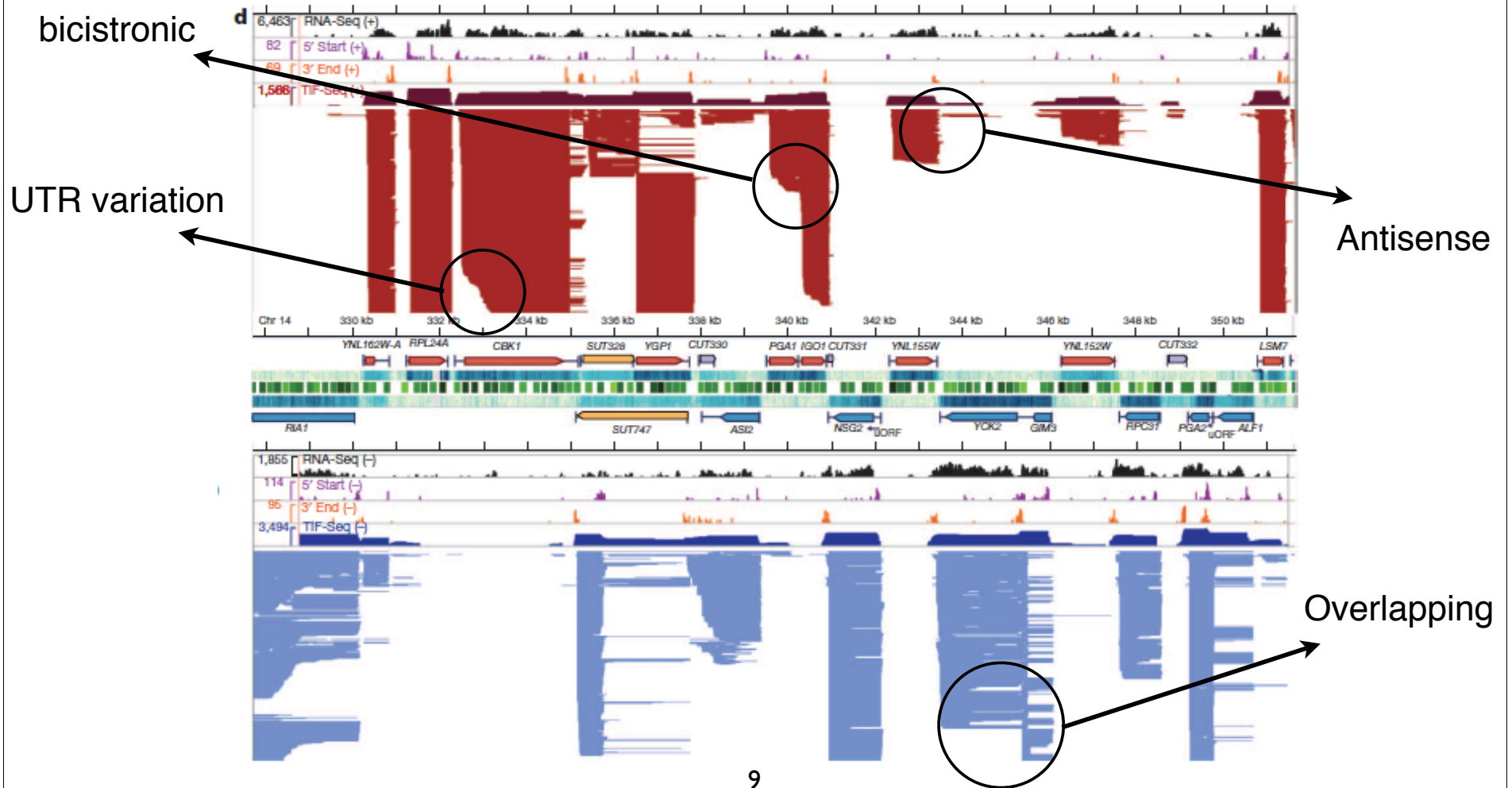


371,087 mTIFs genome-wide

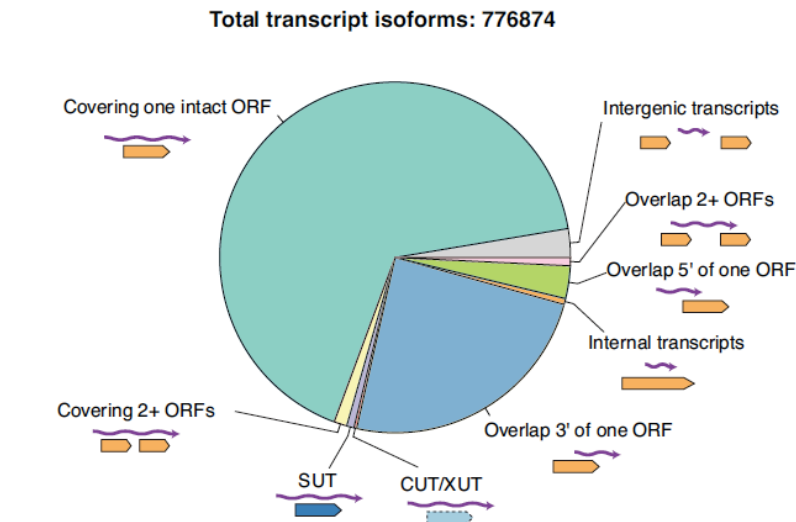
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- Identify Transcript isoforms (TIFs) with TIF-Seq
- **TIF variations and their categories**
- Potential biological functions of TIFs

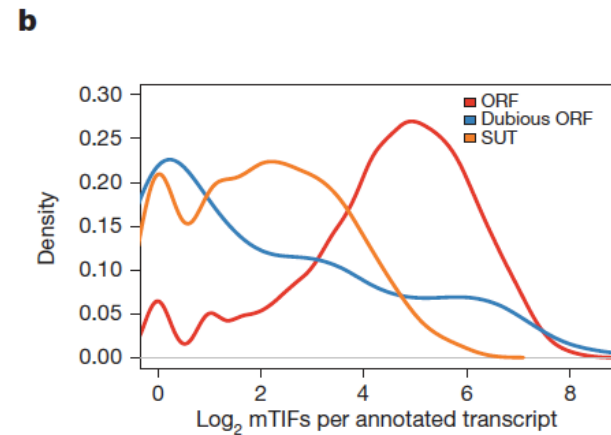
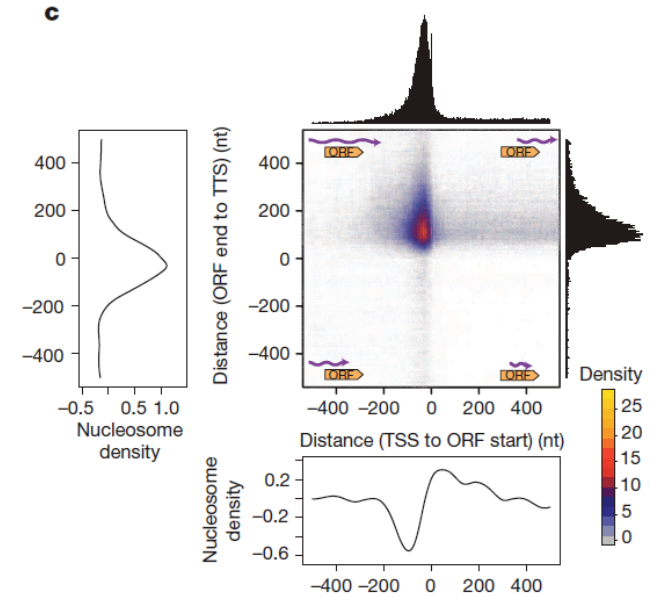
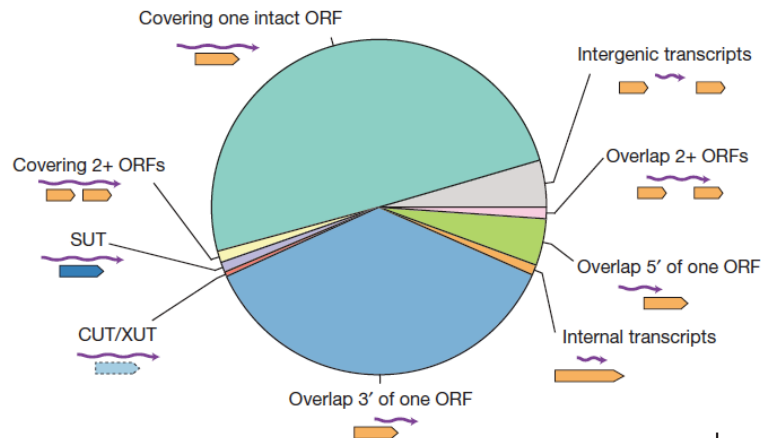
mTIF variation



mTIF variation categories



a Major transcript isoforms (mTIFs): 371,087



Outline

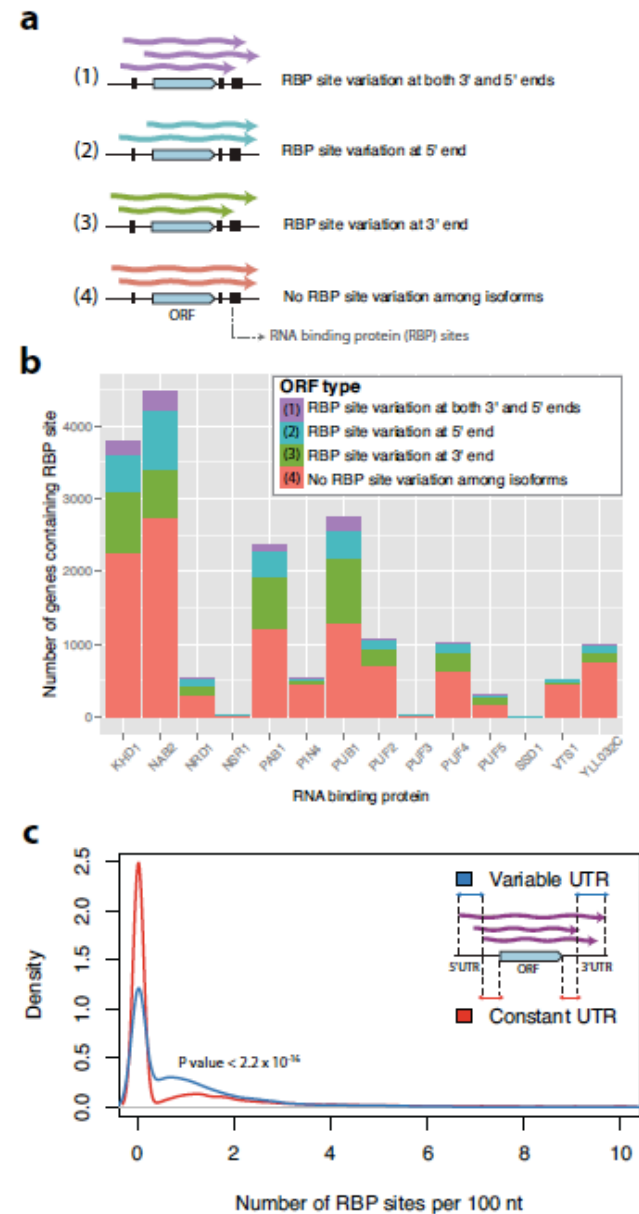
- Find Transcript isoform (TIF) with TIF-Seq
- TIF variations and their categories
- **Potential biological functions of TIF**

Functional correlation of TIF variations

- RBP binding sites variation
- uORF variation and re-annotation
- Contribute to protein diversity: truncated N-terminal transcripts, C-terminal truncation

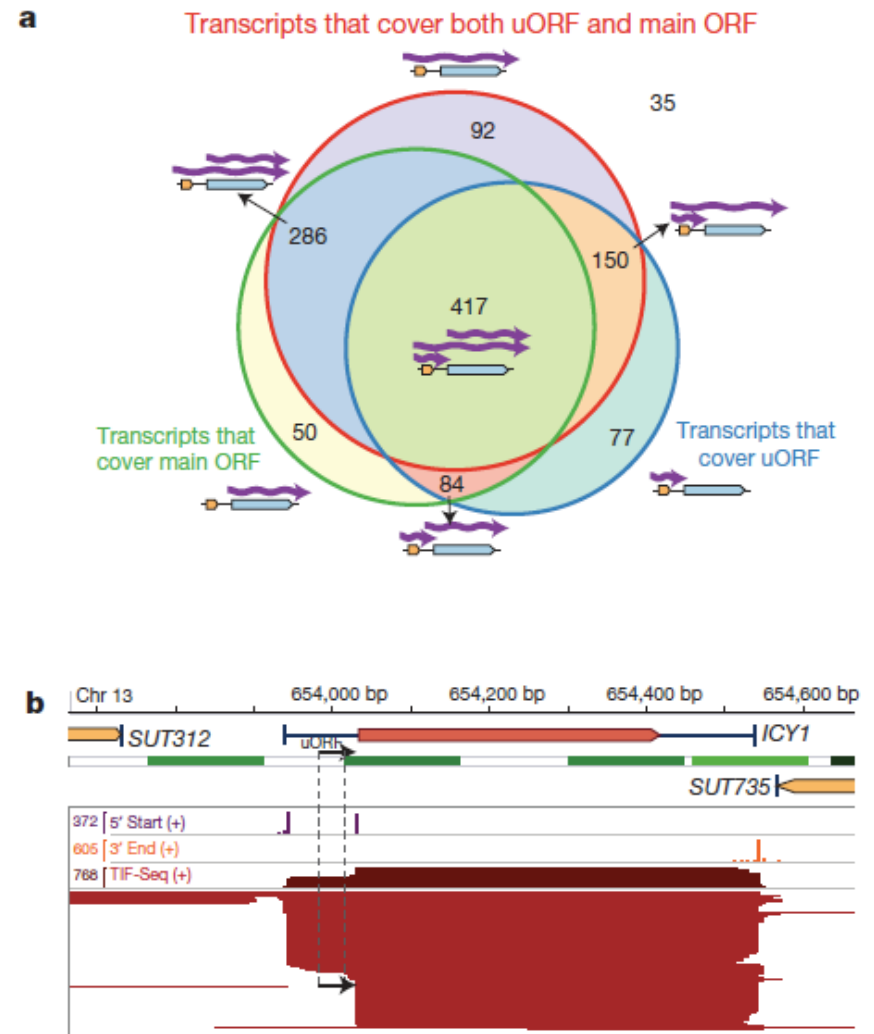
RBP binding sites

- Many genes with putative RBP binding sites express mTIFs with different combinations of binding sites
- Variable UTR regions between mTIFs are enriched for binding sites



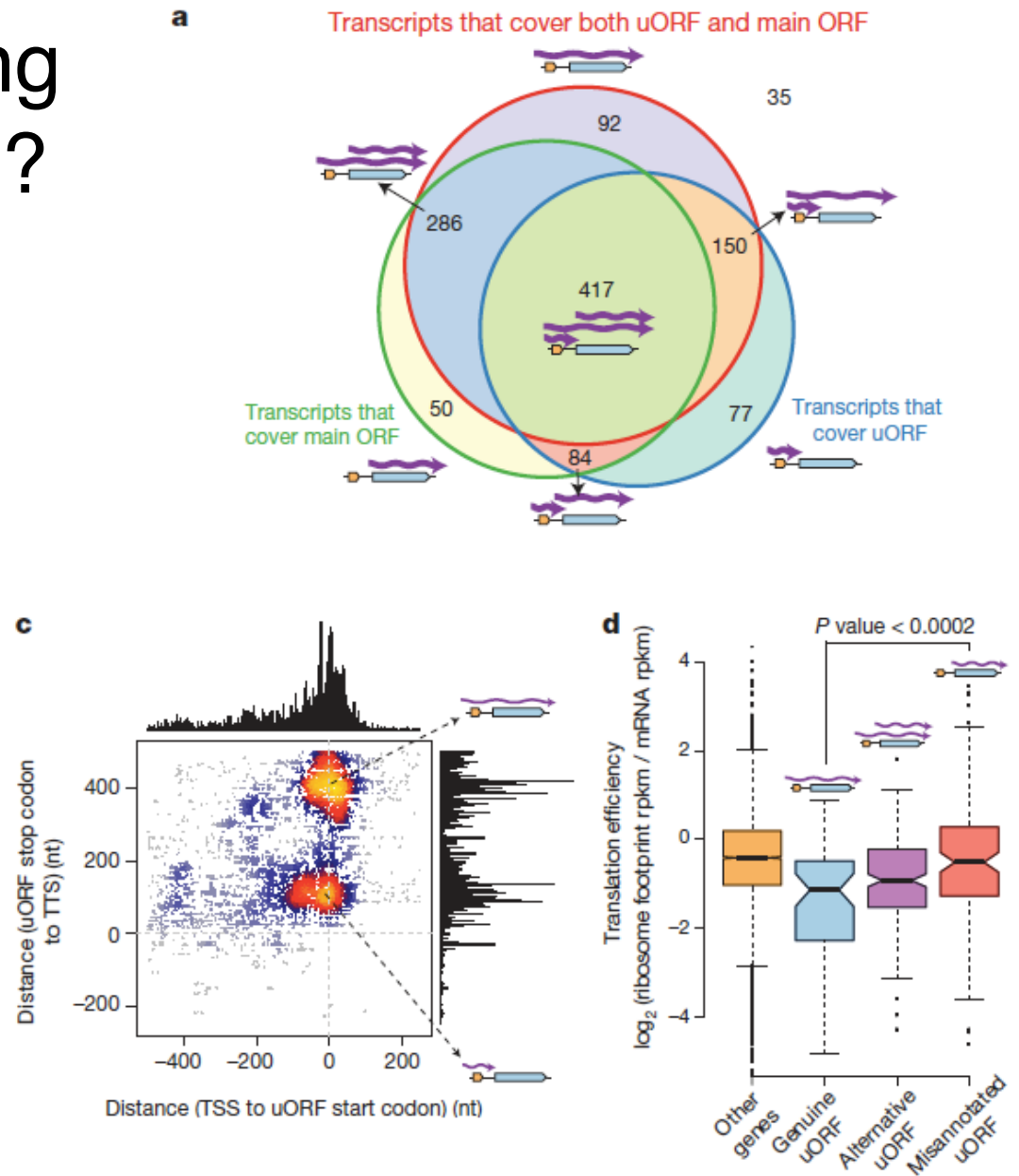
uORF

- 703 genes (286 + 417) express alternative mTIFs both with and without uORF. A possible transcriptional control of post-transcriptional regulatory potential

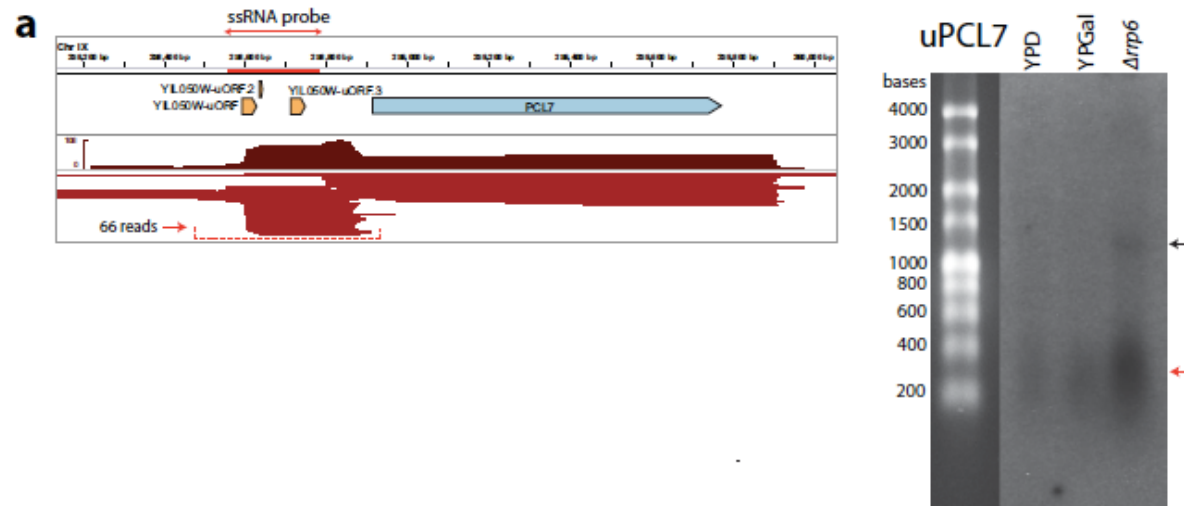


Re-annotating some uORF?

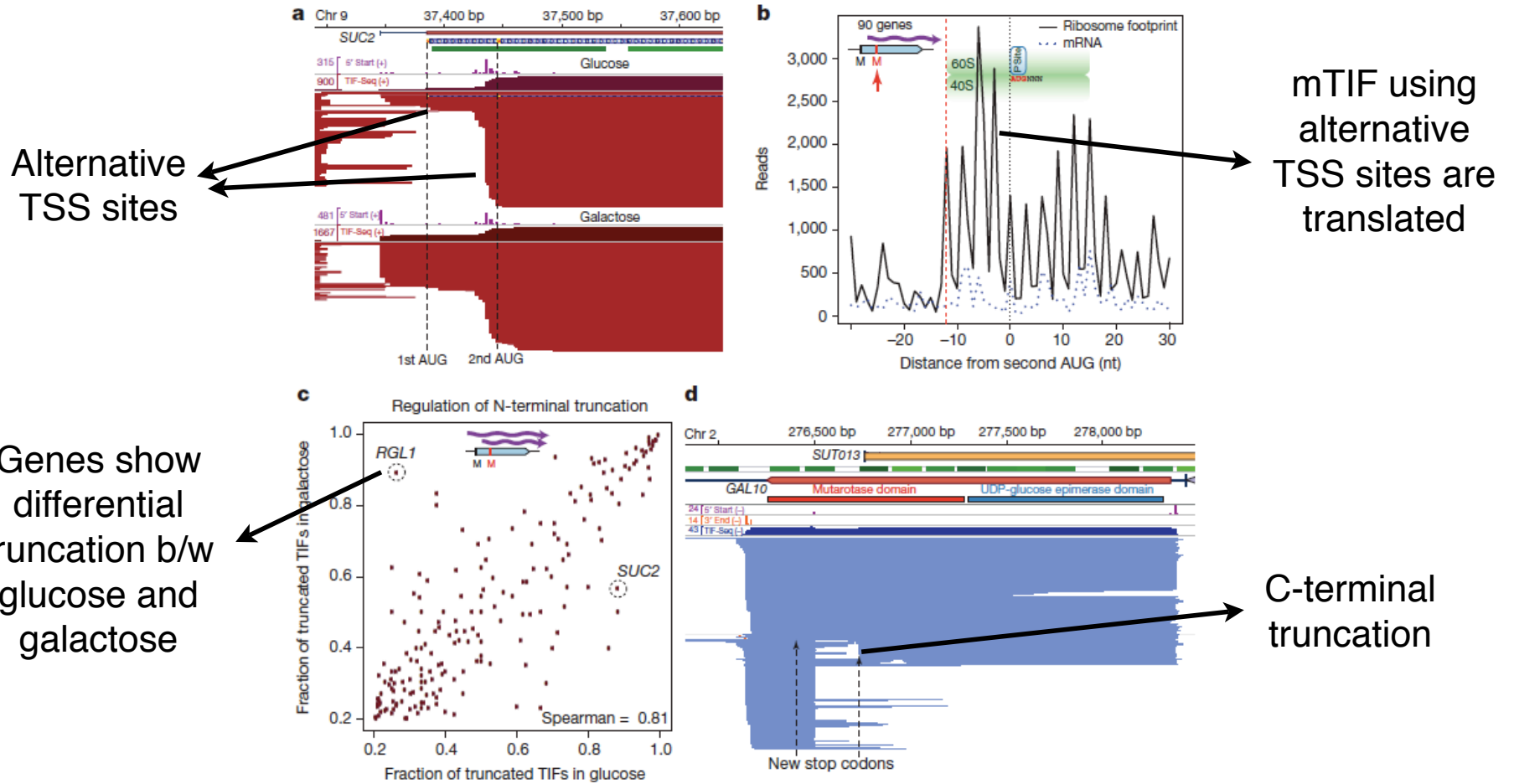
- mTIFs containing only the uORF were detected
- Genes containing genuine uORF are significantly less translated than those where the uORFs are independent



Re-annotating uORF - Example



Protein Diversity



Summary

- Nearly 2 million different RNA transcripts identified for a yeast genome with about 6,000 protein coding genes
- Different TIFs have the potential to alter the coding and regulatory capacity of RNA

Some caveats:

- TIF-Seq only works on mature mRNA;
- Efficiency of reverse transcription is an issue;
- Can not handle alternative splicing