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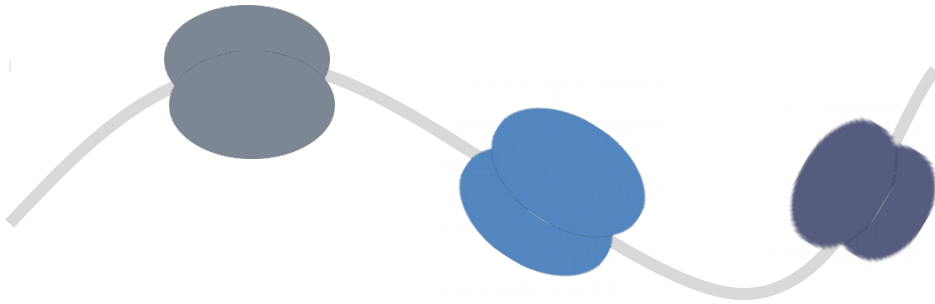


ANTONI VAN LEEUWENHOEK

How to decipher the structural secrets of RNA behind its translational efficiency?

**Ferhat Alkan
Postdoc
NKI - Faller Lab**

**34th TBI Winterseminar - Bled
February 5th 2019**



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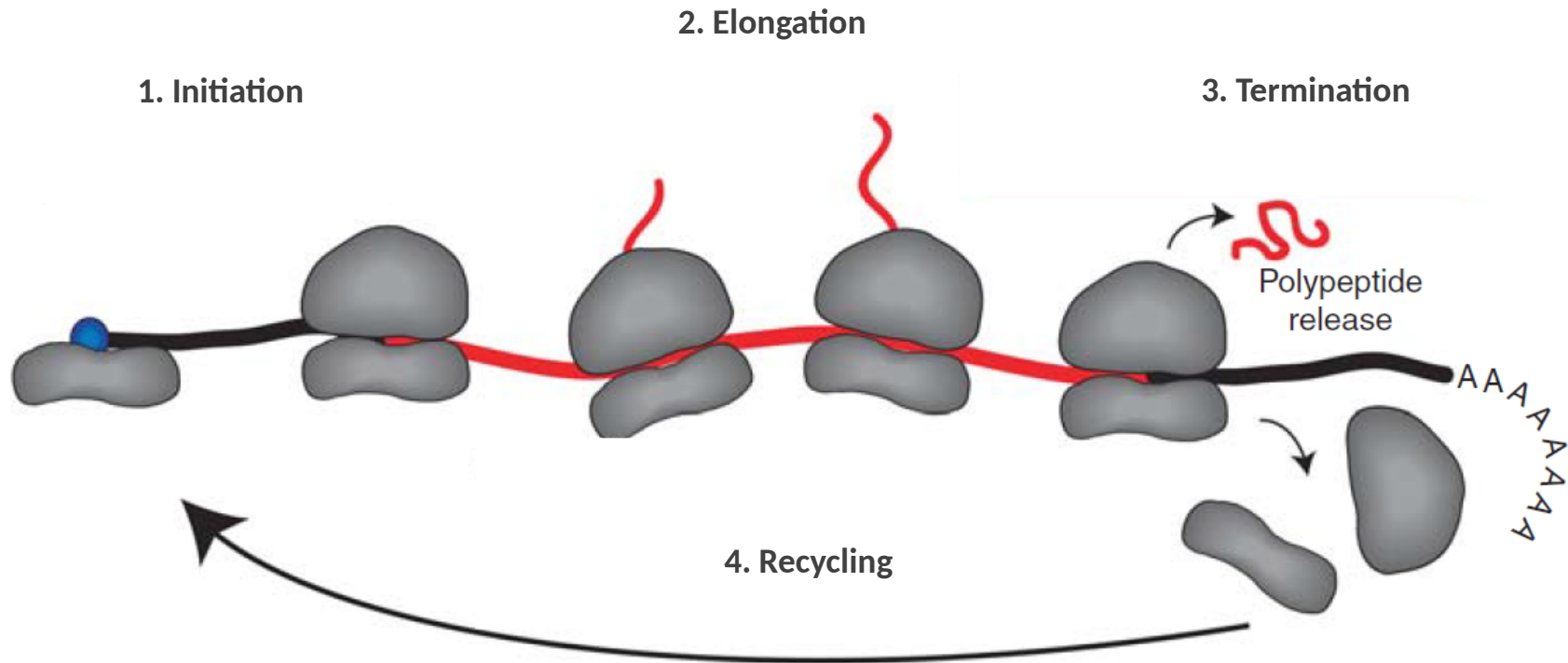
The Faller Lab



In the Faller lab, we study the role that RNA translation plays in cancer models.

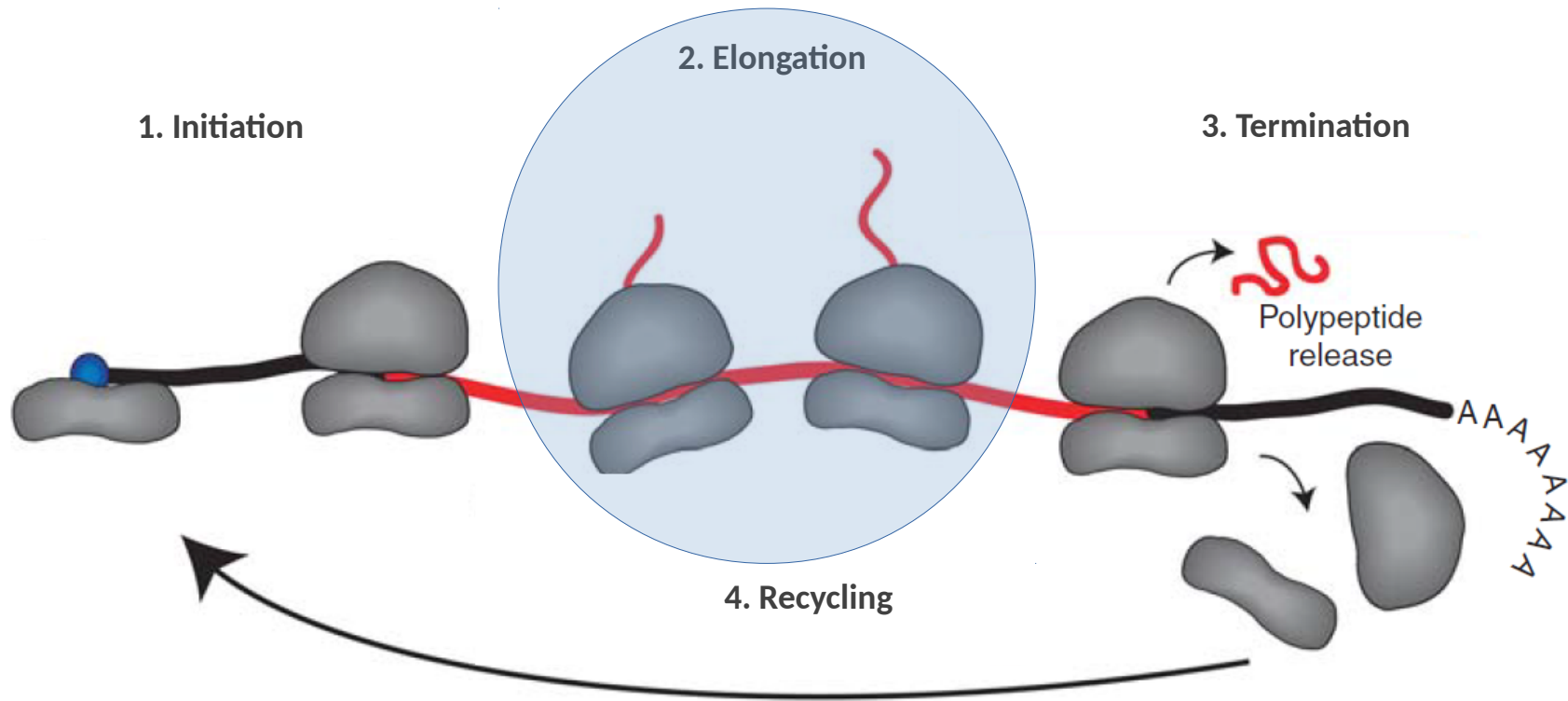


Eukaryotic RNA translation



Adapted from Sokabe et al. Cold Spring Harb Perspect Biol 2018

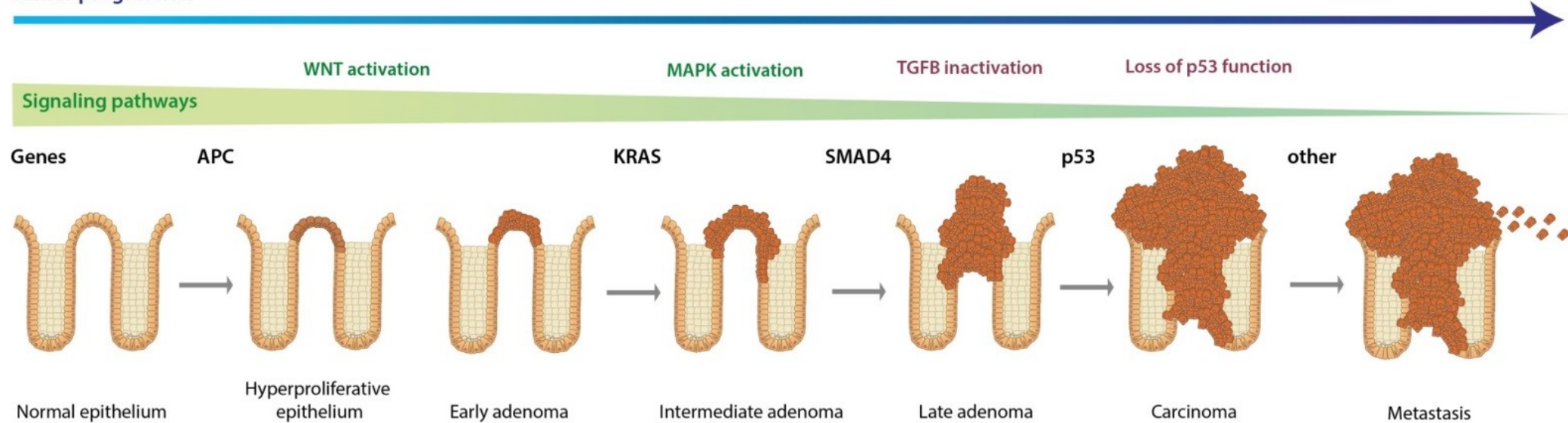
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Specific focus on Colorectal Cancer

Tumor progression



LETTER

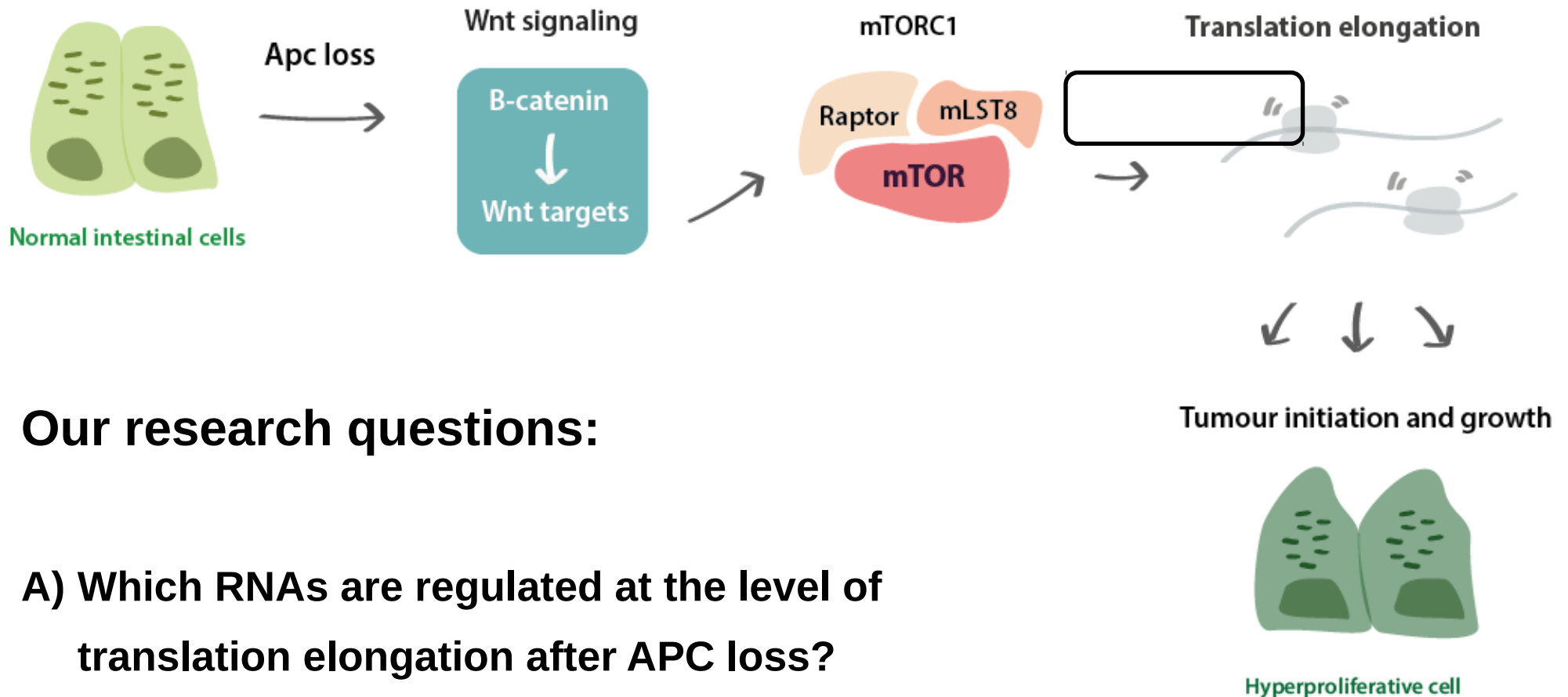
doi:10.1038/nature13896

mTORC1-mediated translational elongation limits intestinal tumour initiation and growth

William J. Faller¹, Thomas J. Jackson^{2*}, John R. P. Knight^{2*}, Rachel A. Ridgway¹, Thomas Jamieson¹, Saadia A. Karim¹, Carolyn Jones², Sorina Radulescu¹, David J. Huels¹, Kevin B. Myant¹, Kate M. Dudek², Helen A. Casey¹, Alessandro Scopelliti¹, Julia B. Cordero¹, Marcos Vidal¹, Mario Pende³, Alexey G. Ryazanov⁴, Nahum Sonenberg⁵, Oded Meyuhas⁶, Michael N. Hall⁷, Martin Bushell², Anne E. Willis² & Owen J. Sansom¹

*Faller et al. Nature 2015

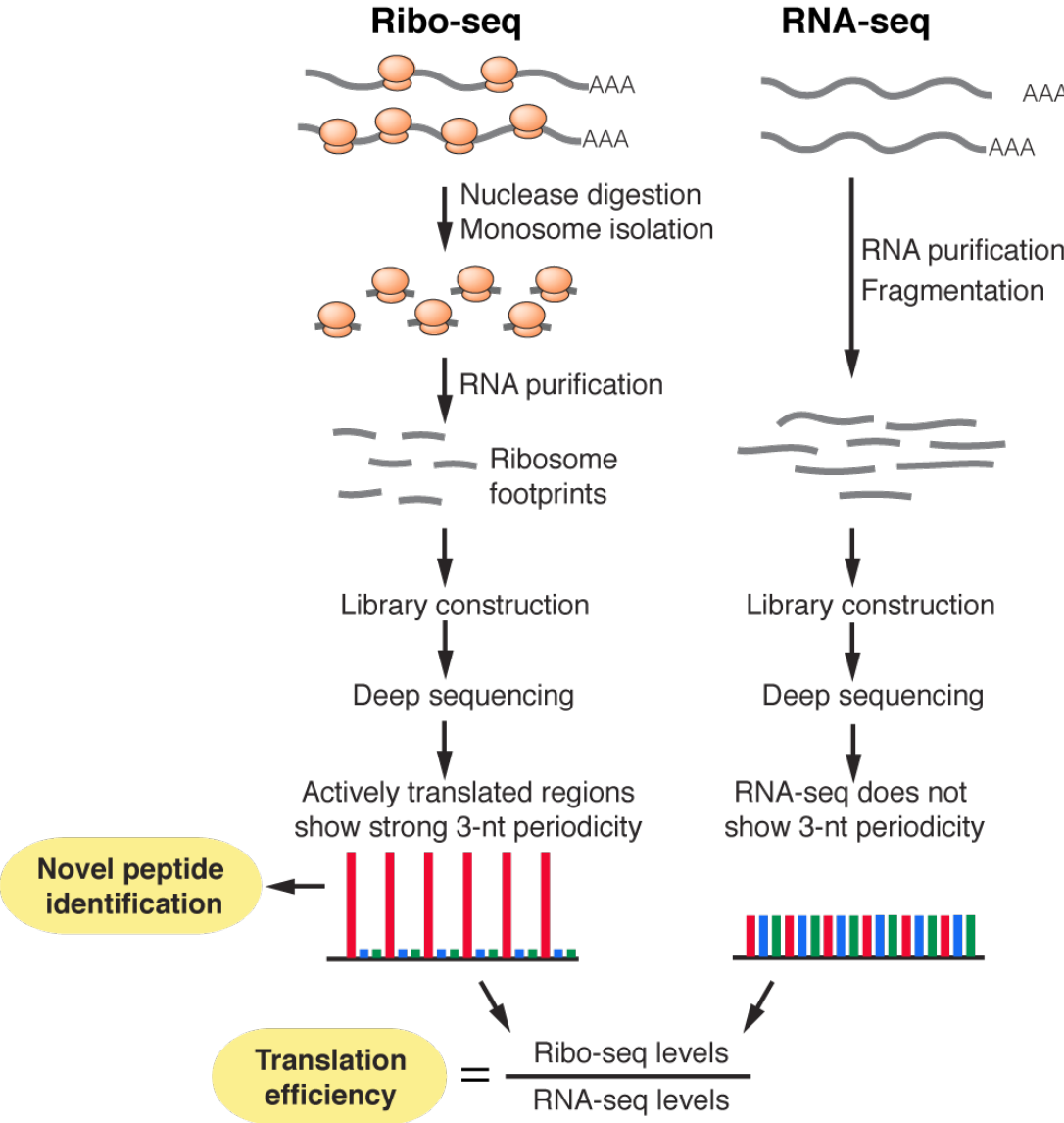
Our research model



Our research questions:

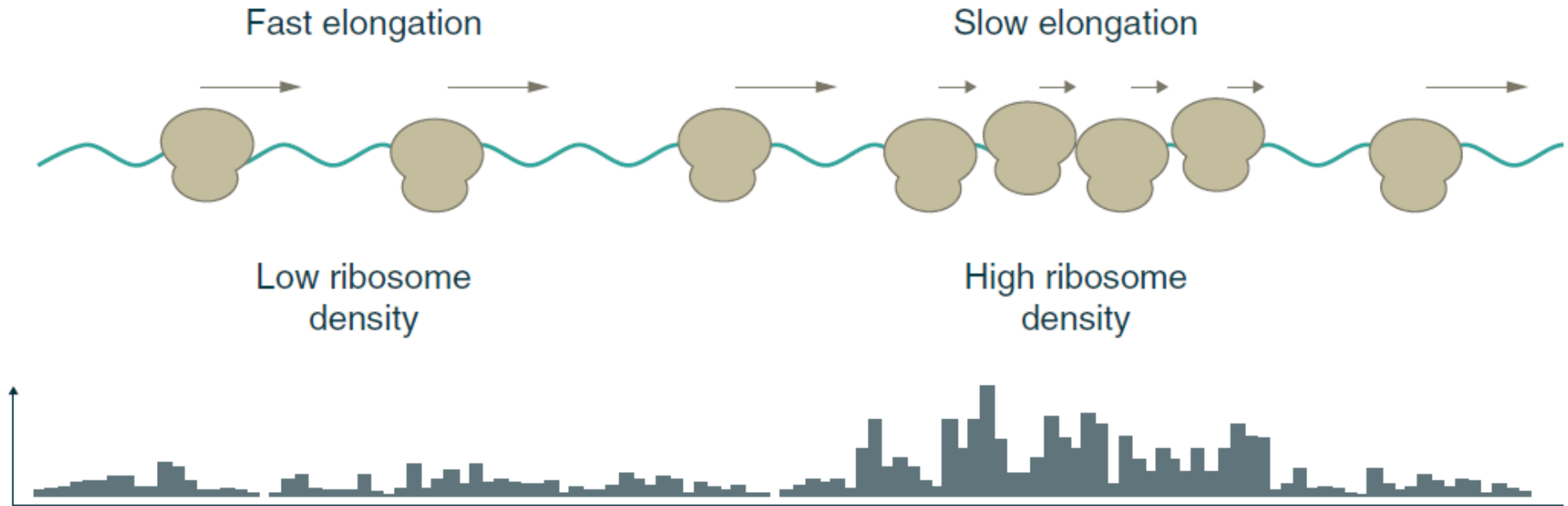
- A) Which RNAs are regulated at the level of translation elongation after APC loss?
- B) What are the determinants of elongation changes?

Measuring translation : RiboSeq vs RNAseq

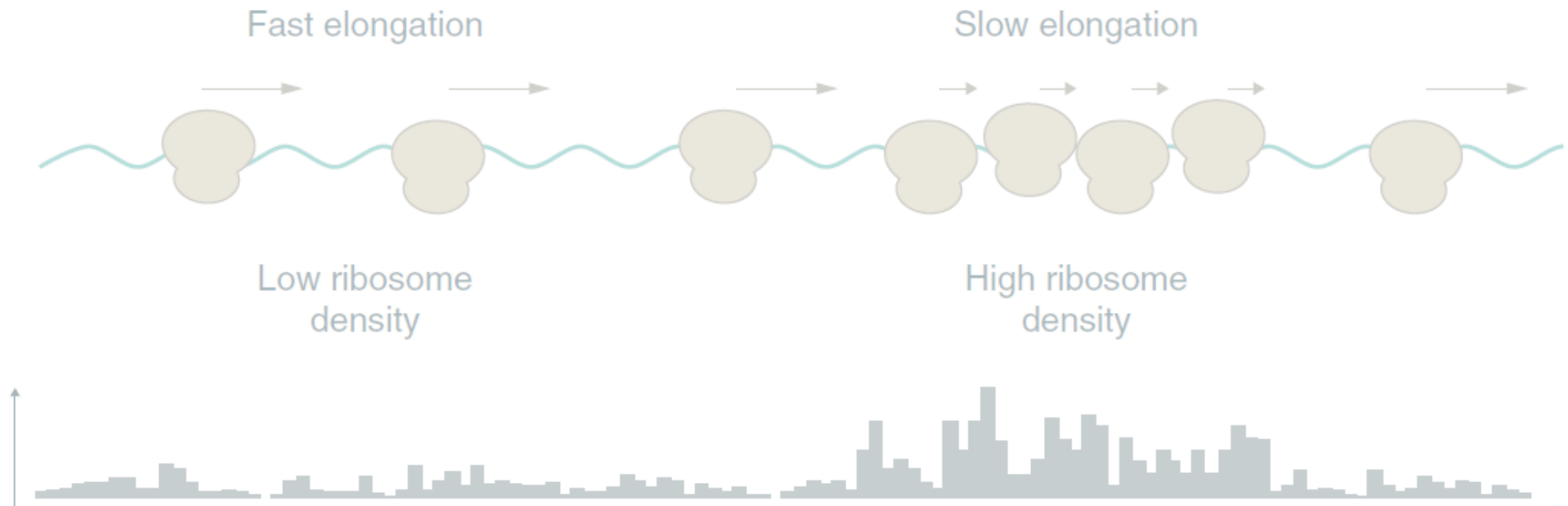


Adapted from Hsu *et al.* 2016

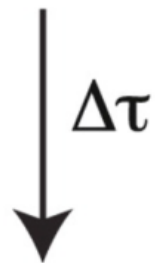
RiboSeq read profiles



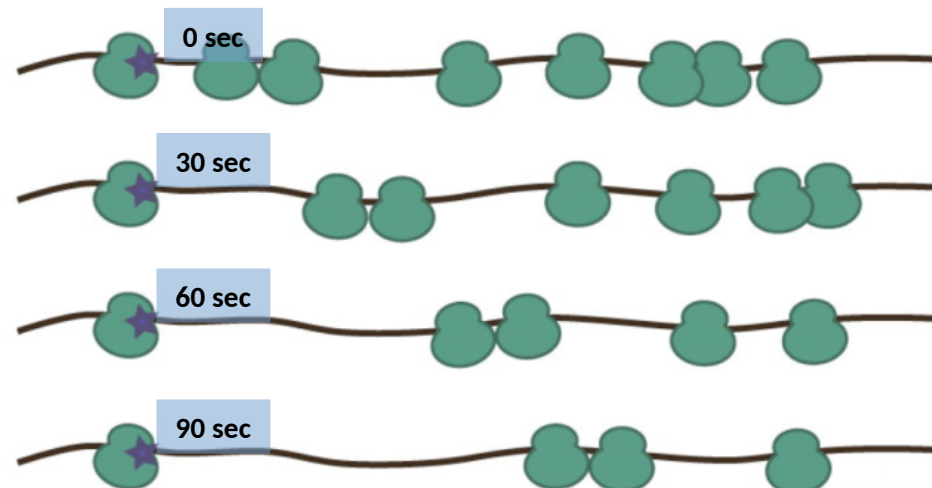
RiboSeq vs ElongationSeq



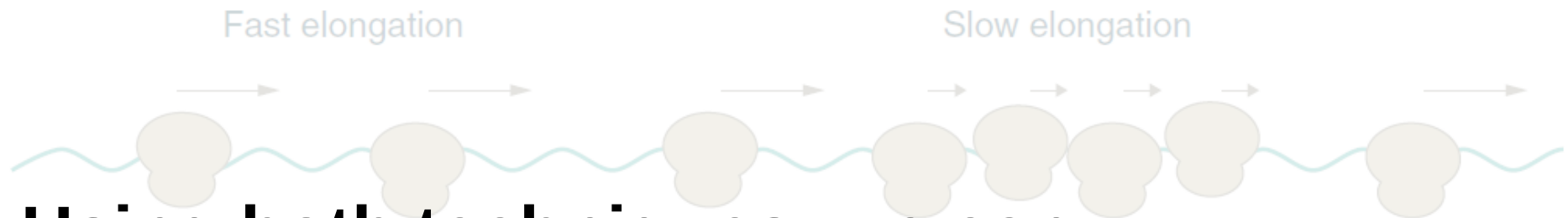
Harringtonine



Cycloheximide



RiboSeq vs ElongationSeq



Using both techniques, we can

Low ribosome
density

High ribosome
density

(1) determine the transcripts that are regulated at the level of translational elongation

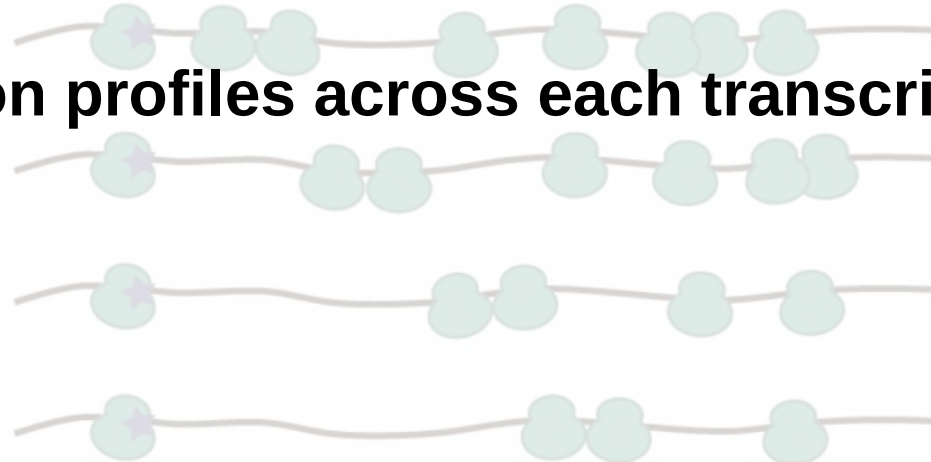
(2) predict ribosome stalling sites in different contrasts

(3) investigate elongation profiles across each transcript

Harringtonine

$\Delta\tau$

Cycloheximide



Potential determinants of elongation speed and ribosome stalling

- tRNA availability
- RBPs and miRNA binding

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➤ co-translational re-folding ??

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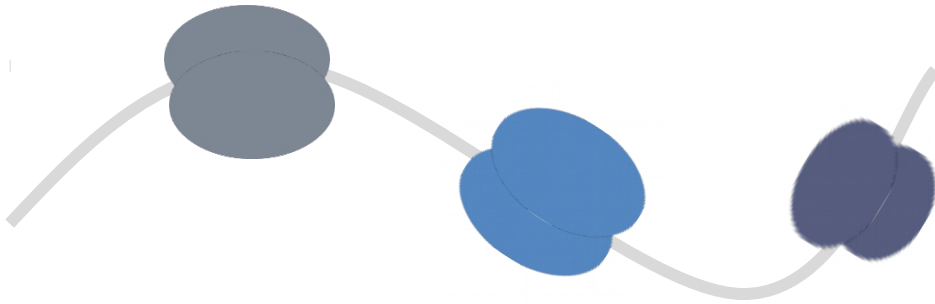
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4) How can we better estimate translational efficiency of transcripts using RNAseq with Ribo-seq and Elongation-seq data?



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