

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

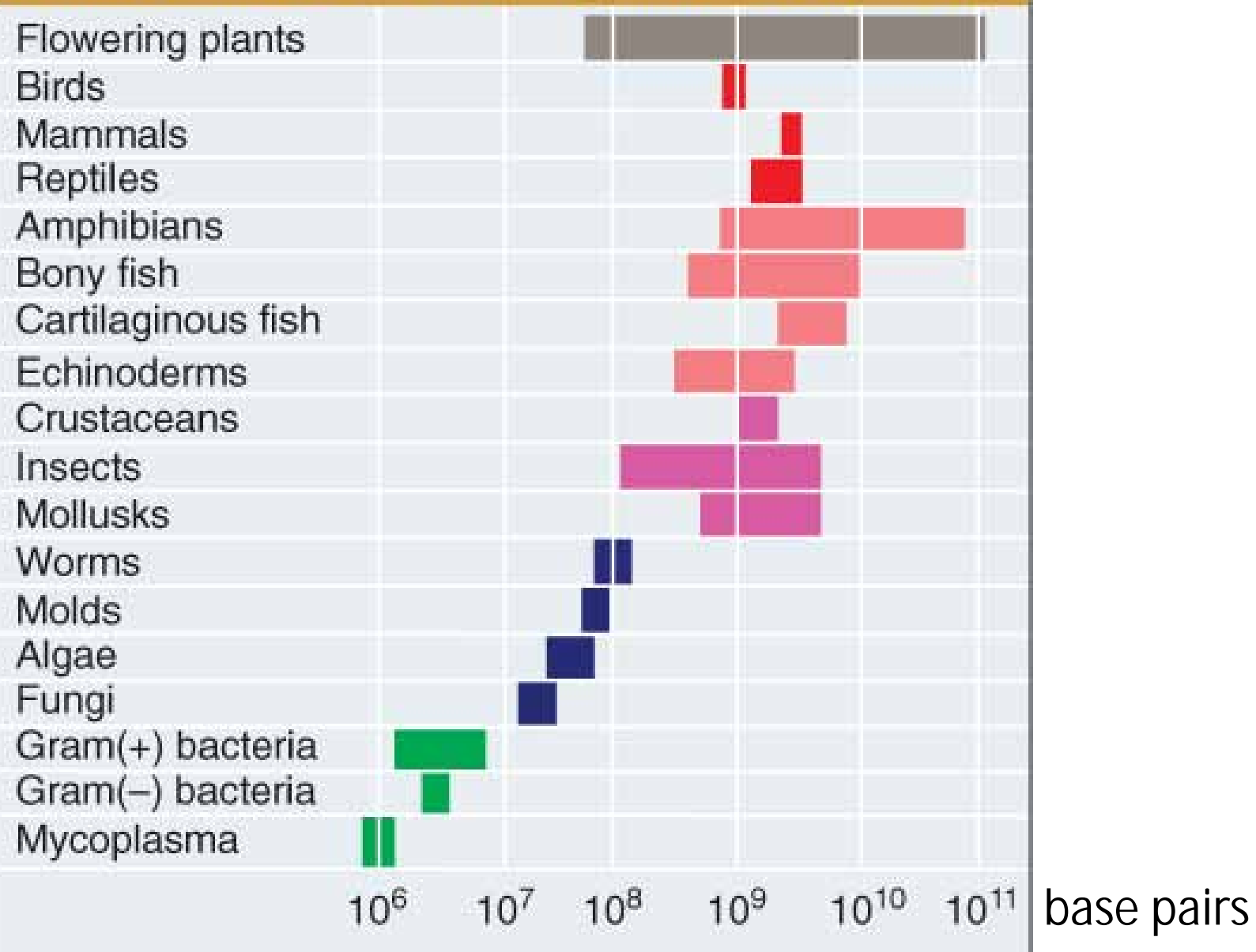
What is the relationship between transcriptome size and organismal complexity?

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?

Is DNA content related to morphological complexity?



From: *Essential Genes*, Lewin

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

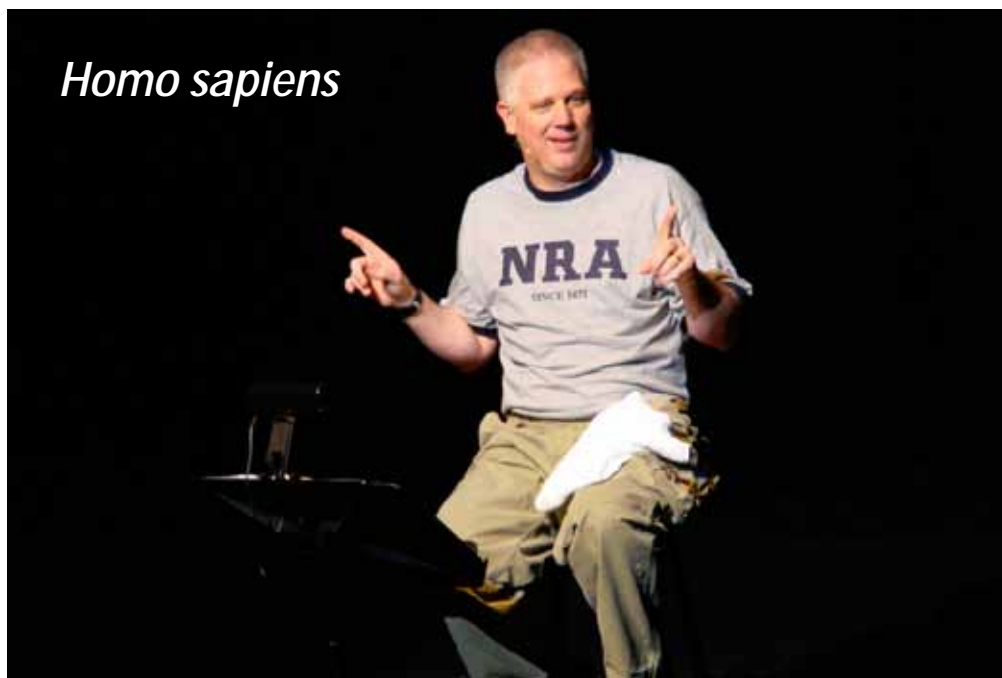


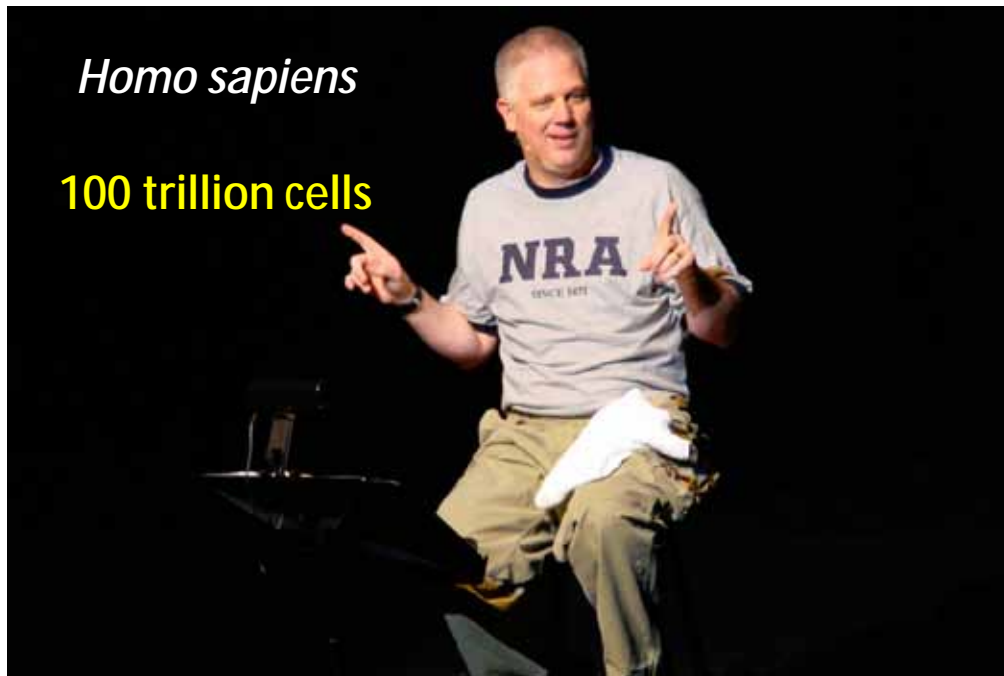
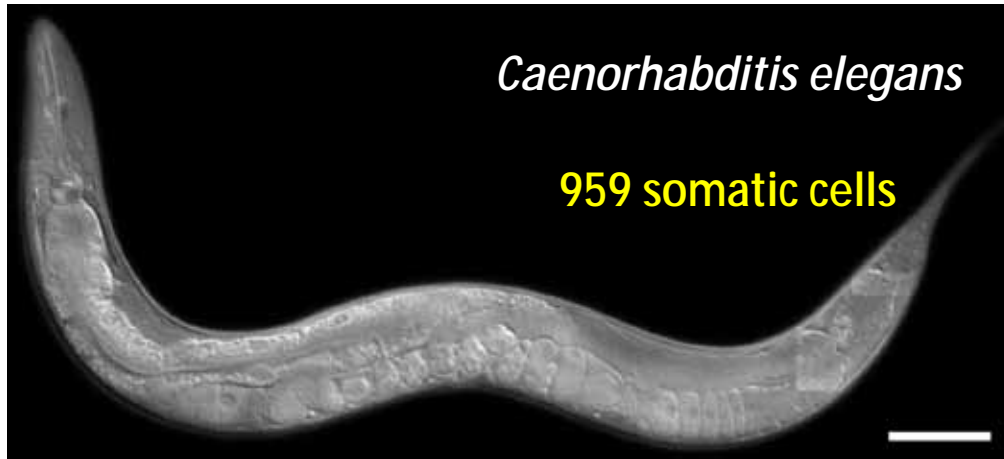
22,000 genes

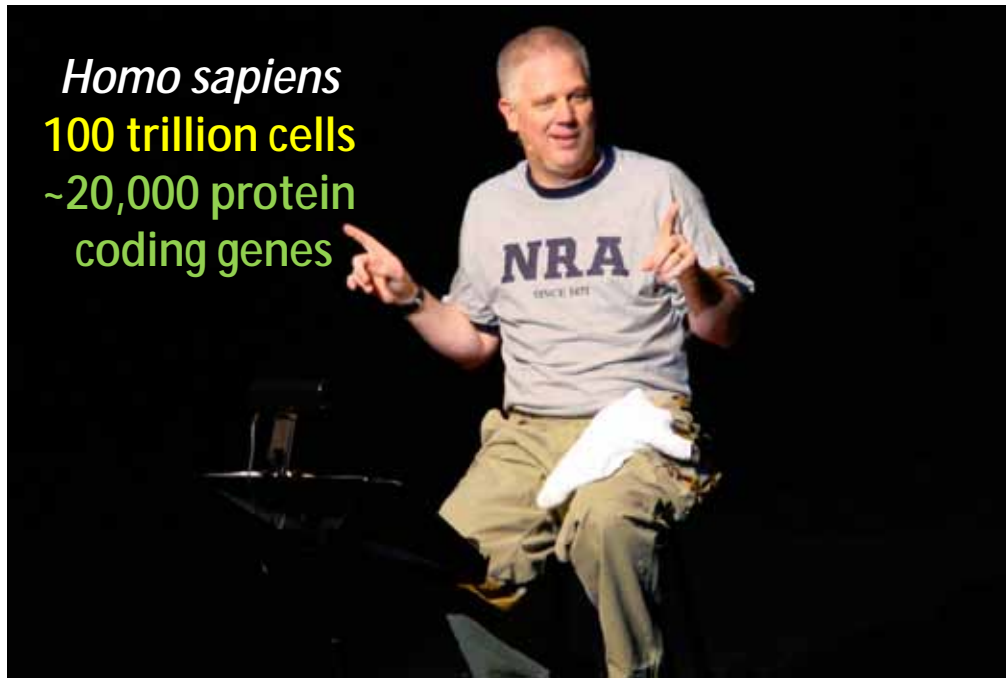
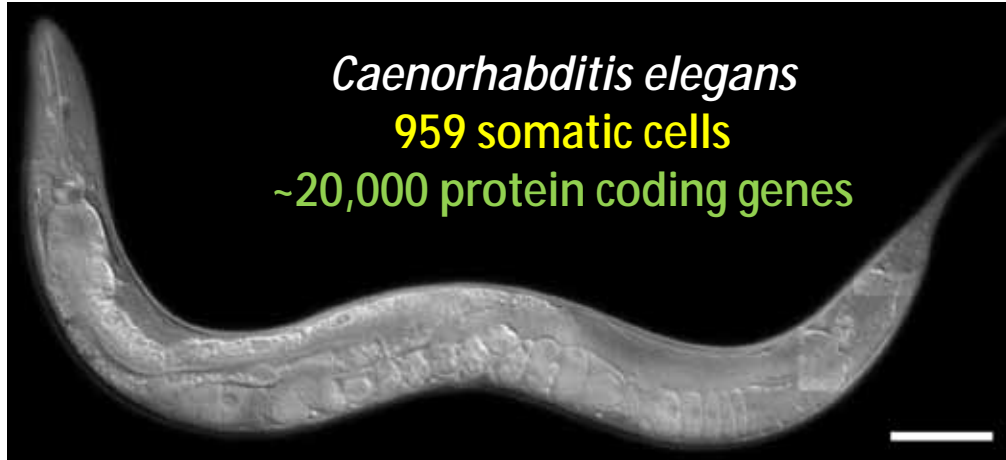
Mammals



From:
Essential Genes, Lewin







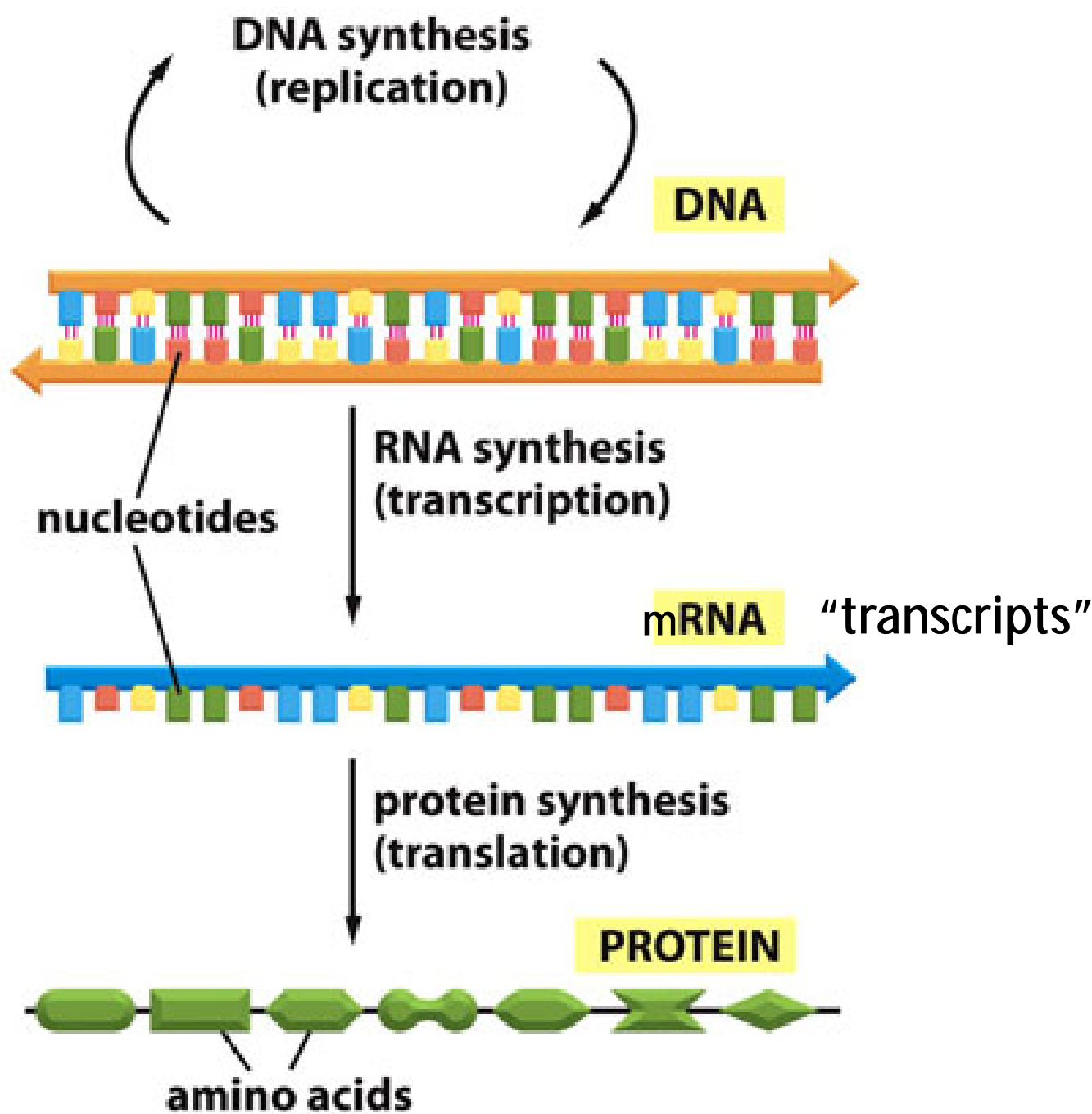
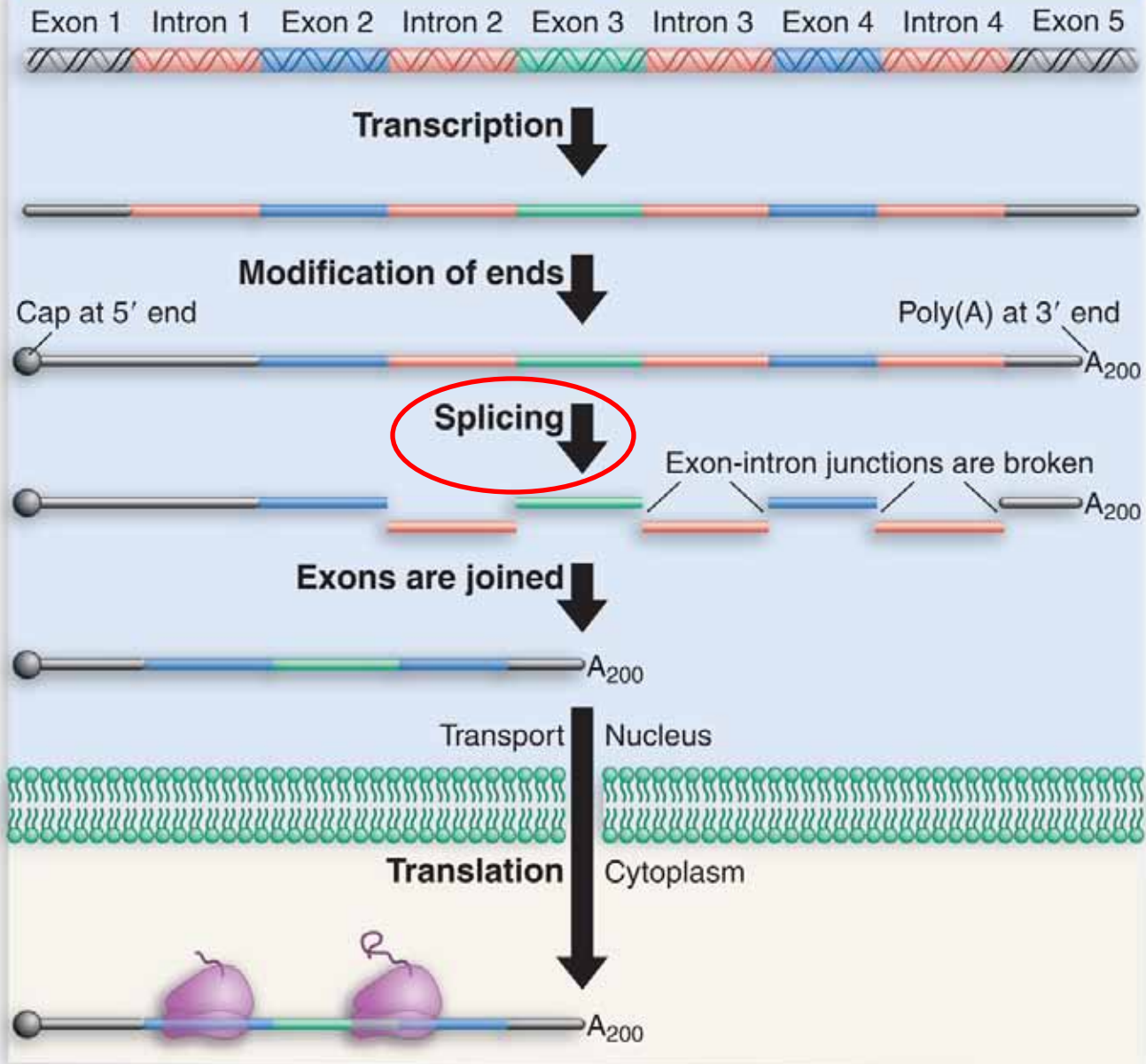
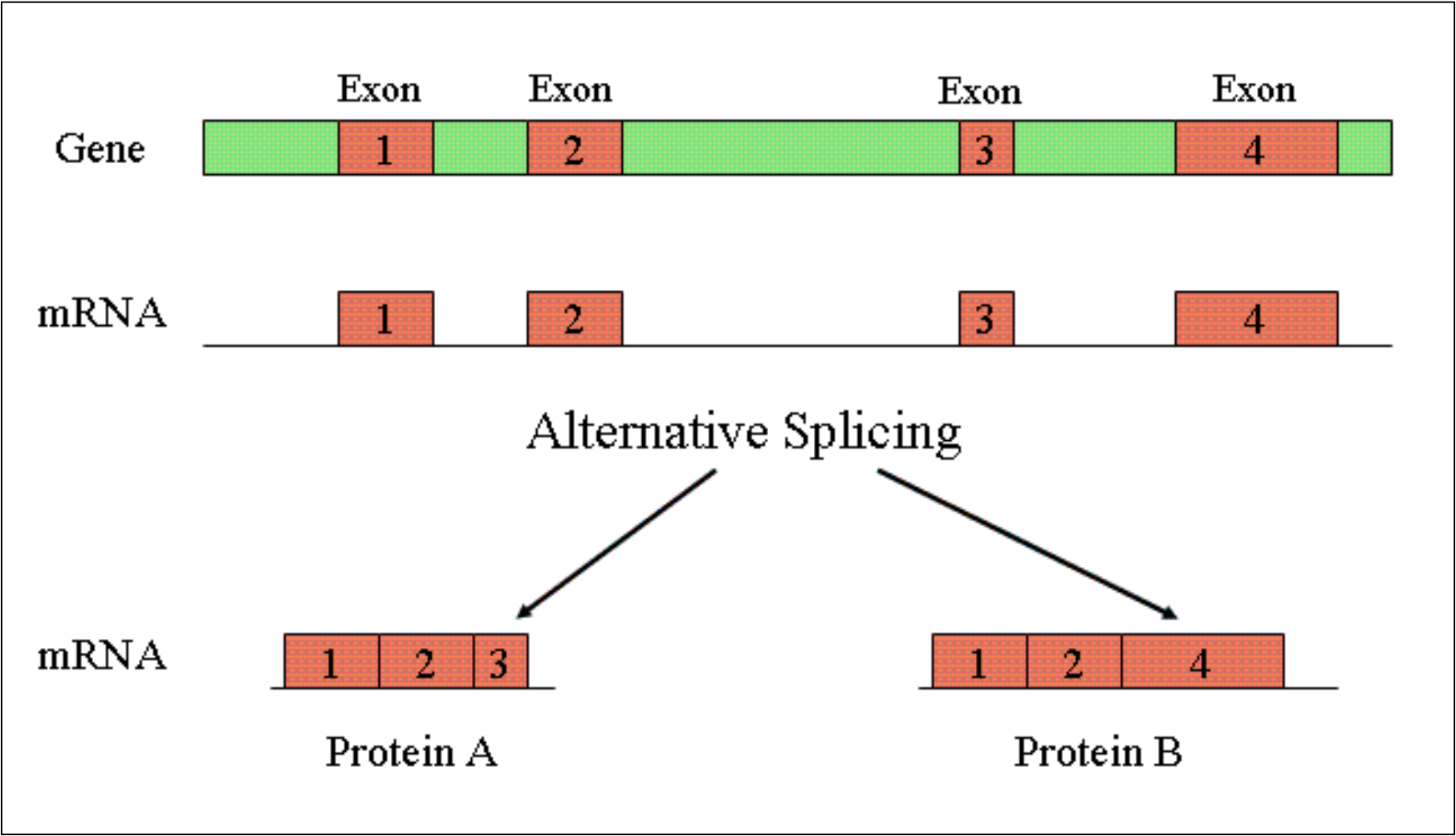


Figure 1-2 Essential Cell Biology 3/e (© Garland Science 2010)

Eukaryotic mRNA is modified, processed, and transported

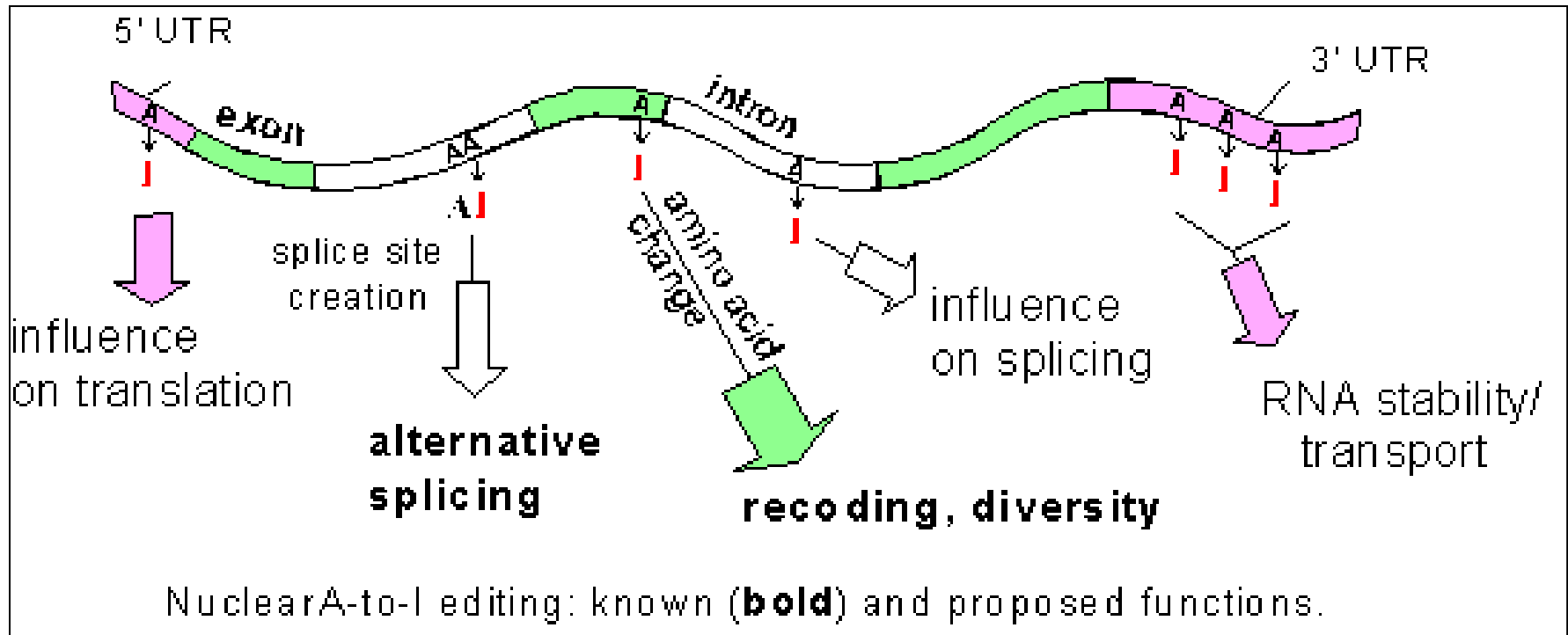


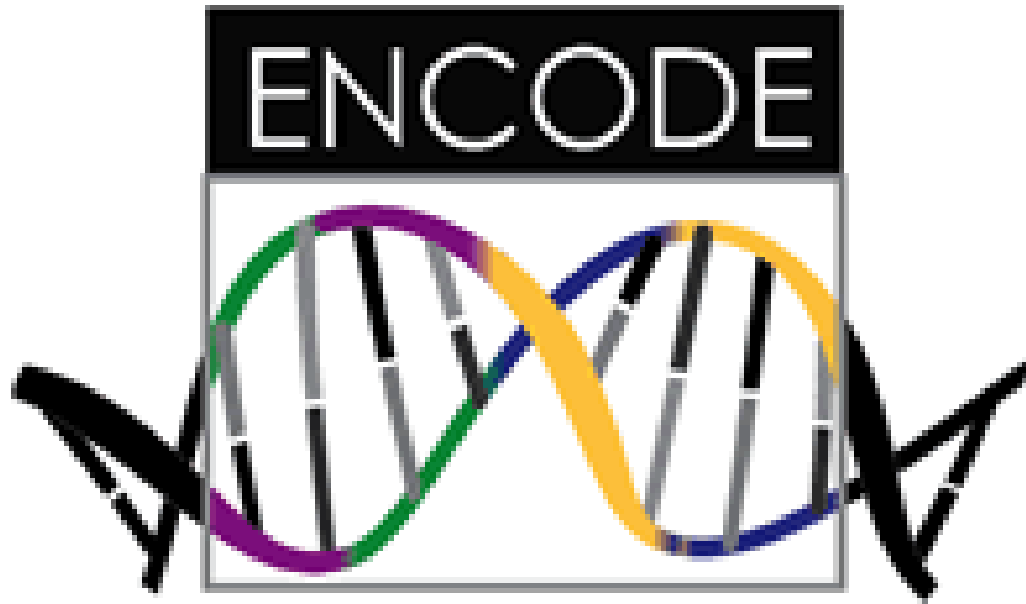
Alternative splicing adds to the size (complexity) of the transcriptome.



From: ncbi.nlm.nih.gov

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

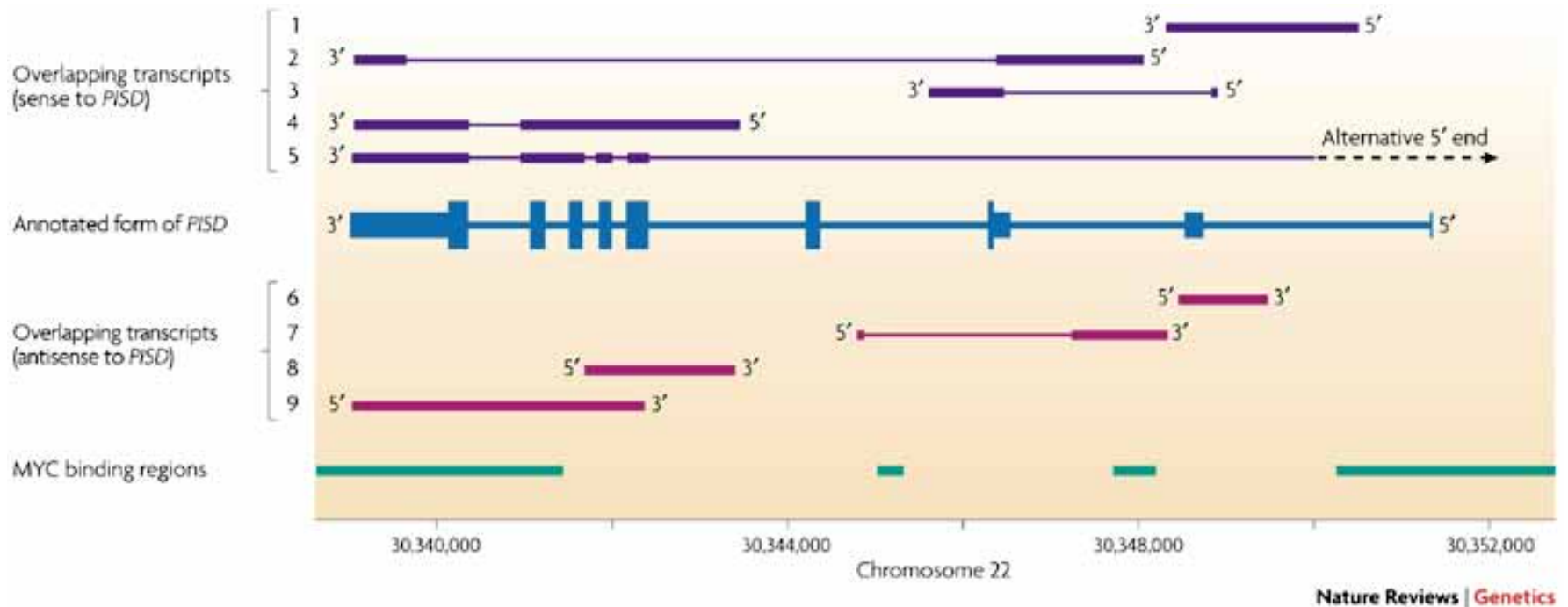




The National Human Genome Research Institute (NHGRI) launched a public research consortium named **ENCODE**, the **Encyclopedia Of DNA Elements**, in September 2003, to carry out a project **to identify all functional elements in the human genome sequence**. The project started with two components - a pilot phase and a technology development phase.

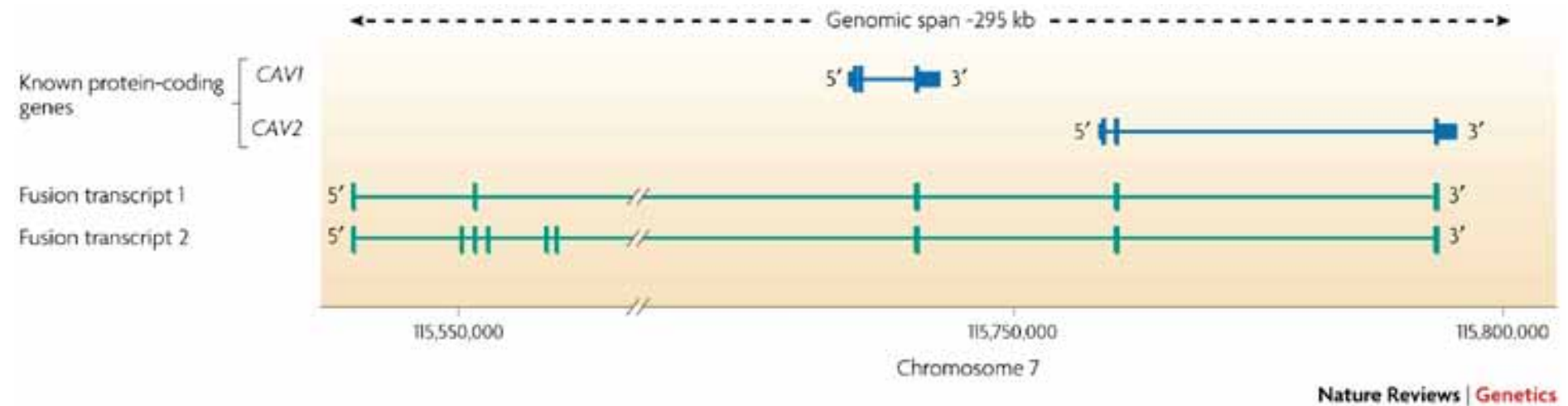
The **pilot phase** tested and compared existing methods to rigorously analyze a defined portion of the human genome sequence. **1 percent (30 Mb)** of the human genome was selected as the target for the pilot project.

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



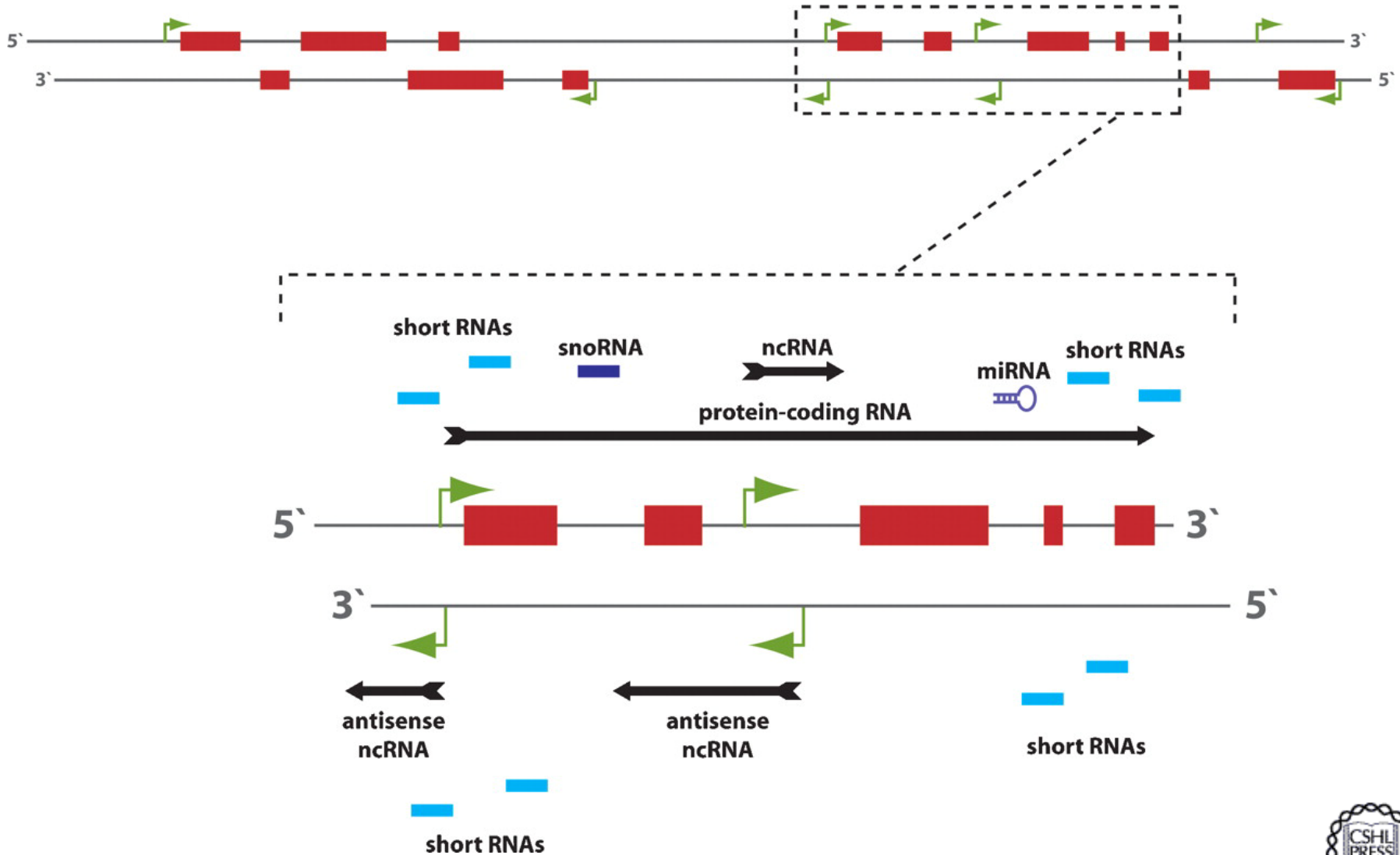
From: Kapranov *et al.* (2007) *Nature Reviews Genetics*, 8: 413 – 423.

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.



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

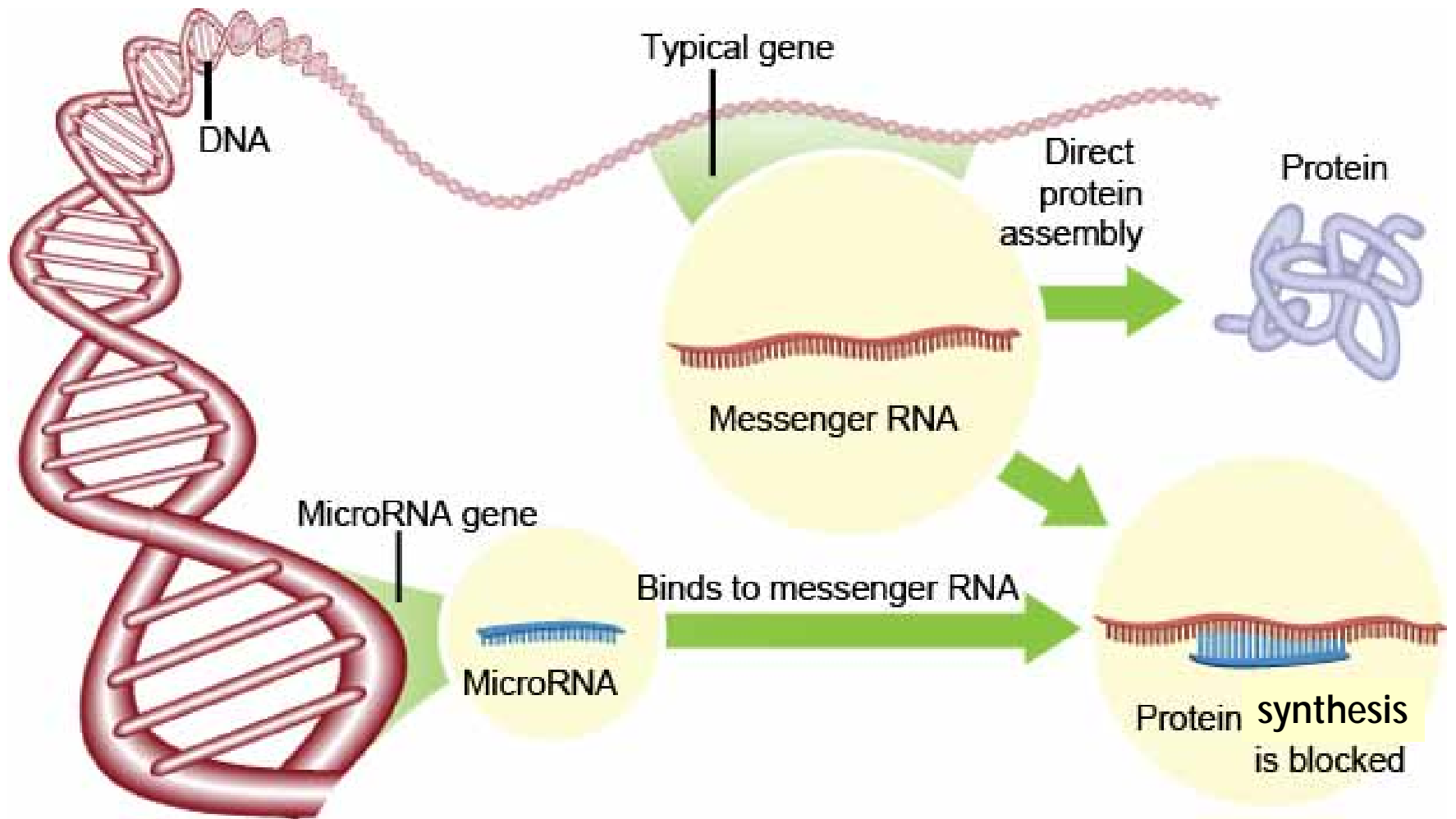
sRNAs

lincRNAs

tasRNAs

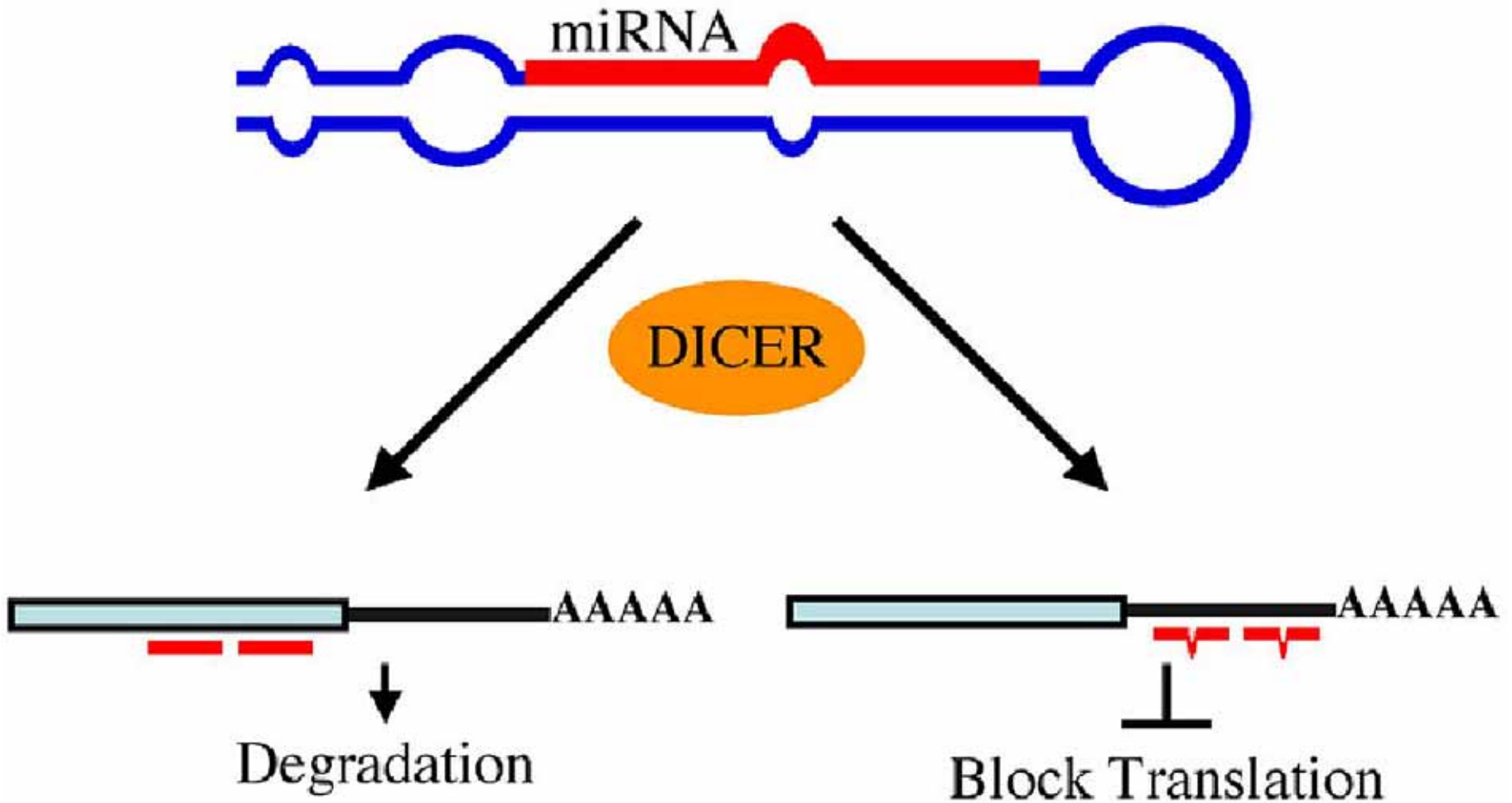
casiRNAs

microRNAs are FUNCTIONAL gene products 21 – 22 nucleotides long .



From: discovermagazine.com

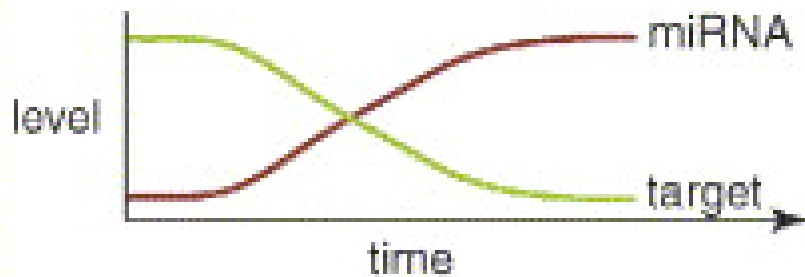
FUNCTIONAL **microRNAs** are cut out of longer RNA molecules by an enzyme called DICER.




From: wormbook.org


- 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*)

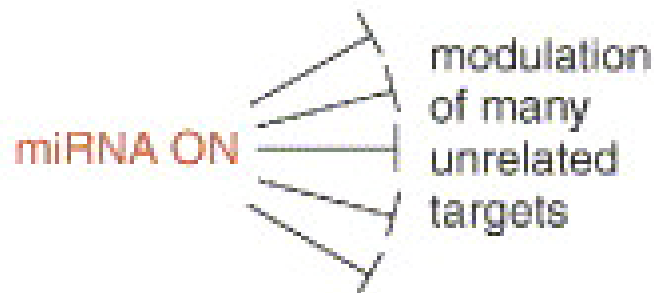


B Spatial switch (*miR-273, lsy-6*)

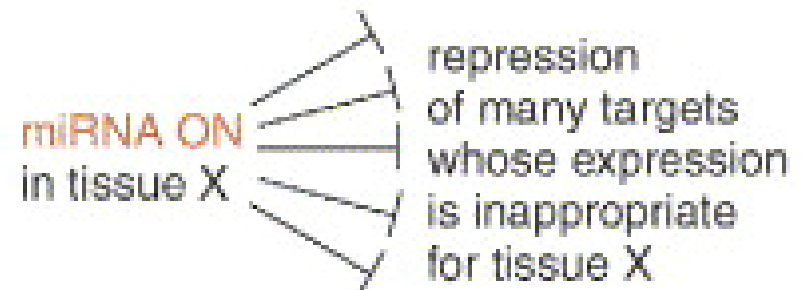
miRNA off, target ON → celltype A 

miRNA ON —| target off, celltype B 

C Fine-tuning expression



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



microRNAs are mis-regulated in human cancers.

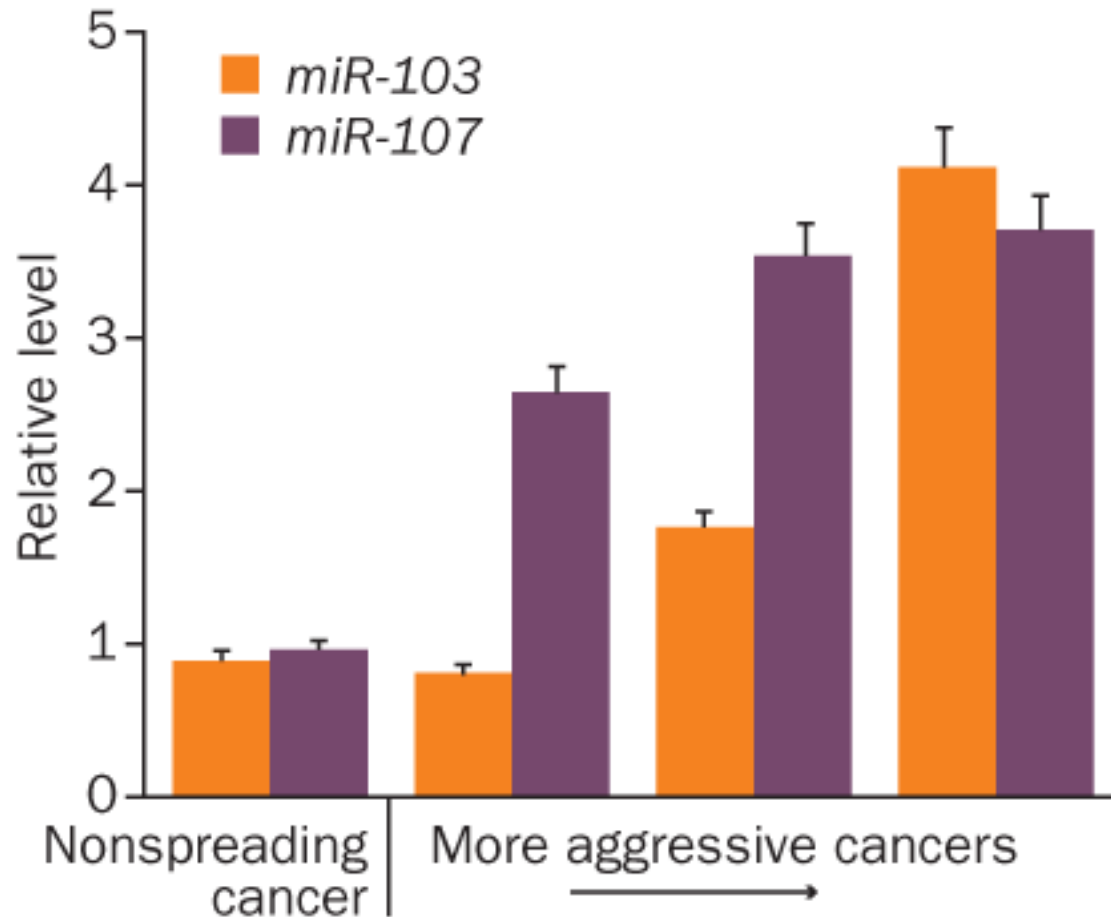
Variations in microRNA genes linked to cancers

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.

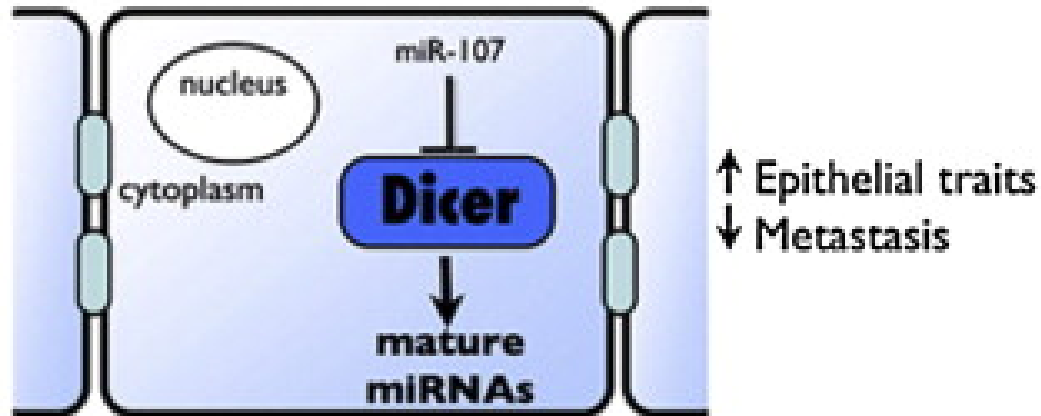
microRNAs are involved in cancer metastasis.

MicroRNA levels and cancer aggressiveness

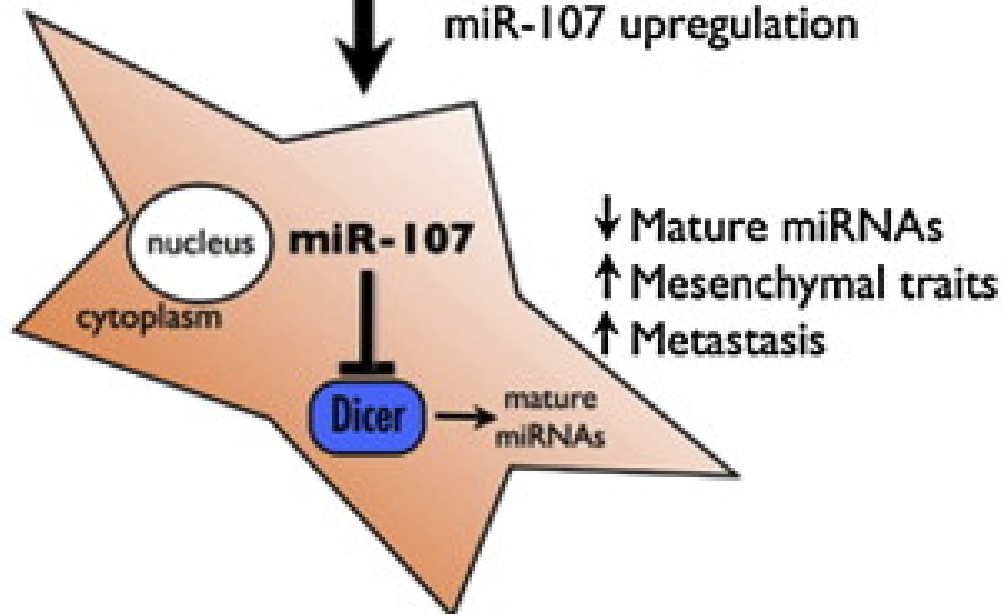


From: Martello *et al.* (2010) *Cell*, 141: 1195 – 1207.

microRNAs are involved in cancer metastasis.

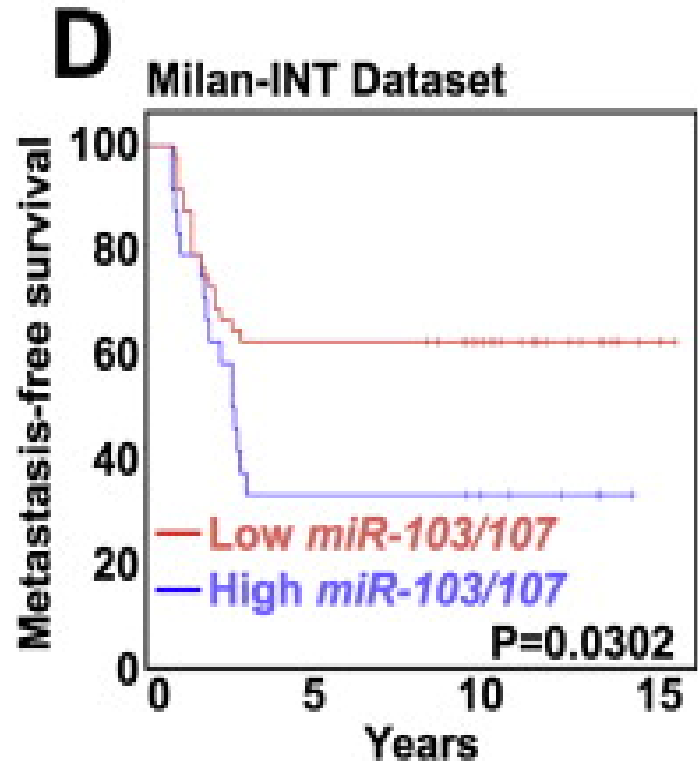
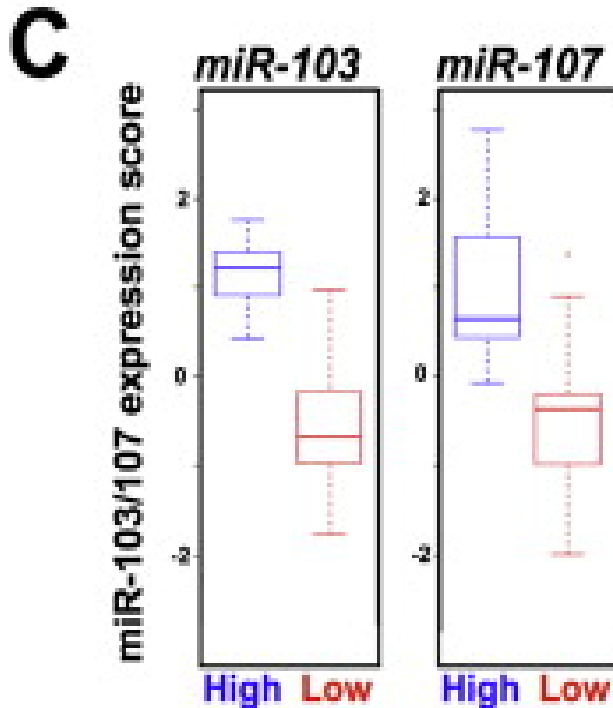


miR-107 upregulation



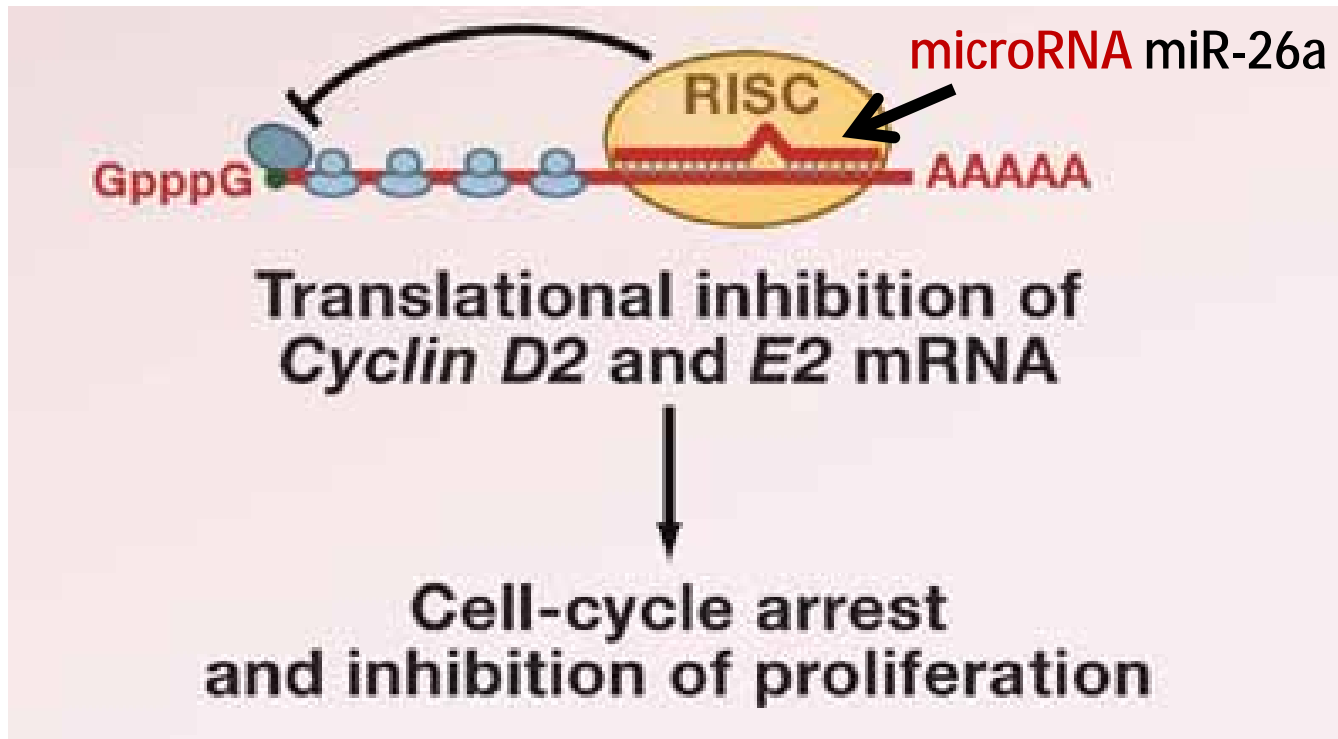
From: Martello *et al.* (2010) *Cell*, 141: 1195 – 1207.

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



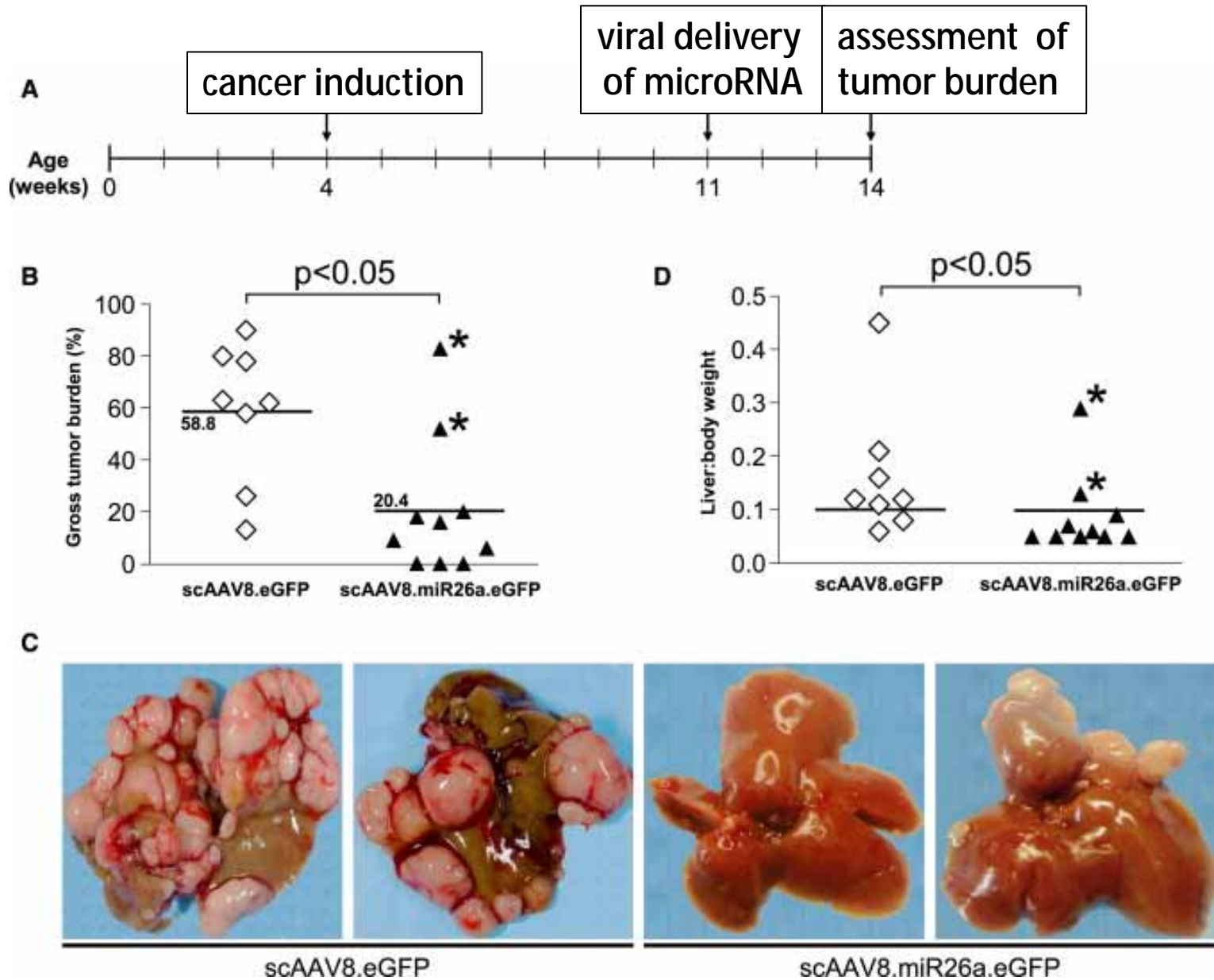
From: Martello *et al.* (2010) *Cell*, 141: 1195 –1207.

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 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?

