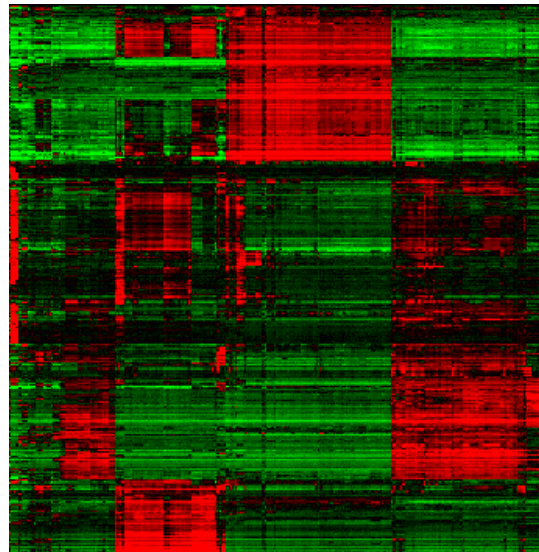


TRANSCRIPTOMICS

The study of the complete set of RNAs (**transcriptome**) encoded by the genome of a specific cell or organism at a specific time or under a specific set of conditions



QUESTIONS

What is the relationship between transcriptome size and organismal complexity?

How do basic steps of gene expression contribute to transcriptome size?

What do new studies tell us about transcriptome size and complexity?

What are the roles of non-coding transcripts?

QUESTIONS

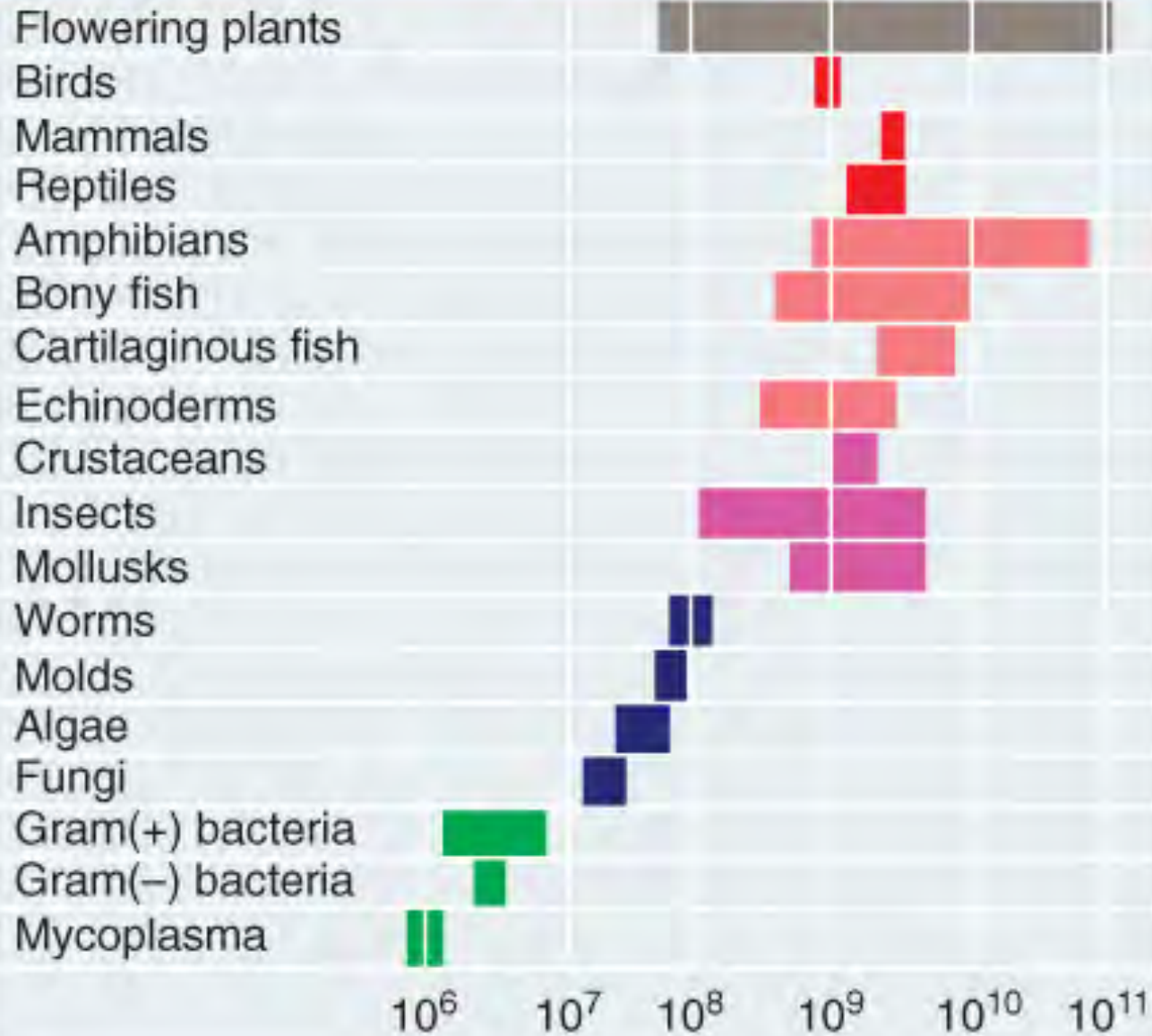
What is the relationship between transcriptome size and organismal complexity?

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What are the roles of non-coding transcripts?

Is DNA content related to morphological complexity?



base pairs

From: *Essential Genes*, Lewin

C-Value
Paradox

Minimum gene numbers range from 500 to 30,000

500 genes

Intracellular (parasitic)
bacterium



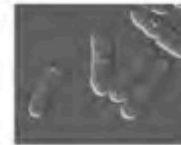
1,500 genes

Free-living bacterium



5,000 genes

Unicellular eukaryote



20,000 genes

Multicellular eukaryote



25,000 genes

Higher plants

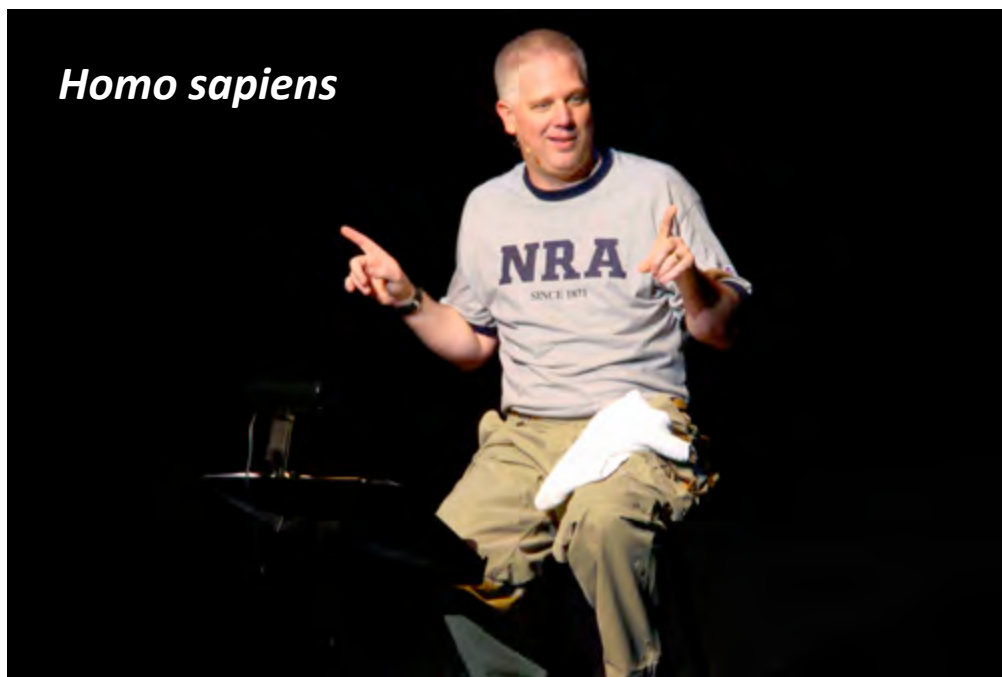


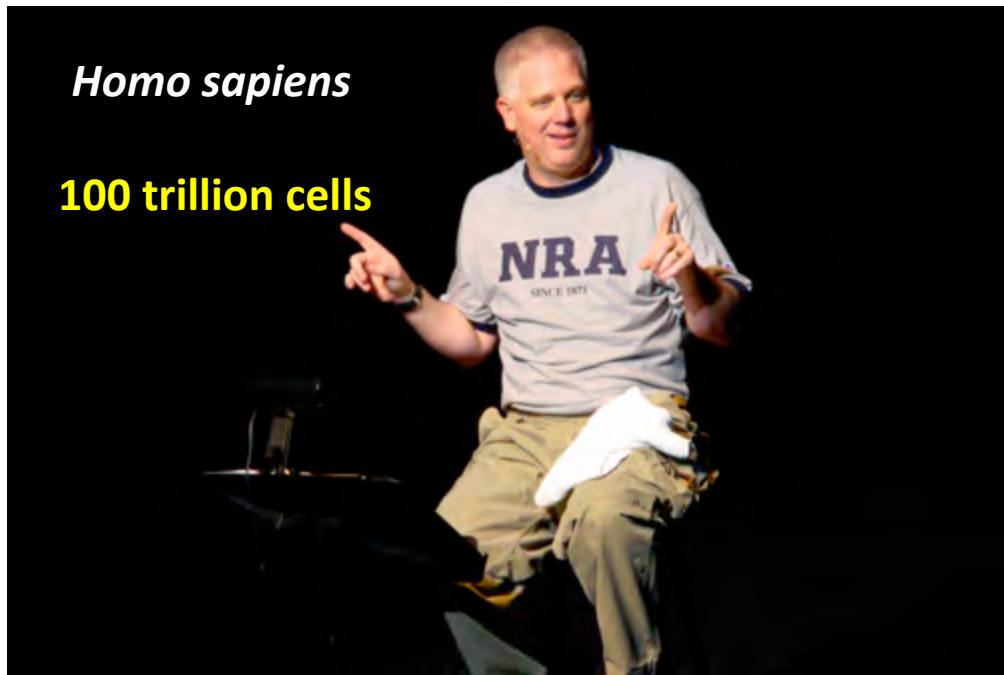
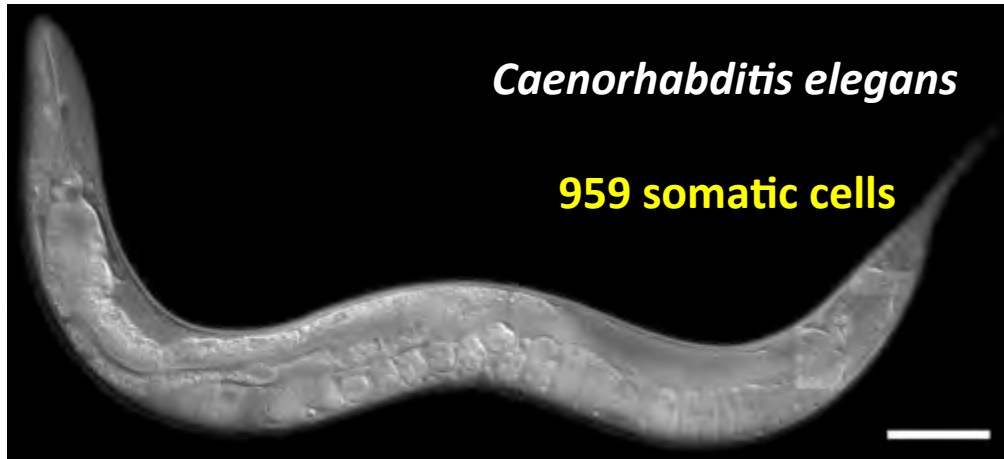
22,000 genes

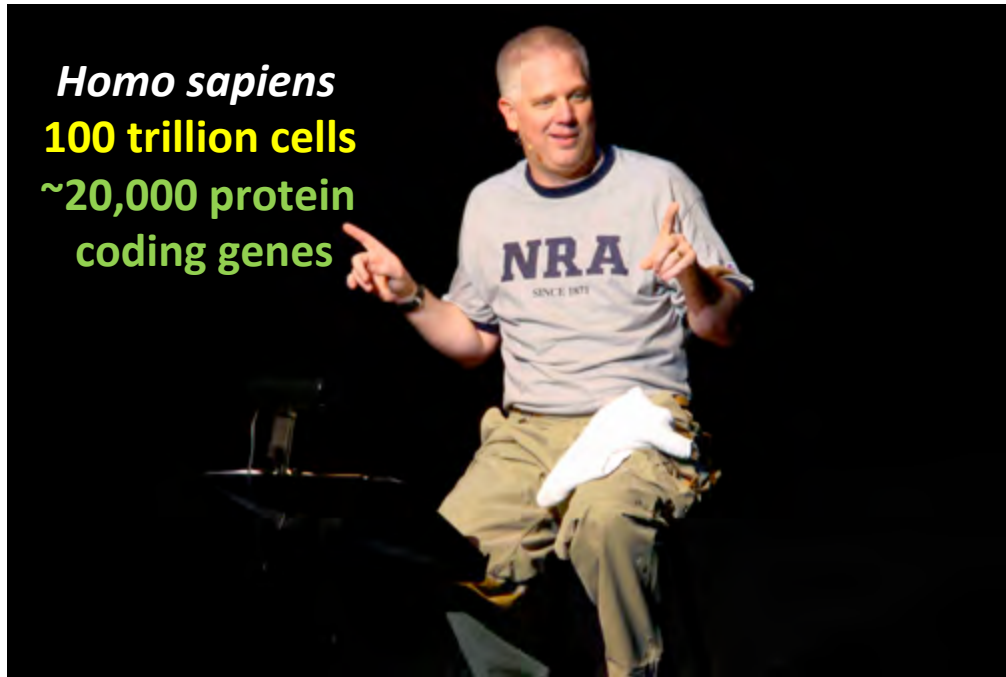
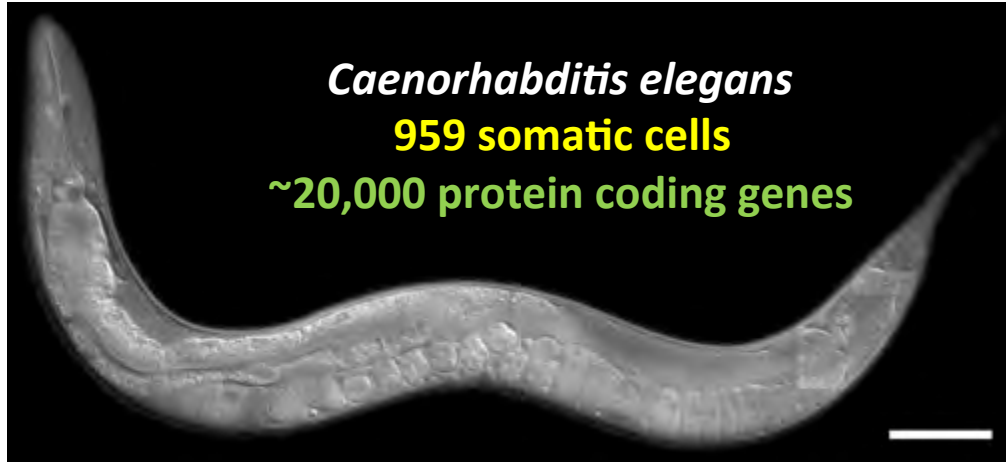
Mammals



From:
***Essential Genes*, Lewin**







QUESTIONS

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BASIC STEPS OF GENE EXPRESSION

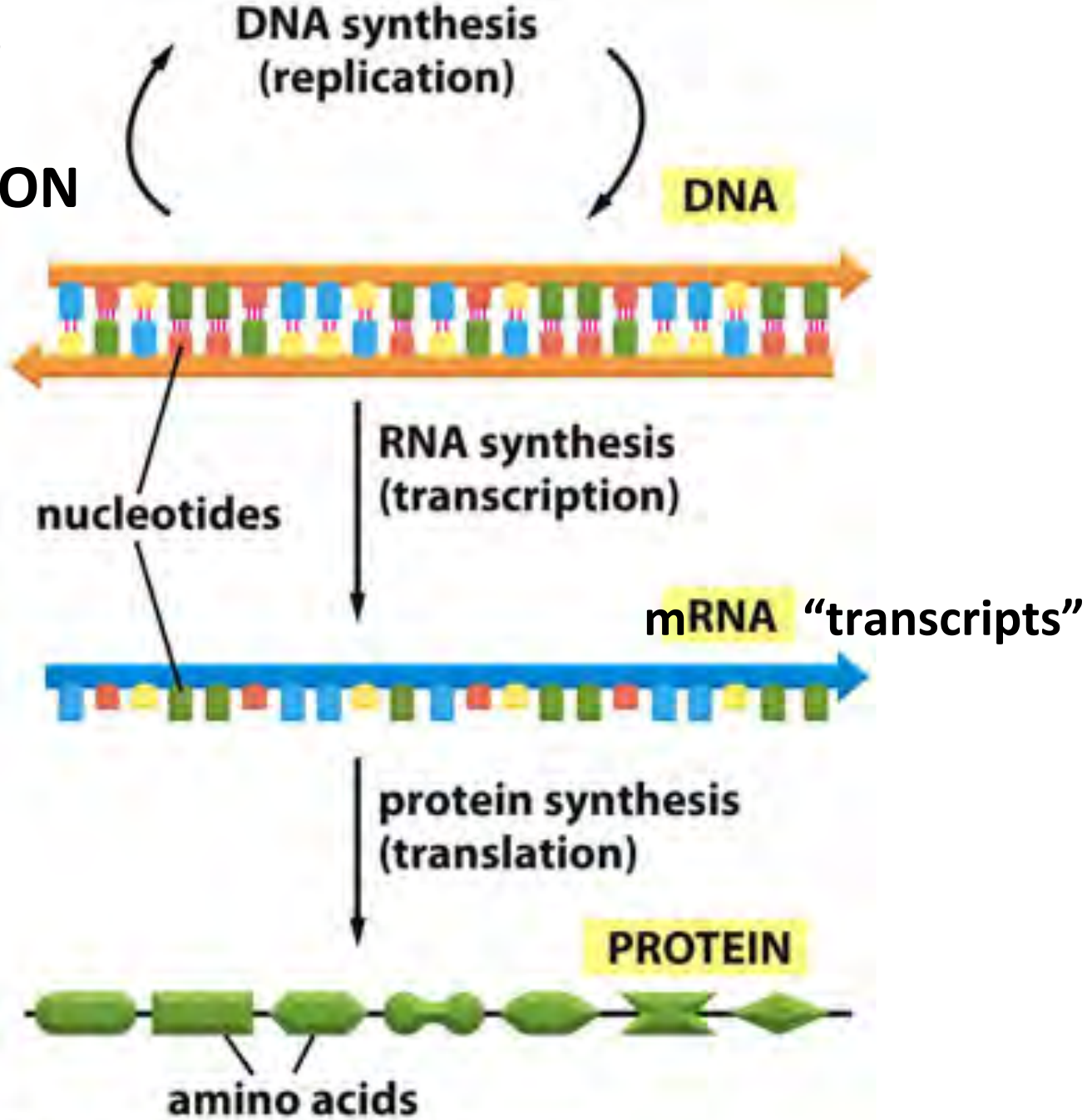
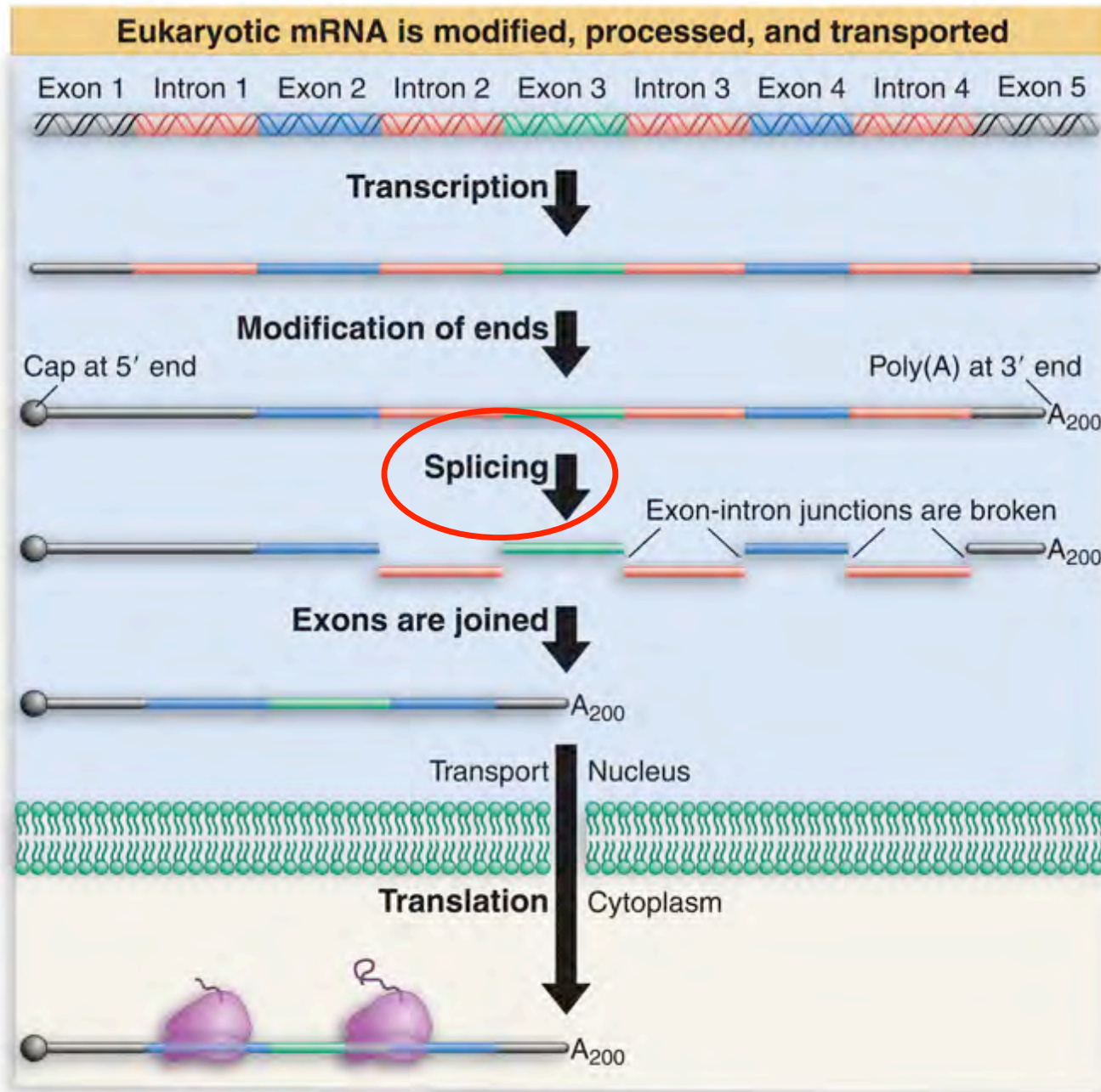


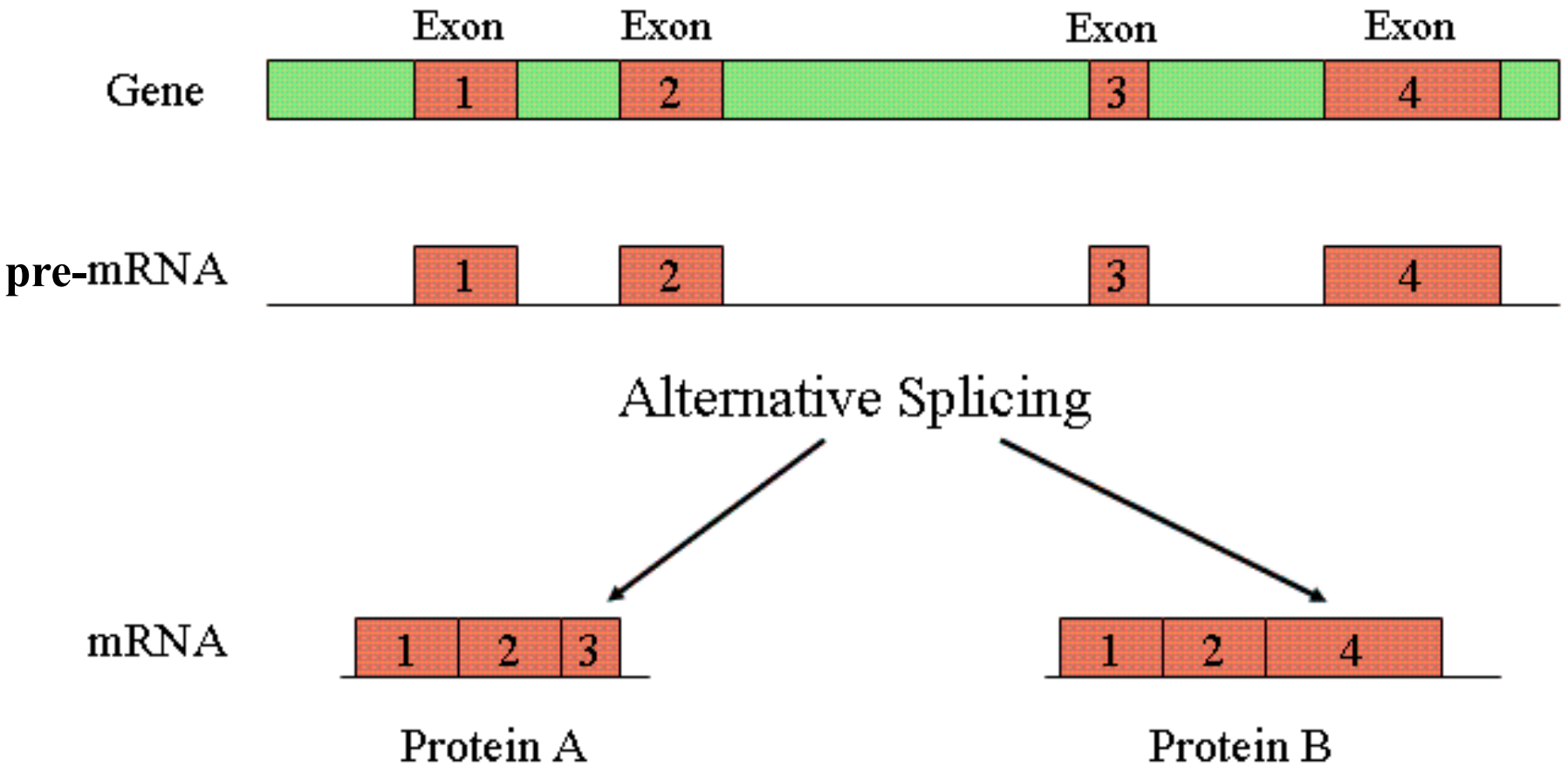
Figure 1-2 Essential Cell Biology 3/e (© Garland Science 2010)

Eukaryotic mRNA is modified, processed, and transported

DNA
pre-mRNA
mRNA
protein

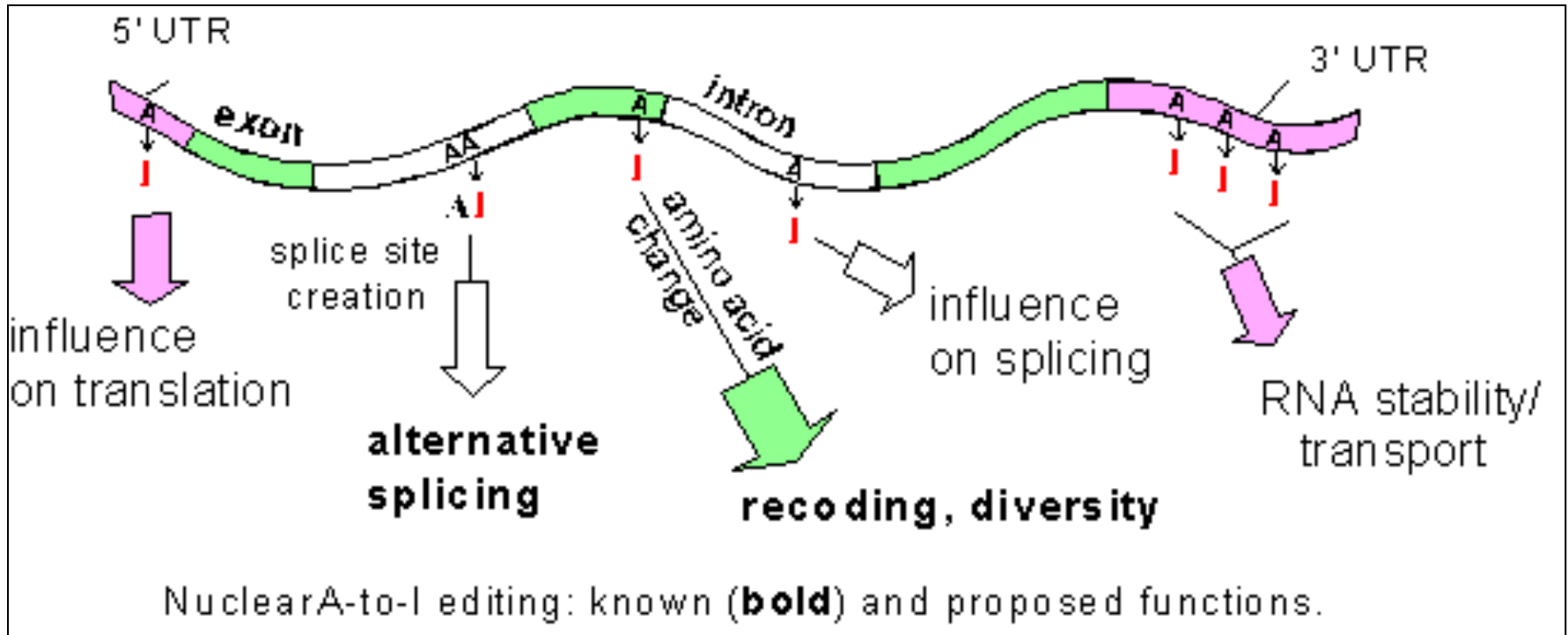


Alternative splicing adds to the size (complexity) of the transcriptome.



From: ncbi.nlm.nih.gov

RNA editing – The enzymatically catalyzed conversion of A to I (Inosine) which is decoded as a G (so an A→G transition)



RNA editing adds to the size (complexity) of the transcriptome.

QUESTIONS

What is the relationship between transcriptome size and organismal complexity?

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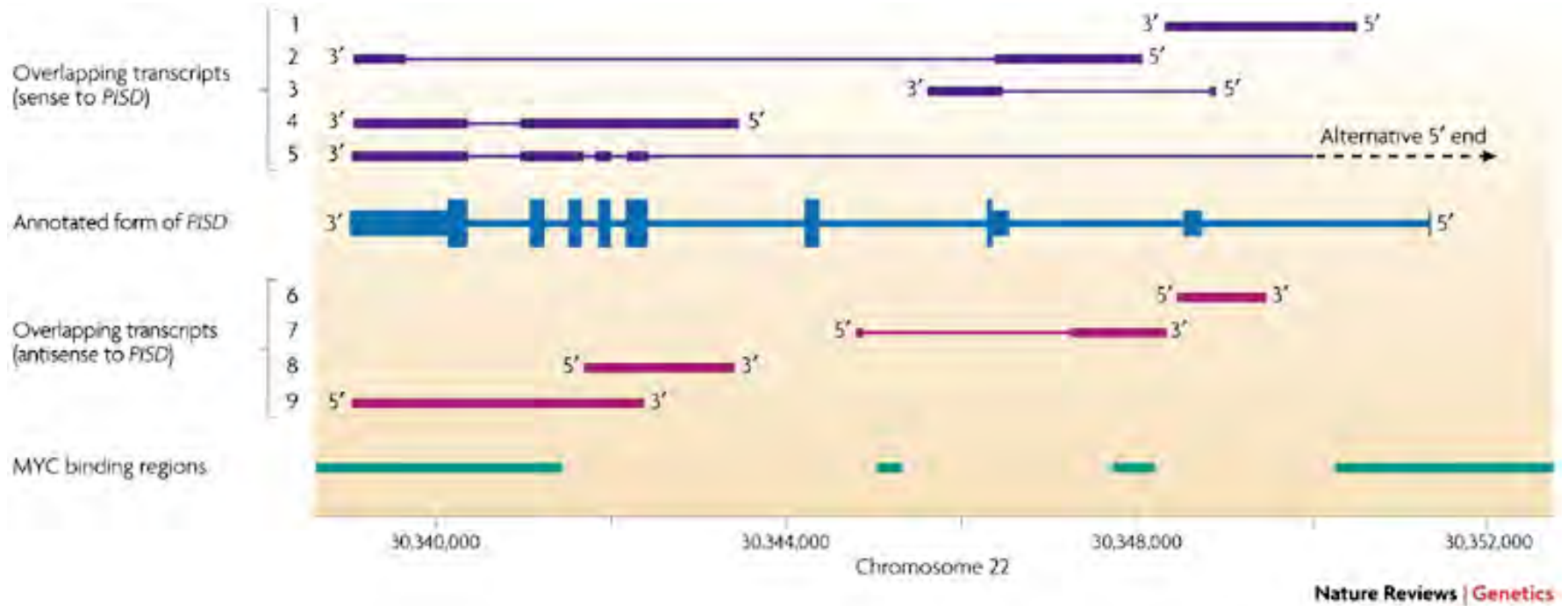
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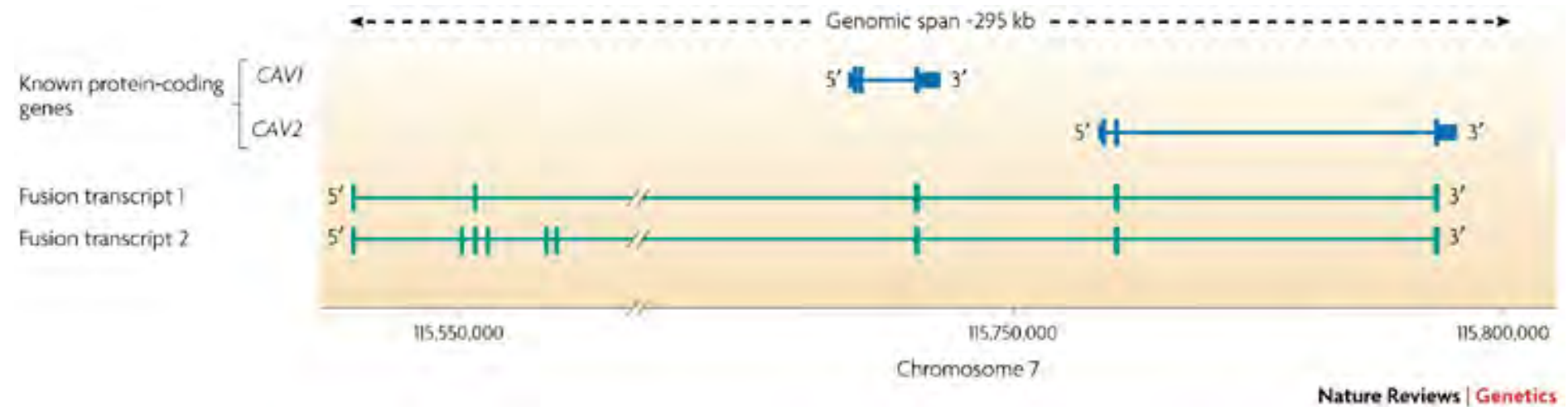
The National Human Genome Research Institute (NHGRI) launched a public research consortium named **ENCODE**, the **Encyclopedia Of DNA Elements**, in September 2003, to carry out a project **to identify all functional elements in the human genome sequence**.

The human genome is pervasively transcribed. One stretch of DNA can encode multiple (m)RNAs.



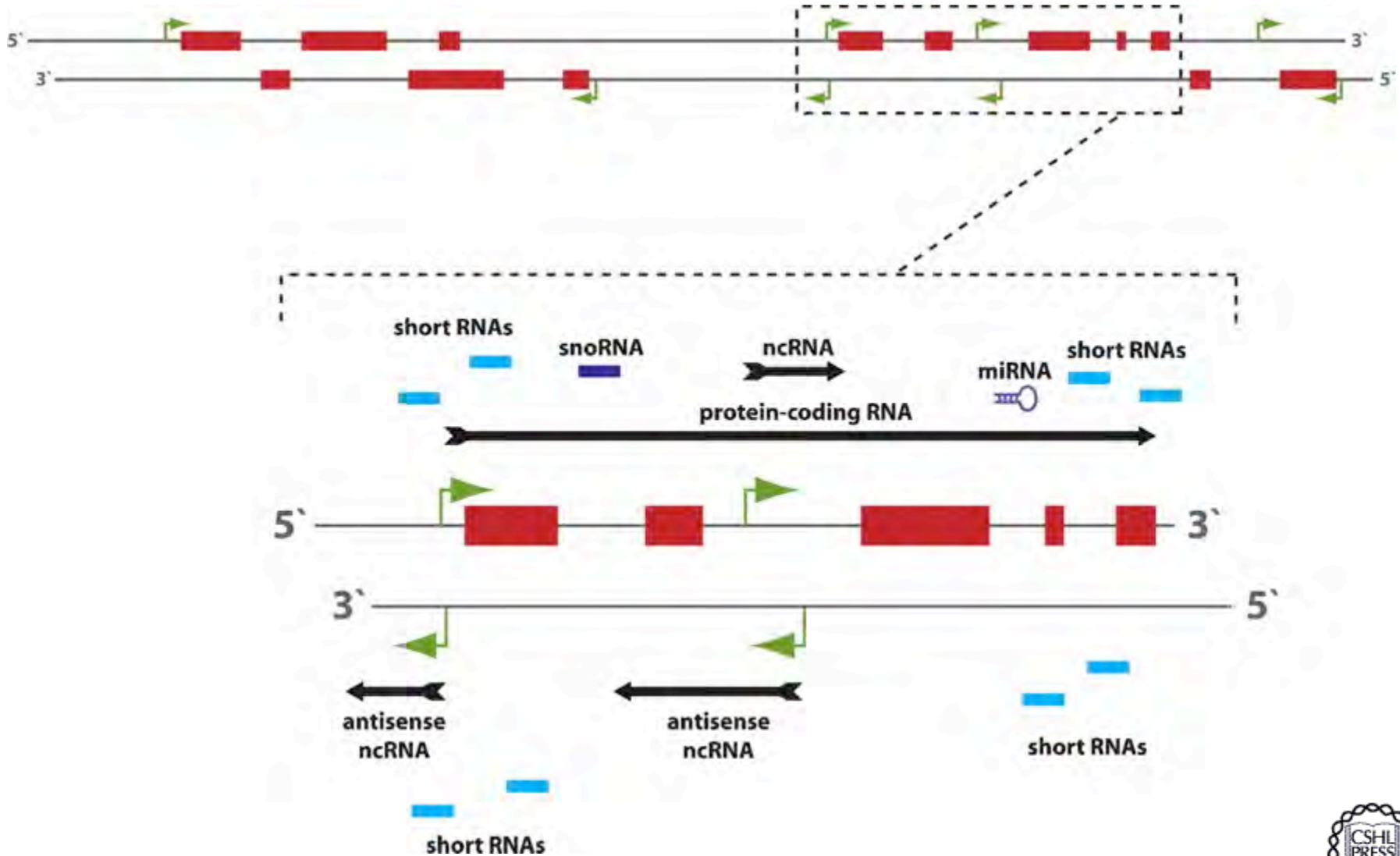
From: Kapranov *et al.* (2007) *Nature Reviews Genetics*, 8: 413 – 423.

The human genome is pervasively transcribed. DNA sequences far apart can be found on a single RNA (“fusion transcripts”).



From: Kapranov *et al.* (2007) *Nature Reviews Genetics*, 8: 413 – 423.

The human genome is pervasively transcribed. One stretch of DNA can encode an mRNA together with many other types of RNAs (“non-coding RNAs”).



natsiRNAs

pasRNAs

rRNAs

tRNAs

endo-siRNAs

tasiRNAs

microRNAs

gRNAs

snoRNAs

snRNAs

piwiRNAs

sRNAs

lincRNAs

tasRNAs

casiRNAs

natsiRNAs

pasRNAs

rRNAs

tRNAs

endo-siRNAs

tasiRNAs

microRNAs

gRNAs

snoRNAs

snRNAs

piwiRNAs

sRNAs

lincRNAs

tasRNAs

casiRNAs

QUESTIONS

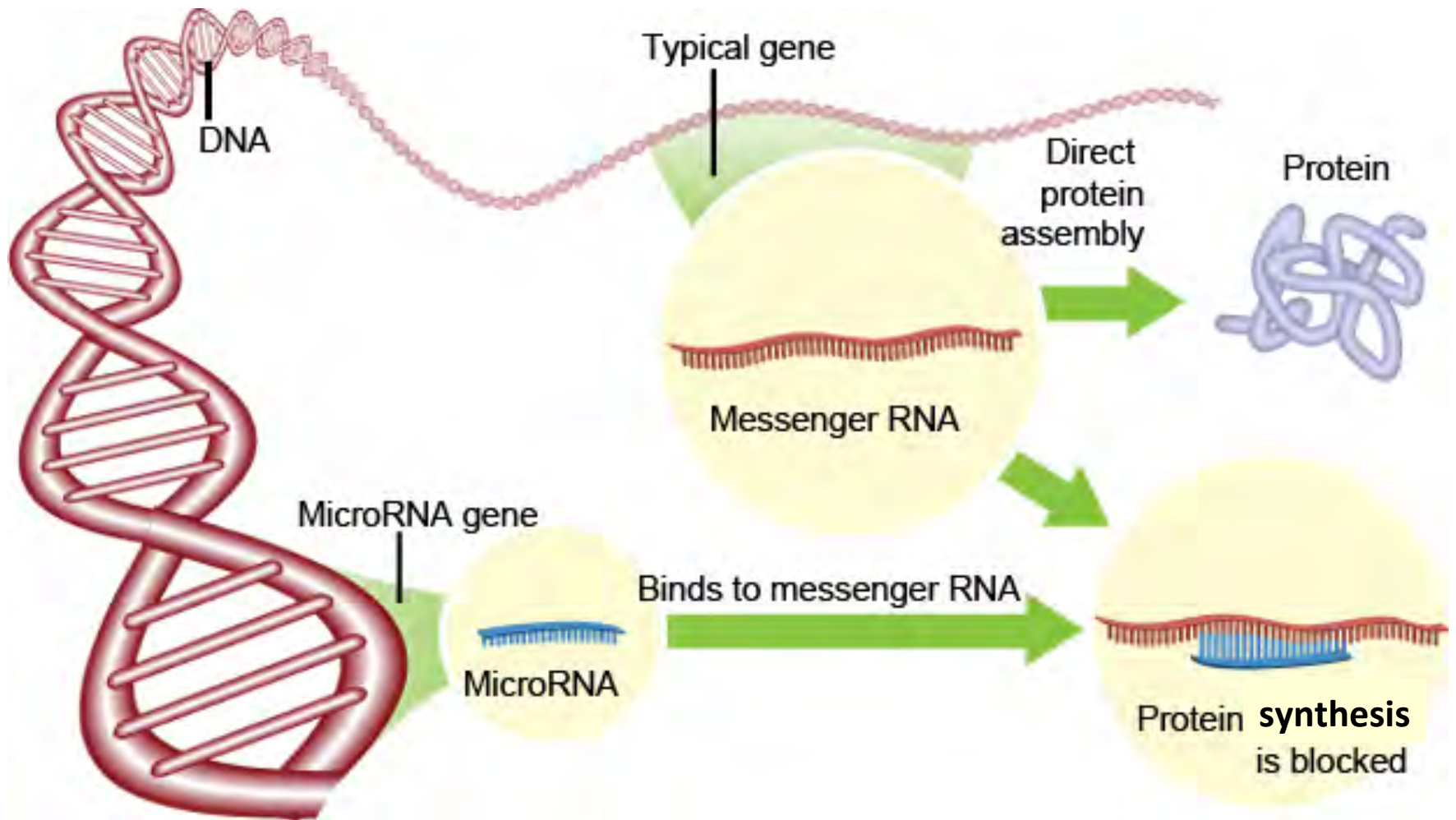
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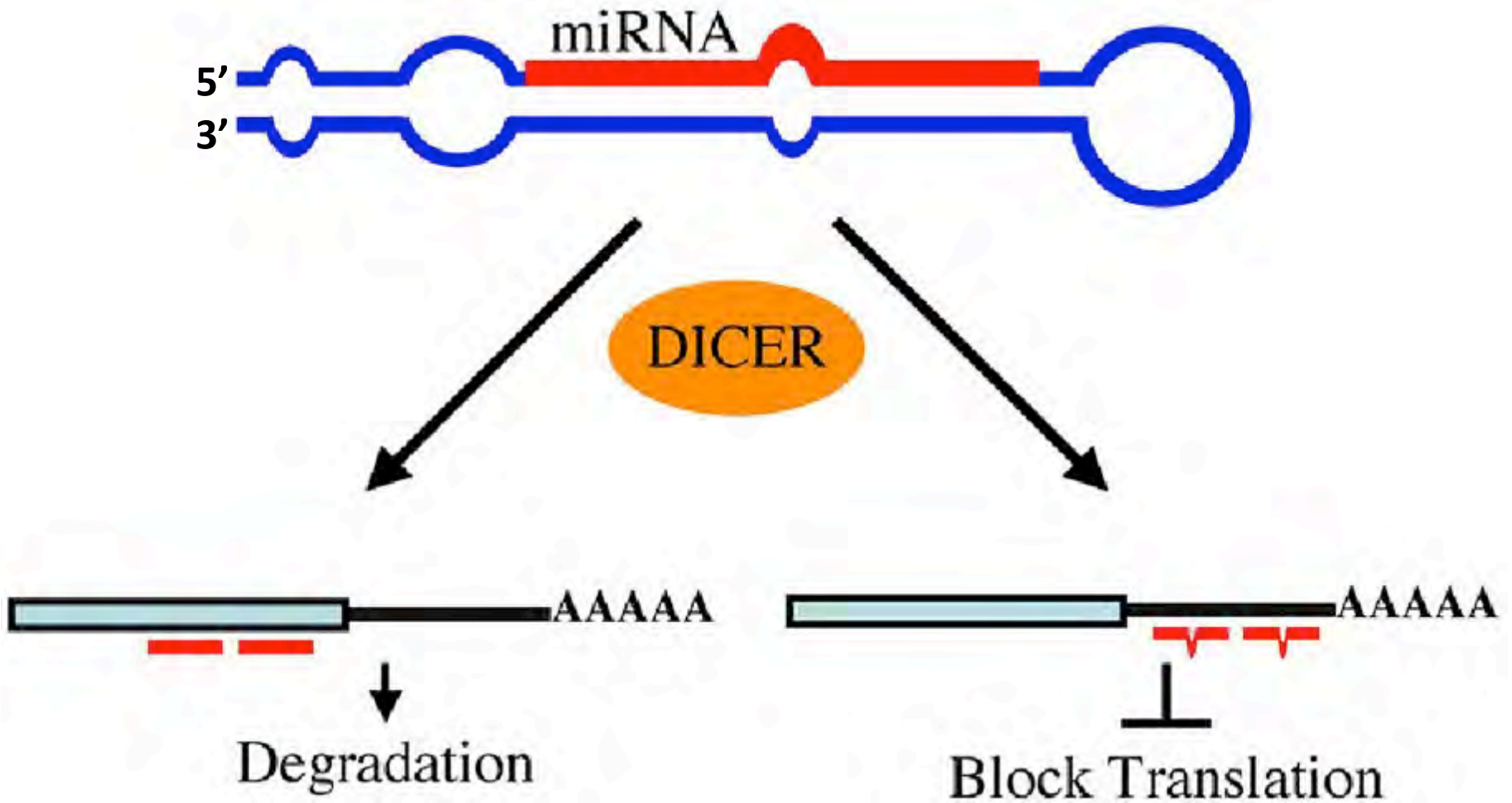
What are the roles of non-coding transcripts?

microRNAs are FUNCTIONAL gene products 21 – 22 nucleotides long.



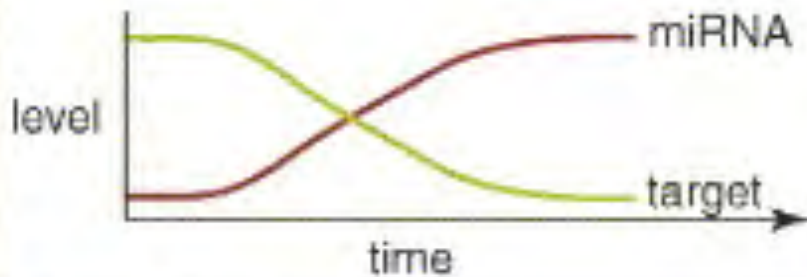
From: discovermagazine.com

FUNCTIONAL **microRNAs** are cut out of longer RNA molecules by an enzyme called DICER.

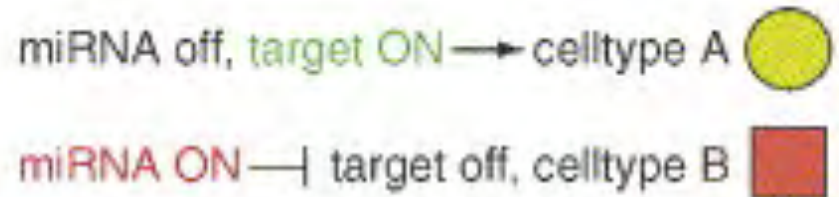


- 1 **microRNA** can control the expression of **many** target mRNAs.
- **microRNAs** are important for **development** and **cell- and tissue-specific** gene expression.

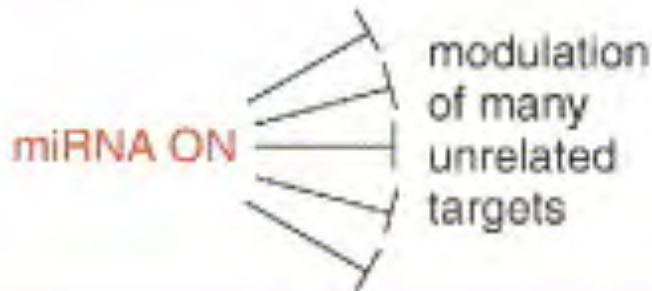
A Temporal switch (*lin-4, let-7*)



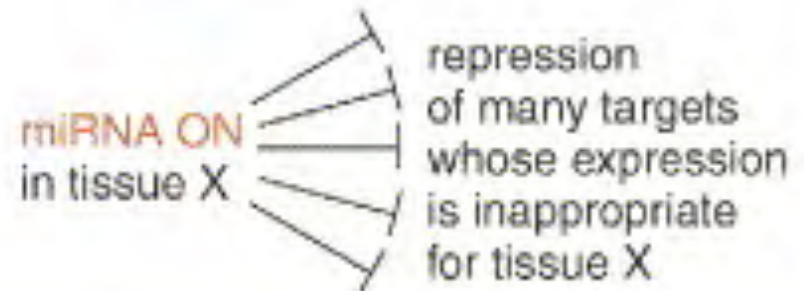
B Spatial switch (*miR-273, Isy-6*)



C Fine-tuning expression



D Tissue identity (*miR-1?*, *miR-124?*)



microRNAs are mis-regulated in human cancers.

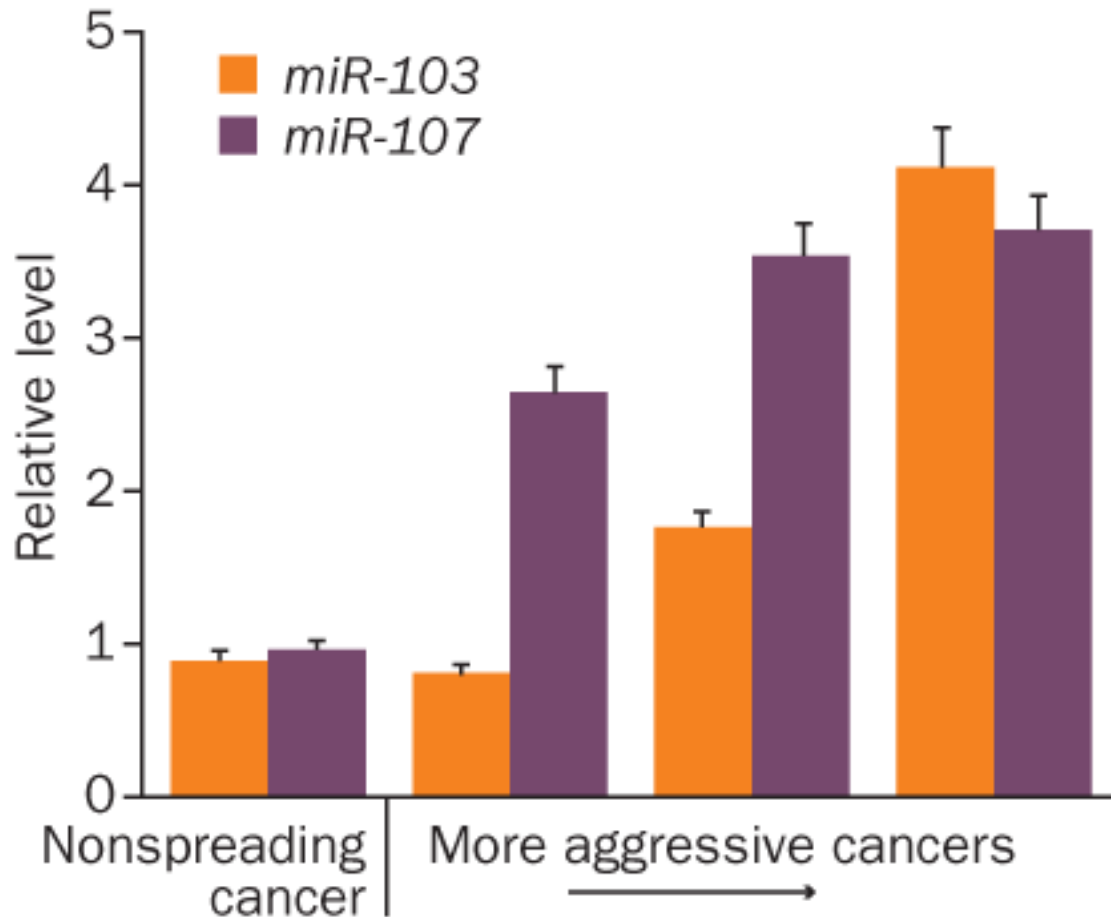
Variations in microRNA genes linked to cancers

Gene for:	<i>miR-146a</i>	<i>miR-196a</i>	<i>miR-423</i>	<i>miR-27a</i>	<i>miR-492</i>	<i>miR-499</i>
Lung cancer		X				
Esophageal cancer		X	X			
Breast cancer		X	X	X		X
Stomach cancer		X				
Liver cancer	X	X				
Bladder cancer			X		X	
Papillary thyroid	X					
Brain cancer		X				

This is important for **cancer diagnosis**.

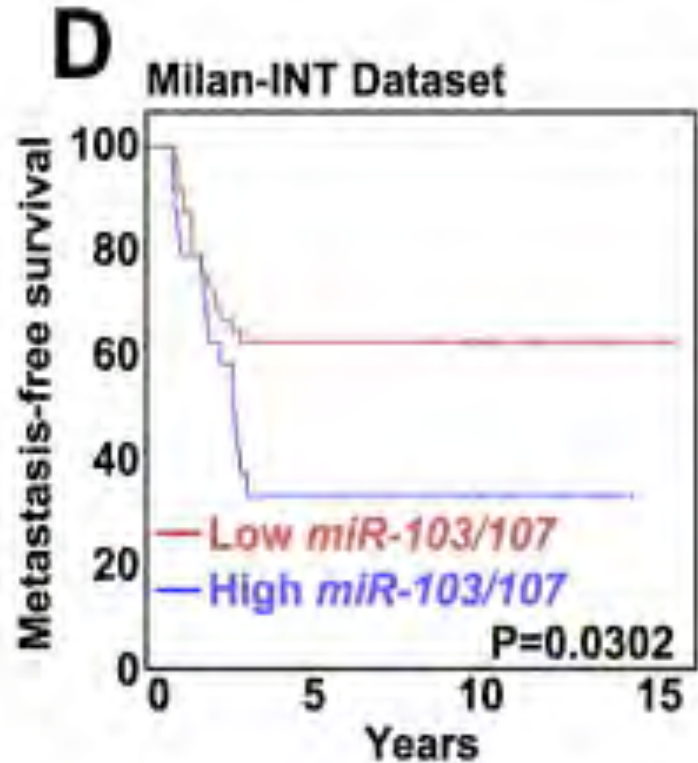
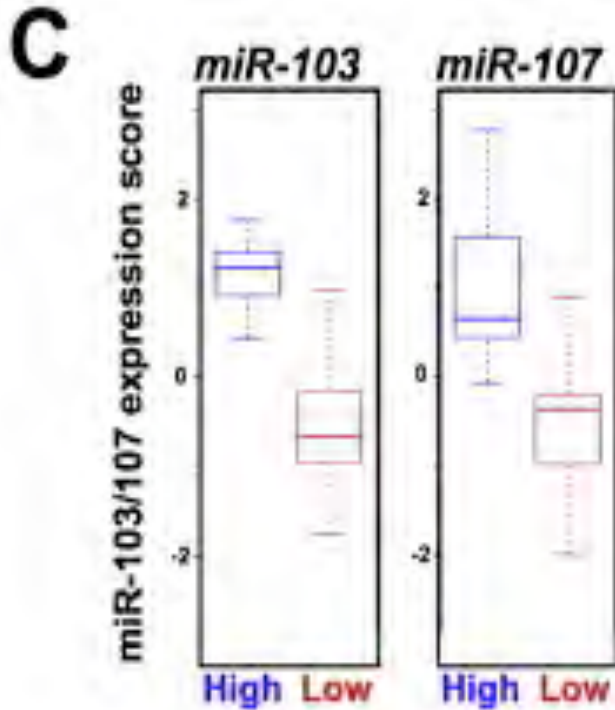
microRNAs are involved in **cancer metastasis**.

MicroRNA levels and cancer aggressiveness



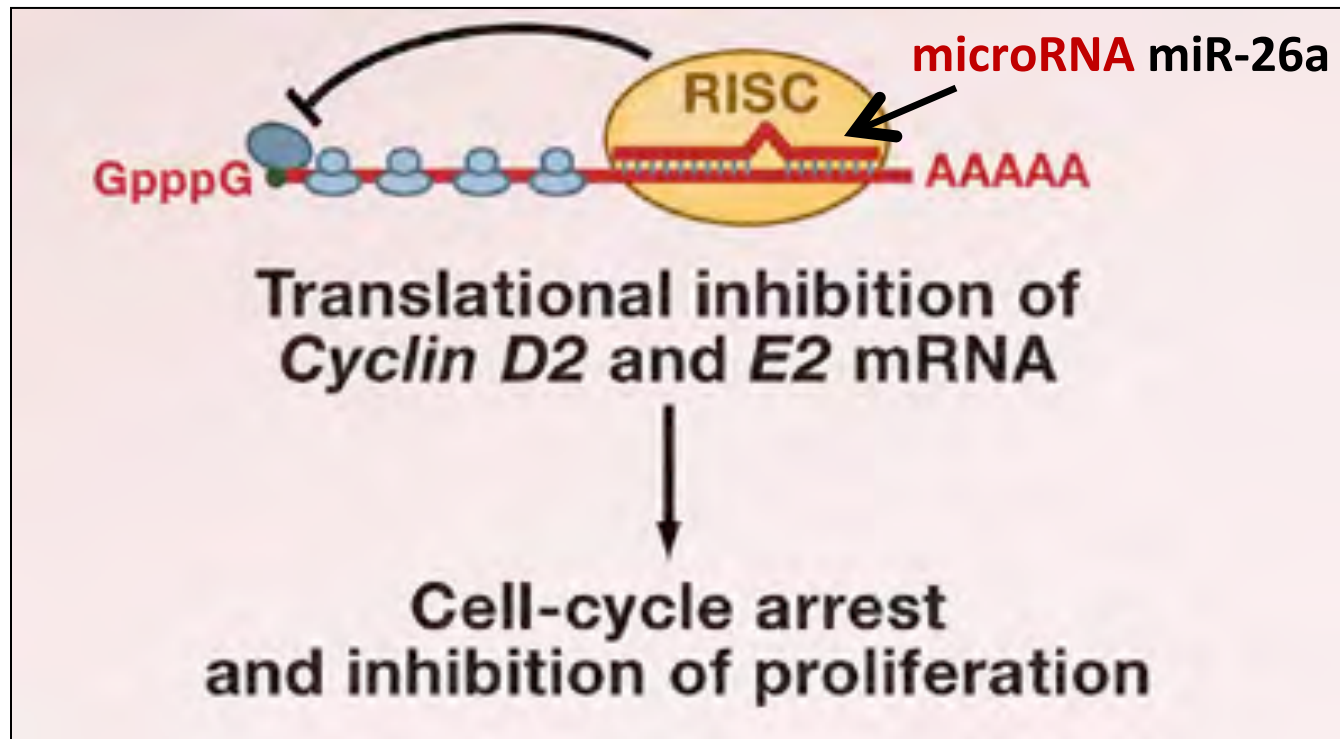
From: Martello *et al.* (2010) *Cell*, 141: 1195 – 1207.

High levels of **microRNAs** miR-103 and miR-107 are associated with poor cancer prognosis.



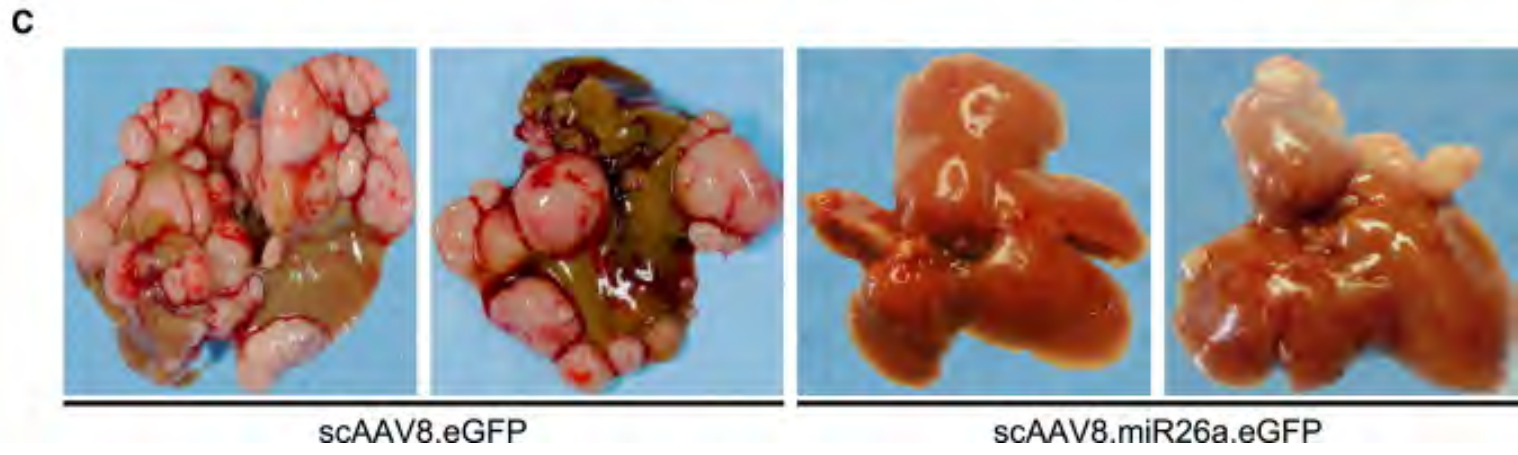
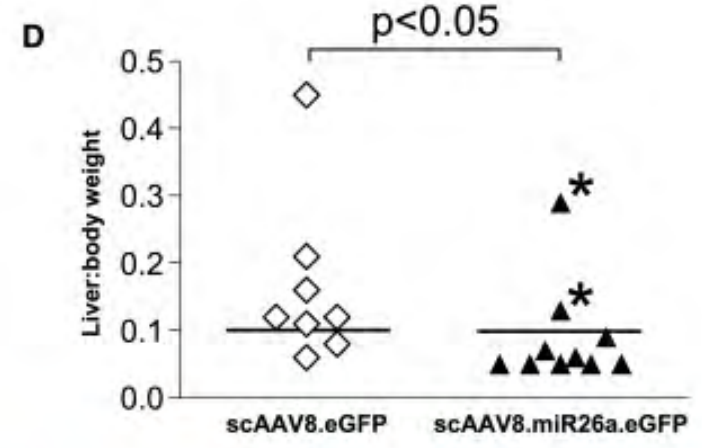
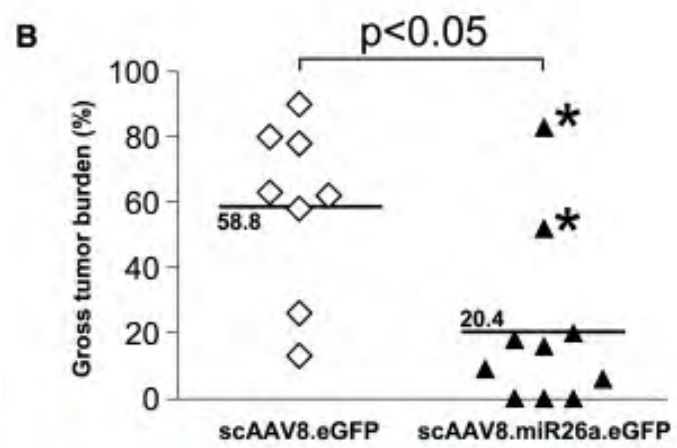
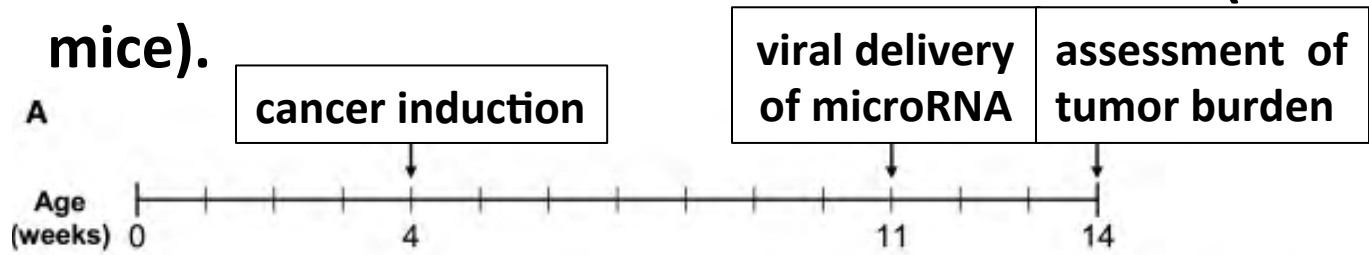
From: Martello *et al.* (2010) *Cell*, 141: 1195 –1207.

microRNAs can be used to treat liver cancer (in mice).



From: Rossi, J. (2009) *Cell*, 137: 990 –992.

microRNAs can be used to treat liver cancer (in mice).



From: Kota, J. et al. (2009) *Cell*, 137: 1005 – 1017.

SOME ANSWERS

Transcriptome size scales with organismal complexity.

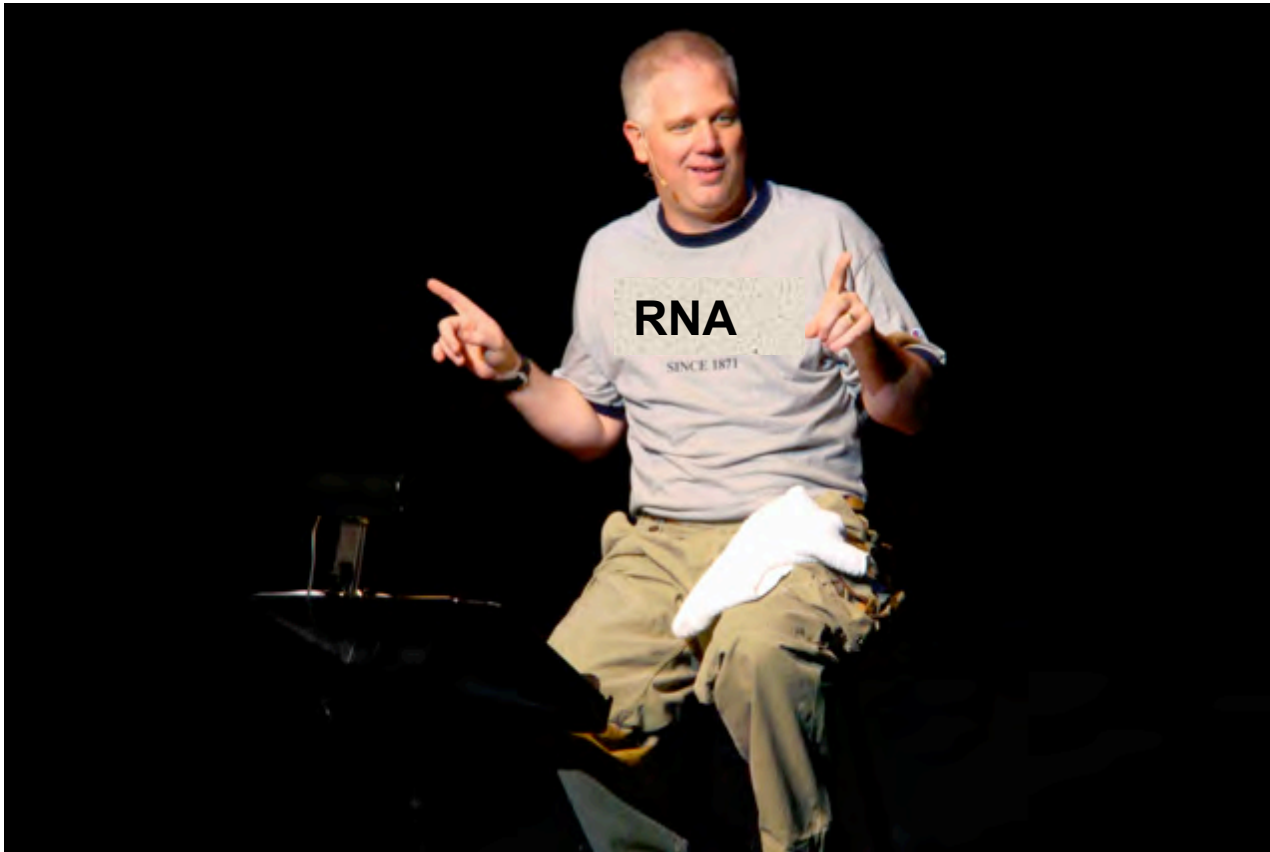
Alternative splicing and RNA editing contribute to and increase transcriptome size.

The human genome is pervasively transcribed. One stretch of DNA can encode many different RNAs.

Many new functional species of RNAs have been identified (*e.g.* microRNAs).

microRNAs control the expression of many mRNAs and are involved in many cellular processes including development and disease, esp. cancer.

The need for a more RNA-centric viewpoint?



REVIEW

- **Relationship of transcriptome size to morphological complexity**
 - Transcriptome size scales with organismal complexity.
 - Alternative splicing and RNA editing increase transcriptome size.
 - The human genome is pervasively transcribed. One stretch of DNA can encode many different RNAs.
 - Many new species of RNAs have been identified.
- **microRNAs**
 - They are 21 – 22 nucleotide long **FUNCTIONAL GENE PRODUCTS**.
 - They are processed from precursor RNAs by Dicer.
 - They control the expression of **MANY** mRNAs.
 - They are involved in many cellular processes including development and disease.