

Hide and Seek: The Complete Transcriptome

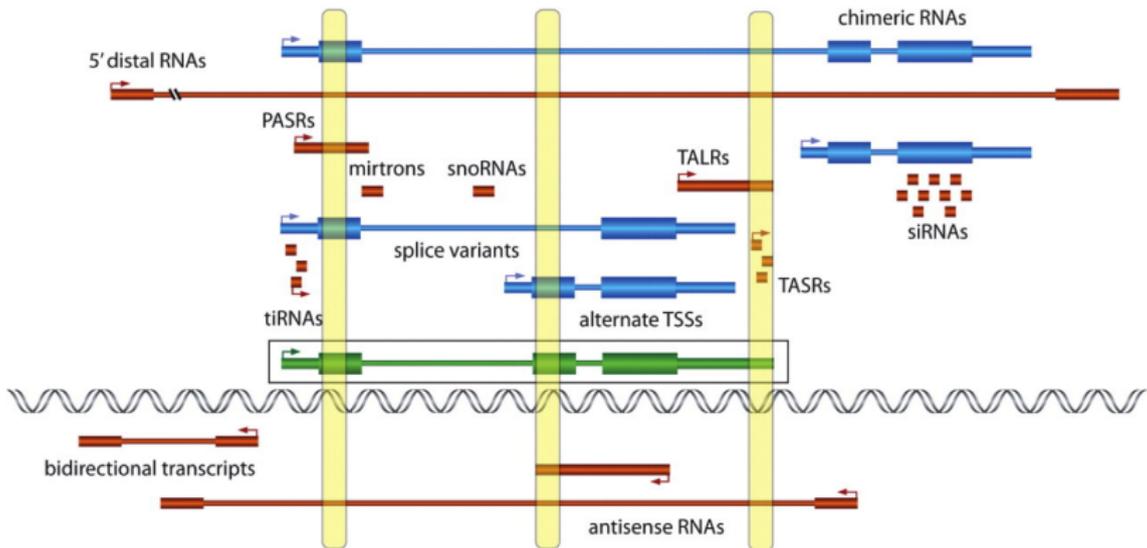
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Computer Science
Robin.Dowell@Colorado.edu

31 July 2012

gene → transcript

gene → isoforms





Chris Madden

www.chrismadden.co.uk

Hide and Seek: Complete Transcriptome

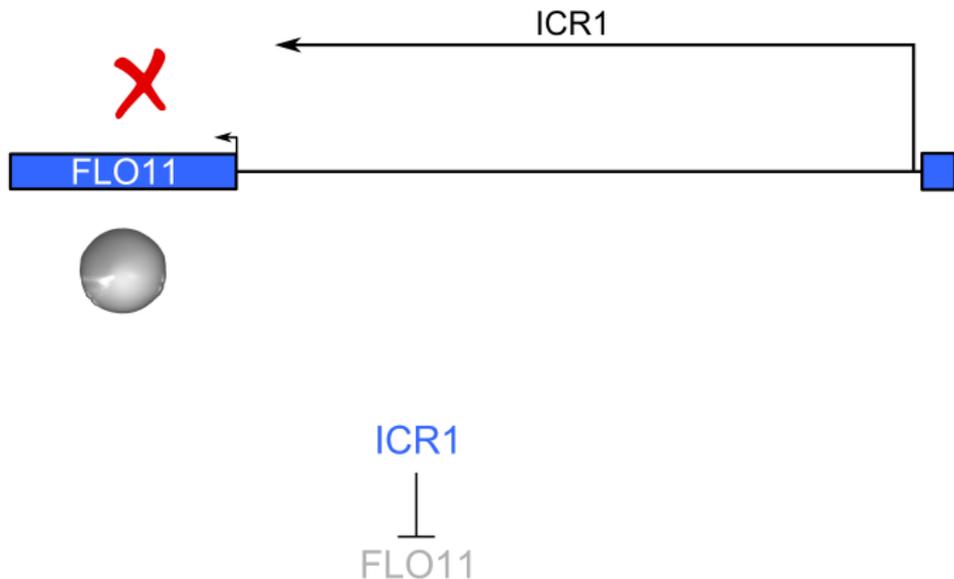
- Overlapping Transcription

- Nascent Transcription

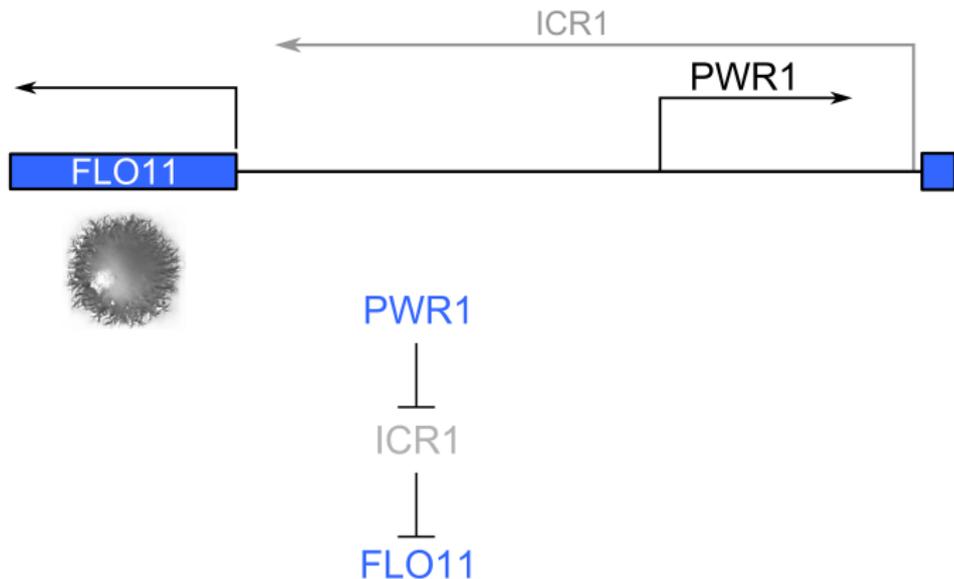


"Don't hide anywhere I can't see you!"

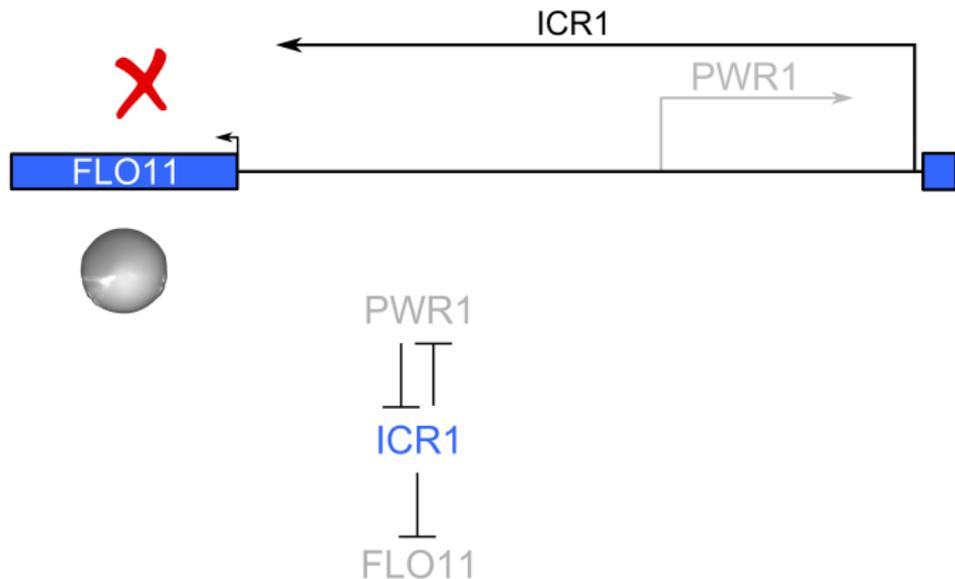
A case study on regulation by act of transcription



A case study on regulation by act of transcription

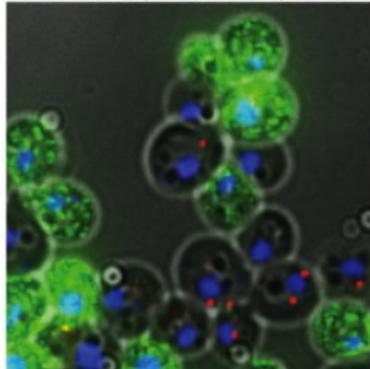


A case study on regulation by act of transcription

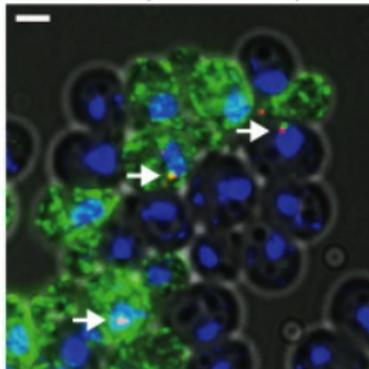


A case study on regulation by act of transcription

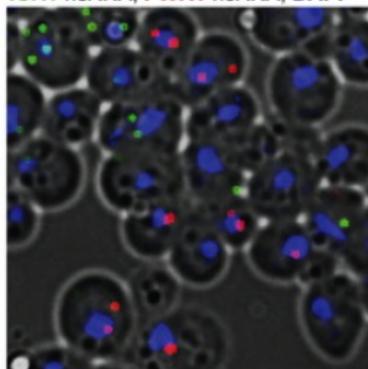
FLO11 mRNA; *ICR1* ncRNA; DAPI



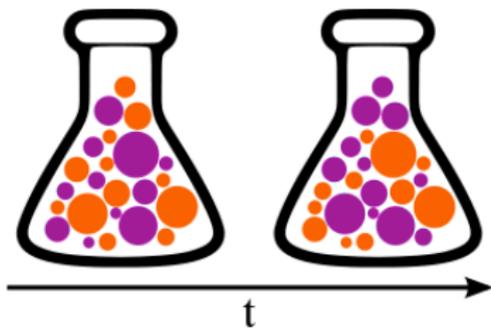
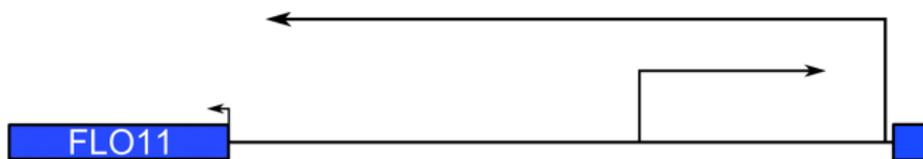
FLO11 mRNA; *PWR1* ncRNA; DAPI



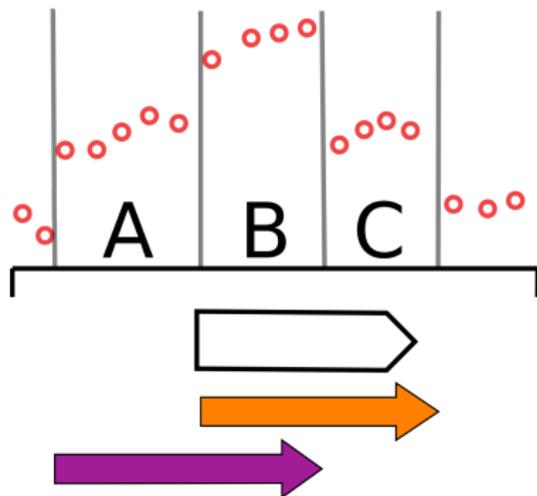
ICR1 ncRNA; *PWR1* ncRNA; DAPI



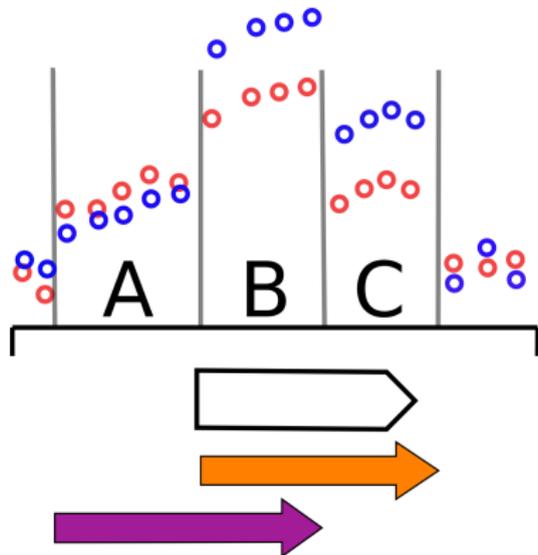
It is time and population averaged assay



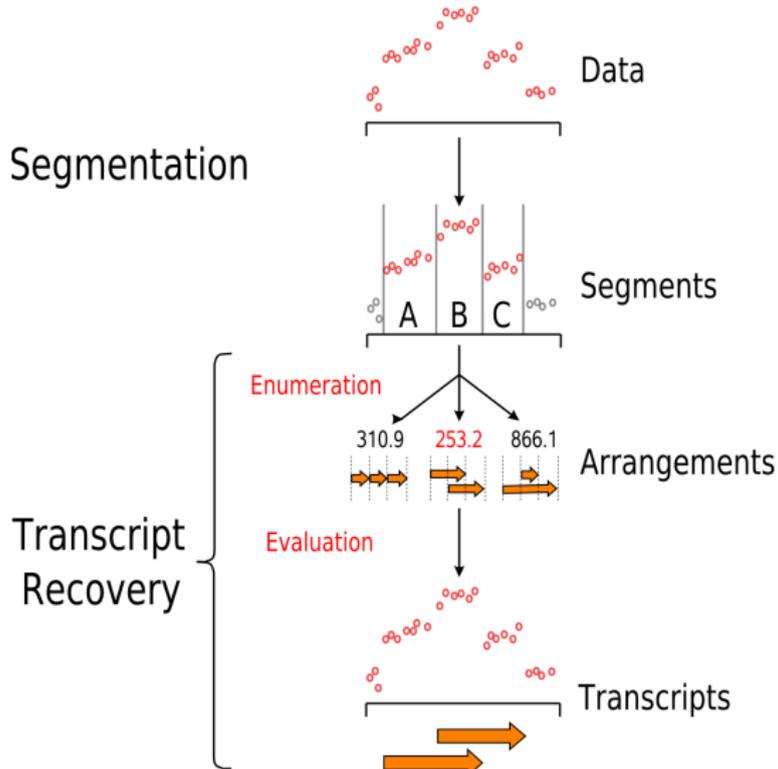
Assume additivity where transcripts overlap



Assume additivity where transcripts overlap



A screen for same strand overlapping transcription



Hide and Seek: Complete Transcriptome

- Overlapping Transcription
- Nascent Transcription
(stable and unstable transcripts)



"Don't hide anywhere I can't see you!"

Mary Allen

If regulation is by the act of transcription,
the transcript need not be stable.

- RNAseq in *rrp6Δ*

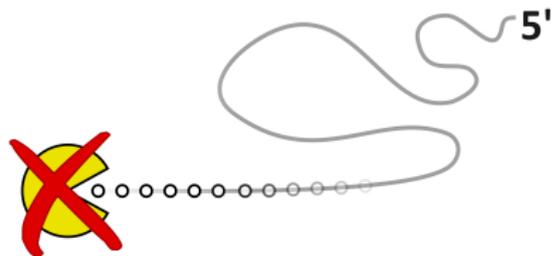
Steinmetz 2009, 2010

- GROseq

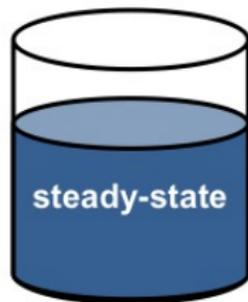
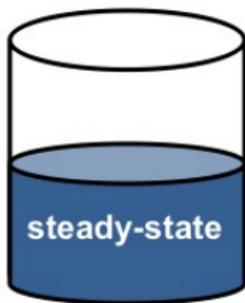
Core and Lis 2008

- NETseq

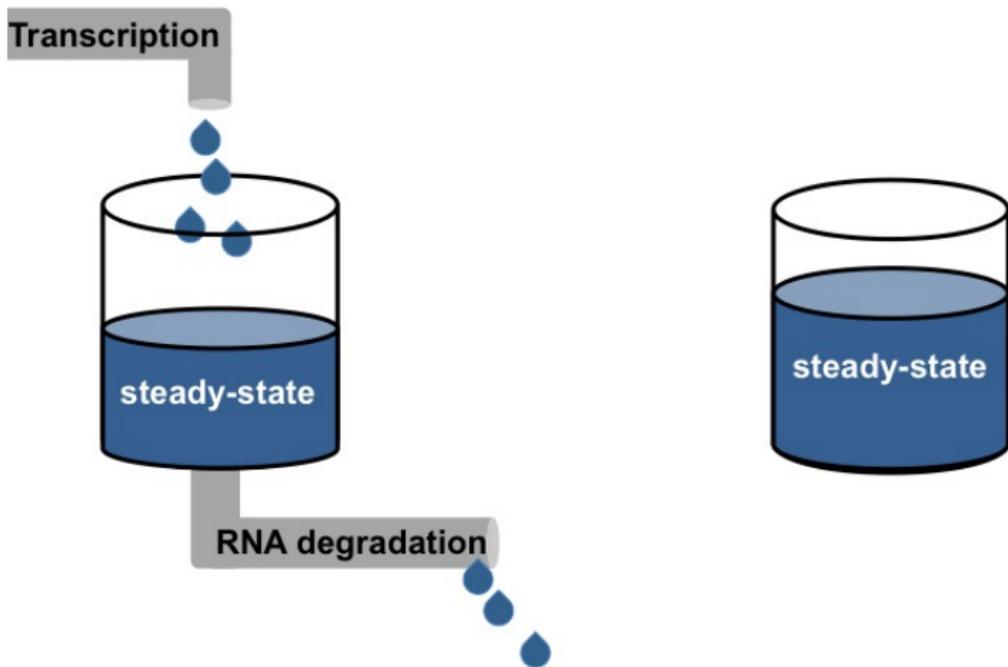
Churchman and Weissman 2011



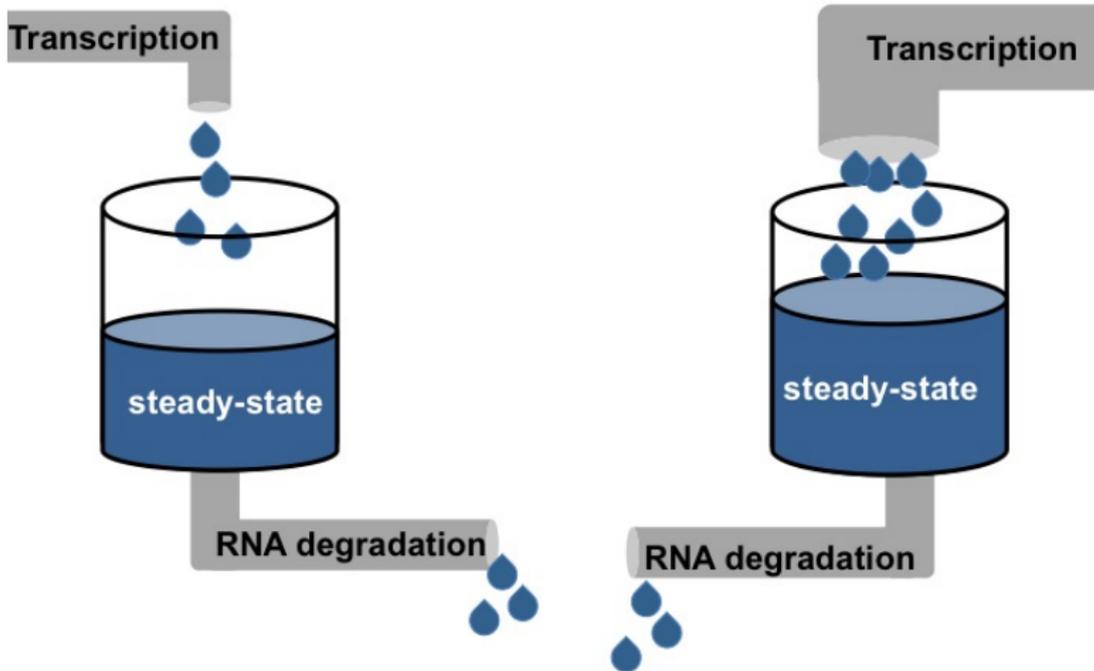
RNA-seq is not necessarily transcription



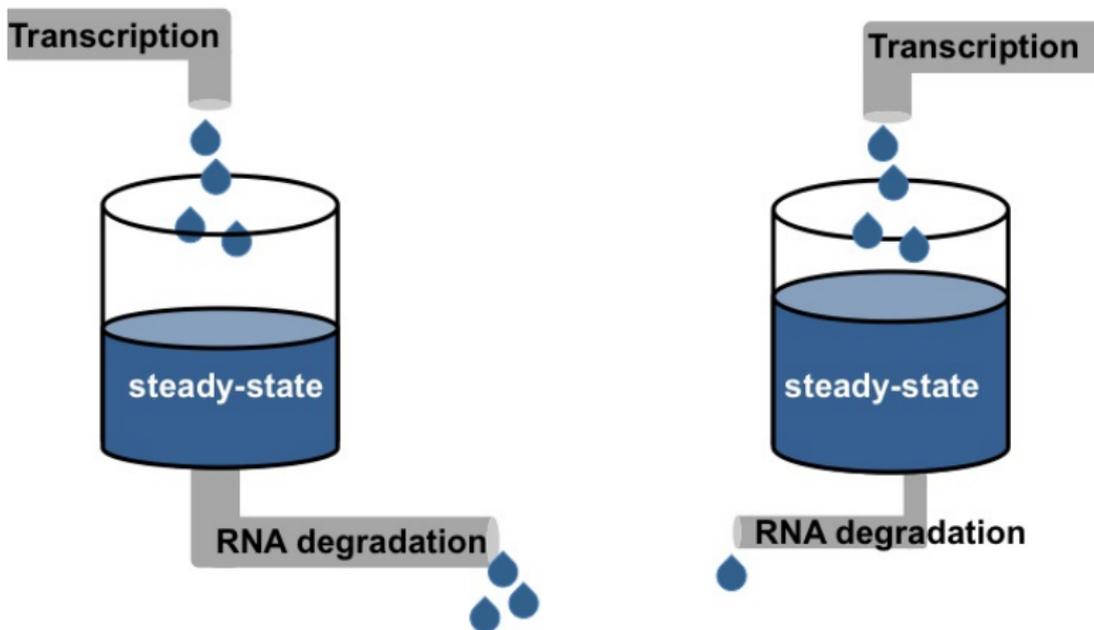
RNA-seq is not necessarily transcription



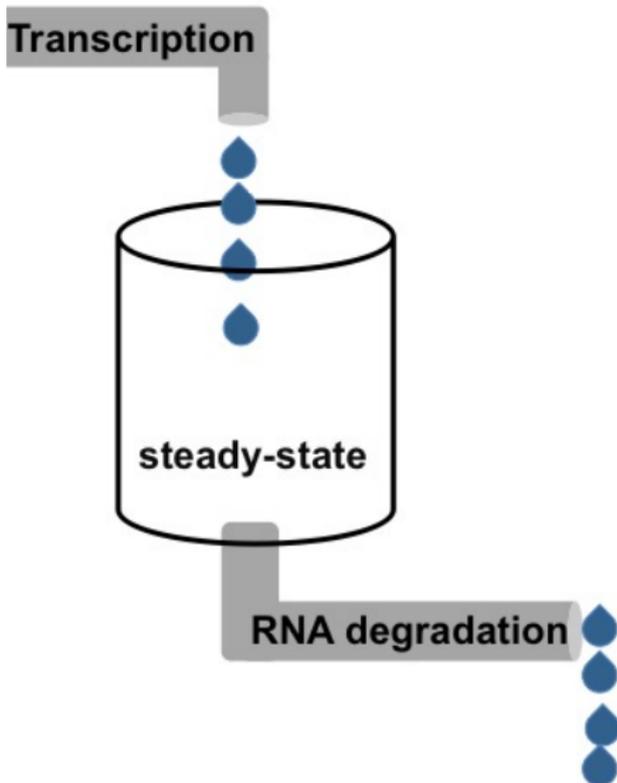
RNA-seq is not necessarily transcription



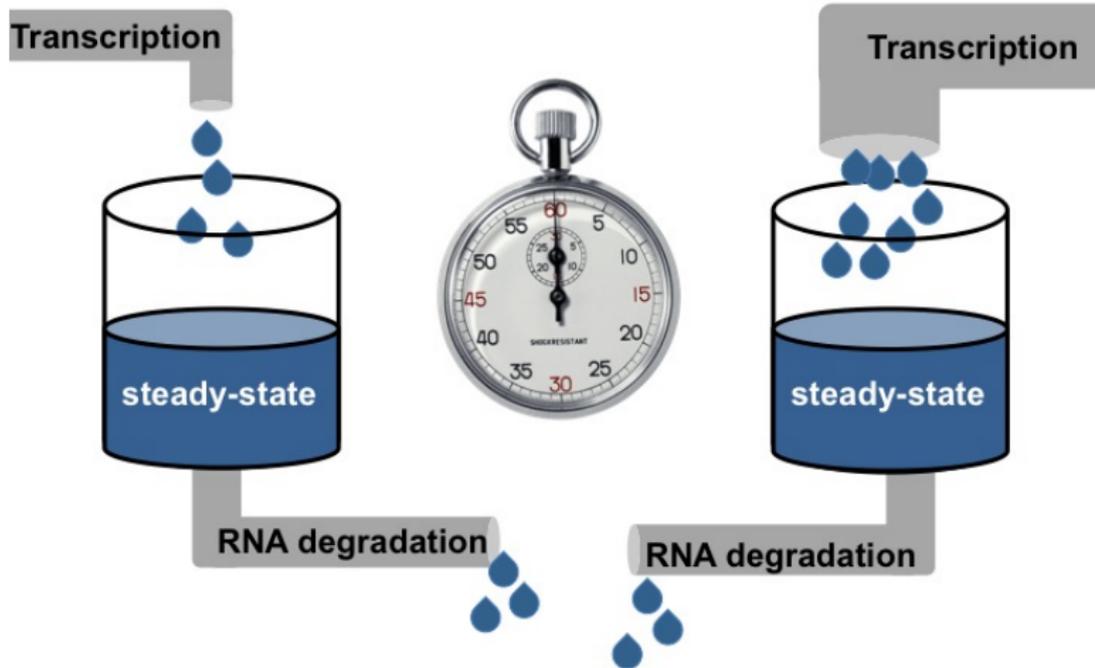
RNA-seq is not necessarily transcription



Degrades too quickly for detection



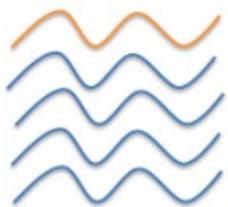
Alterations can not always be detected at early time points



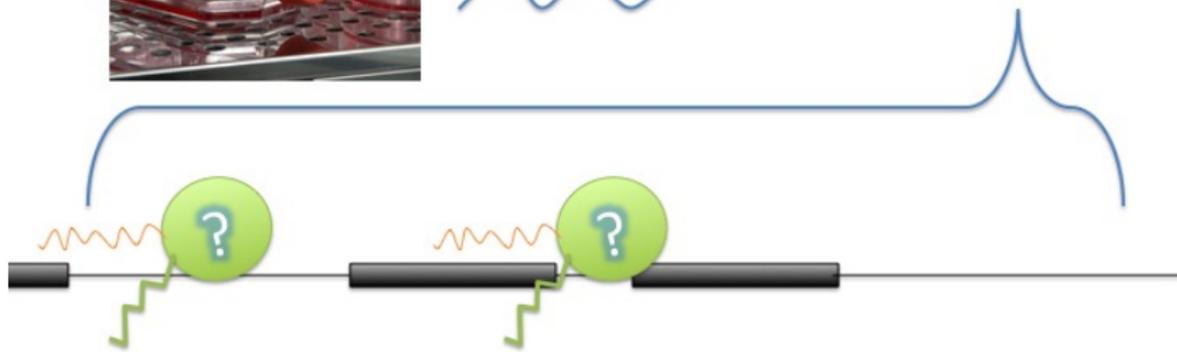
GRO-seq: Picture of current transcription

Global Nuclear Run On Sequencing

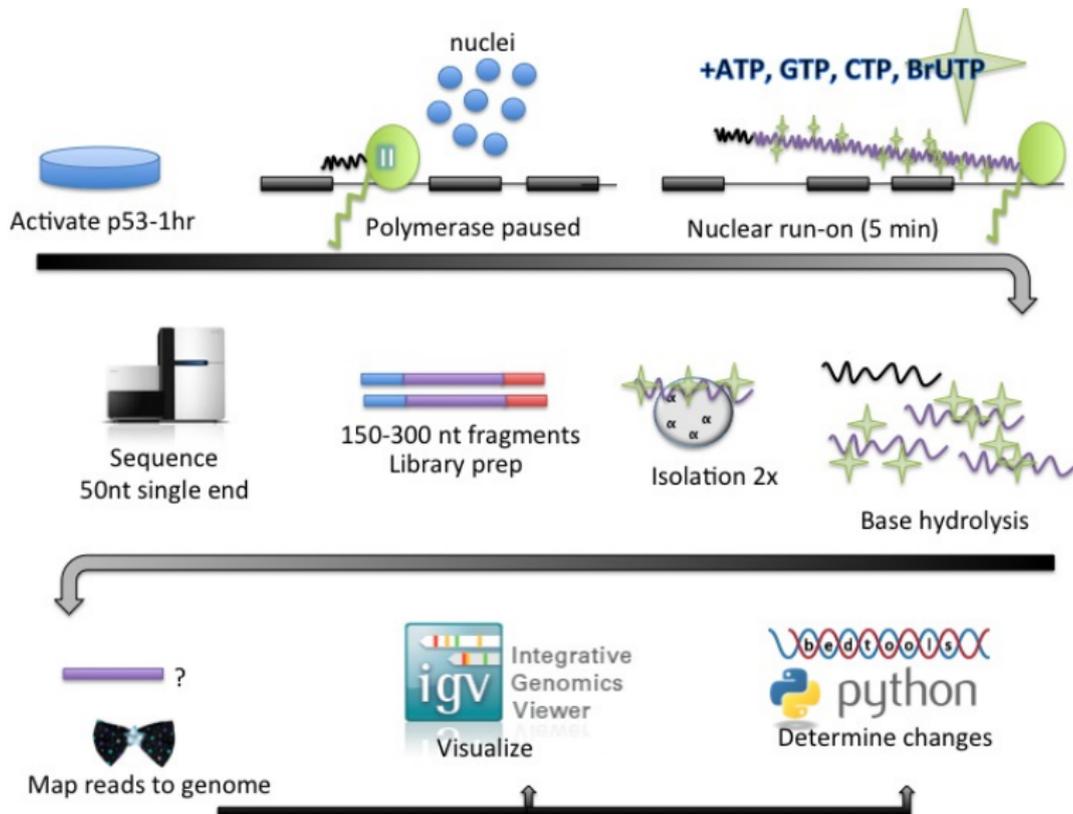
1hr Nutlin treat HCT116



GRO-seq to isolate only nascent RNA

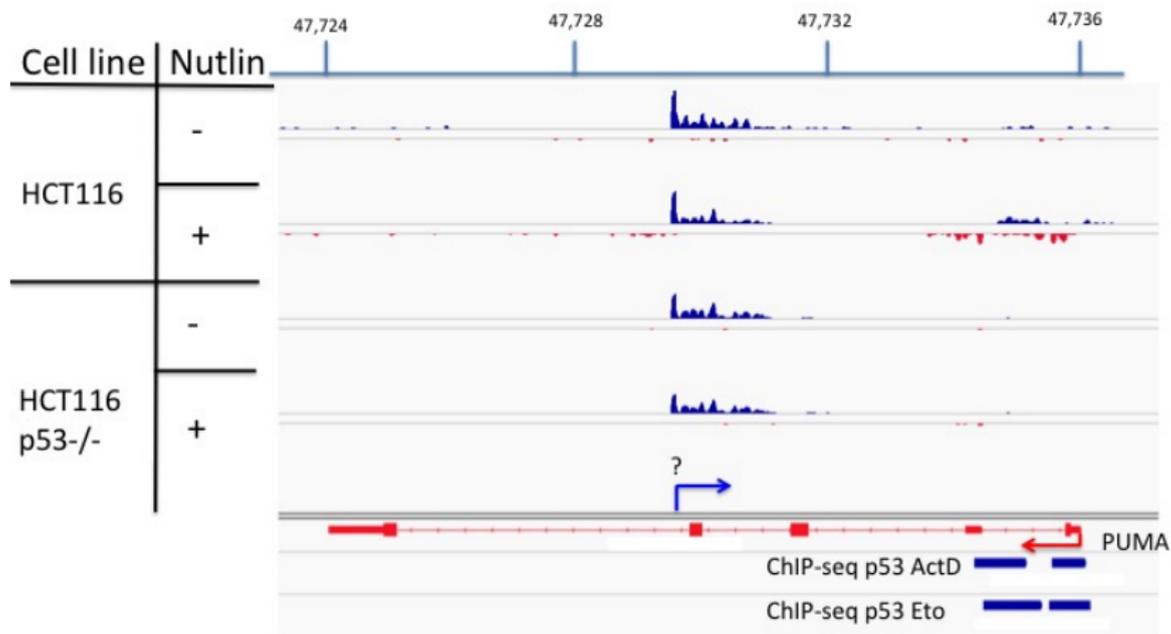


GRO-seq: Picture of current transcription

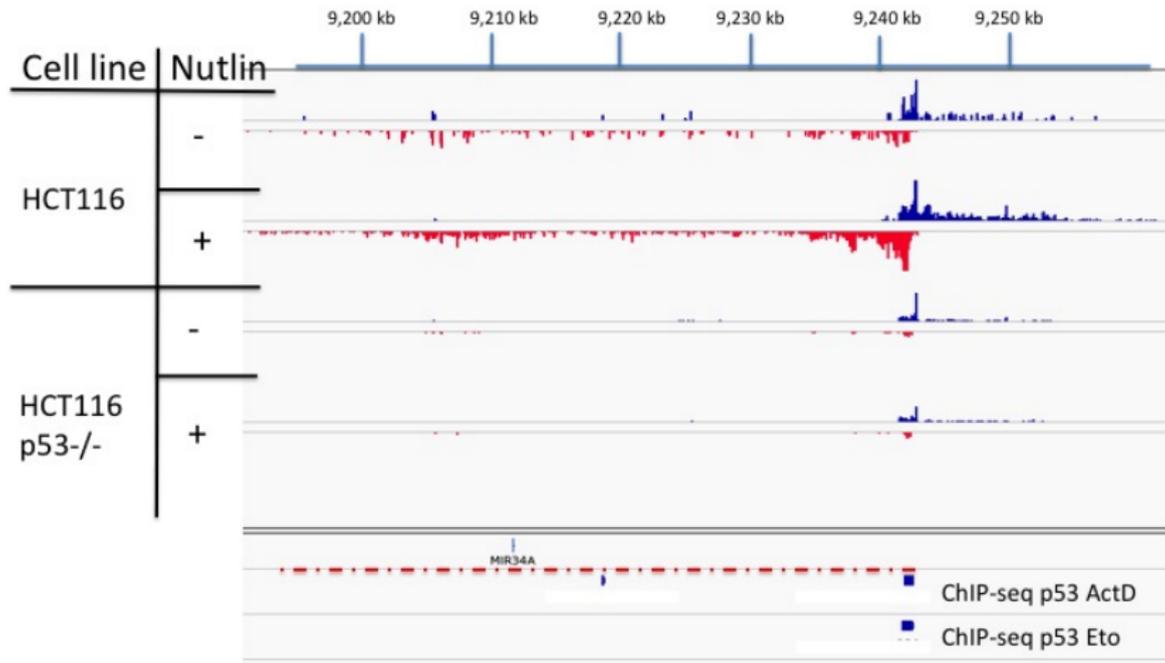


PUMA: known target gene, activated at 1 hr

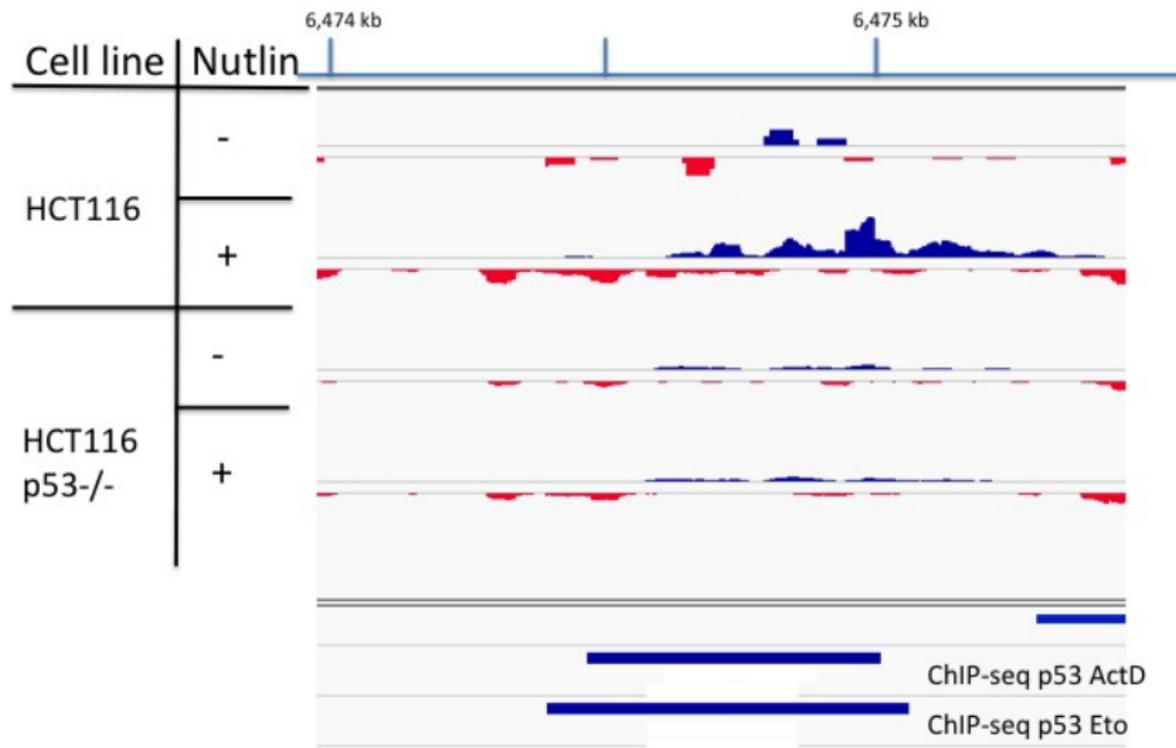
Histogram of coverage: forward strand=blue, reverse strand=red



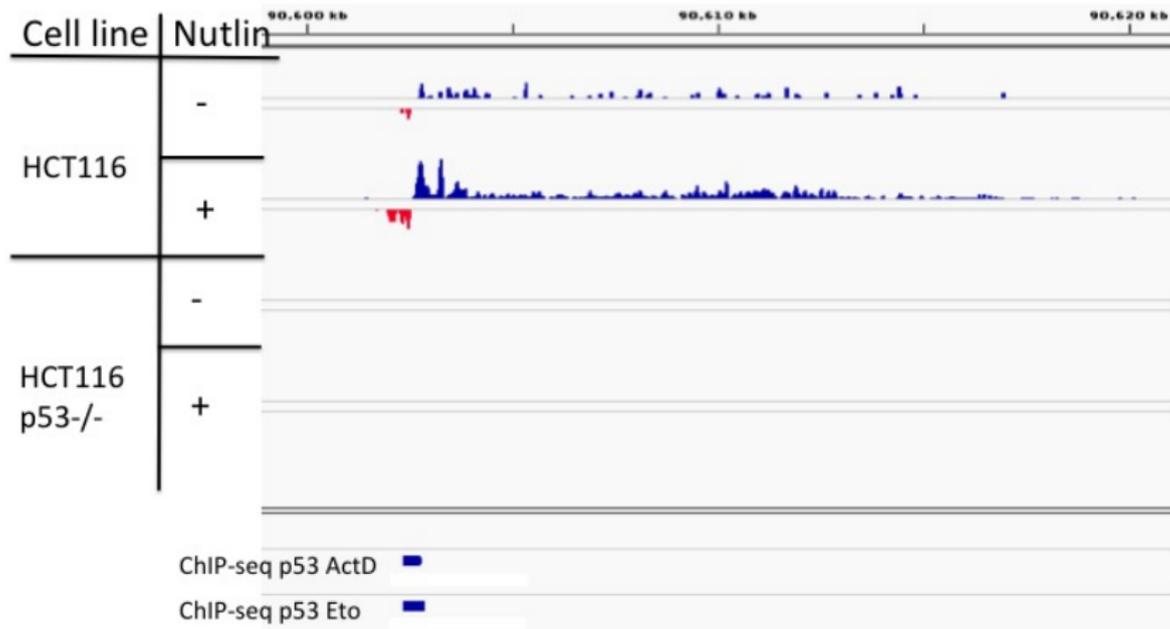
Precursor miRNAs show changes in transcription



eRNAs: expression from TF binding sites



Yes .. we even see novel transcripts



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(stable and unstable transcripts)



"Don't hide anywhere I can't see you!"

Future

- Mary will find her voice.
- Algorithms for identifying patterns in nascent data.
- Where is the act of transcription used as a regulatory mechanism?
- How do novel transcripts arise (evolutionarily)?
- Distinguish “noise” from “function” in transcripts.

Acknowledgments

Univ. Colorado

- Mary Allen
- David Knox
- Alex Poole
- Tim Read
- Jess Vera
- Phil Richmond

Collaborators

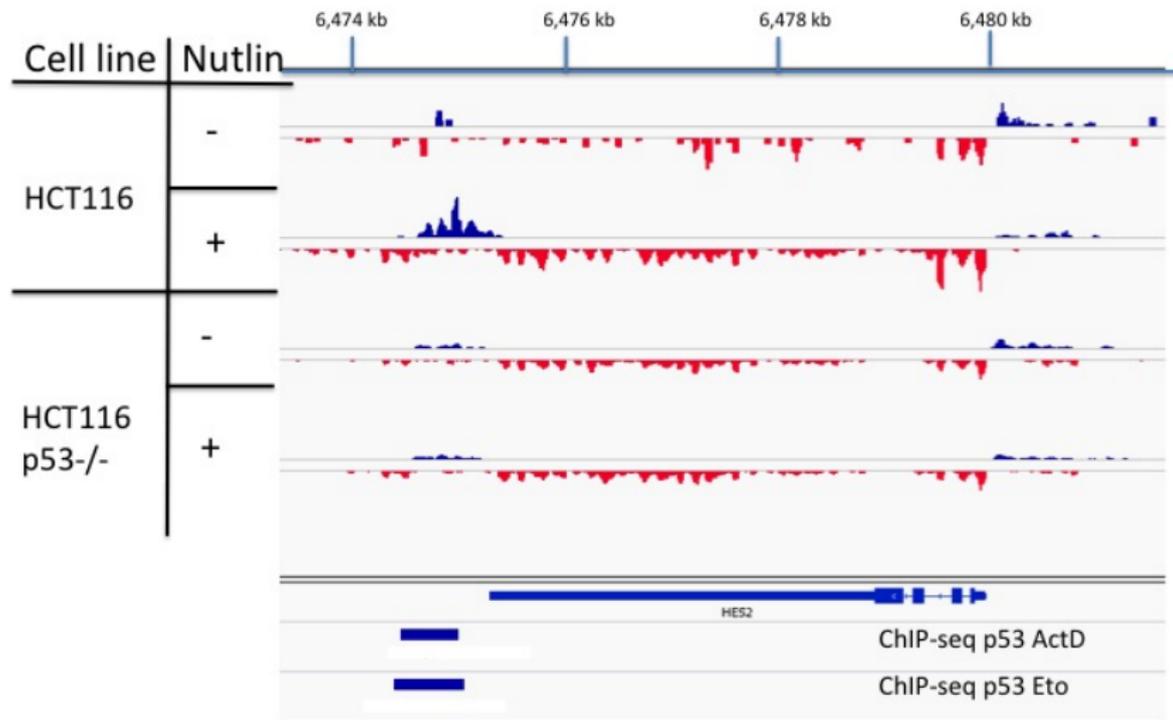
- Stacie Bumgarner
- Gerry Fink
- Joaquin Espinosa
- Manuel Lladser

The Money

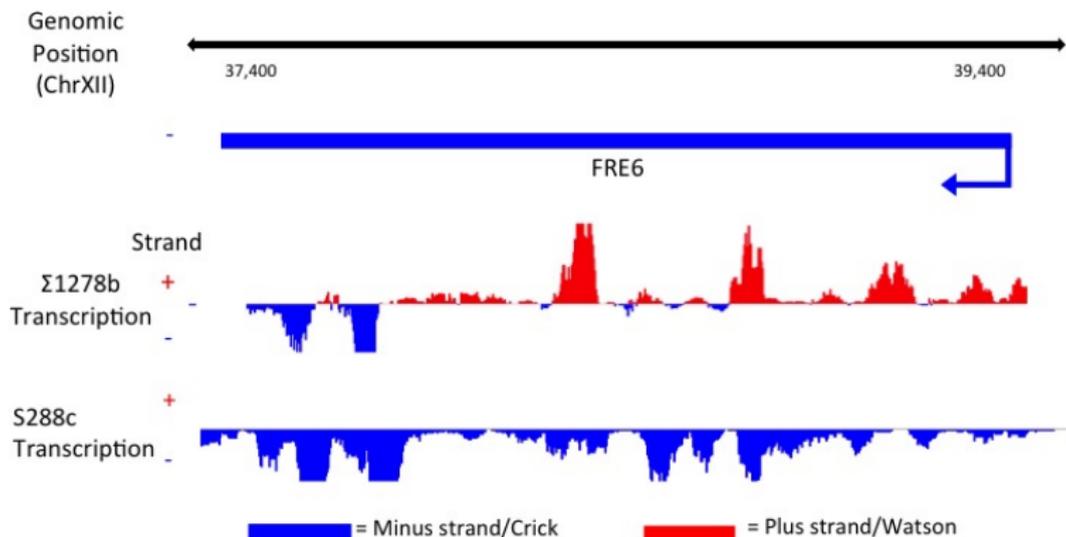
- Boettcher Foundation
- Butcher Seed Grant
- Sloan Foundation



Do eRNAs correlate with TF function?



A strain specific antisense transcript



A strain specific antisense transcript

