

# 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

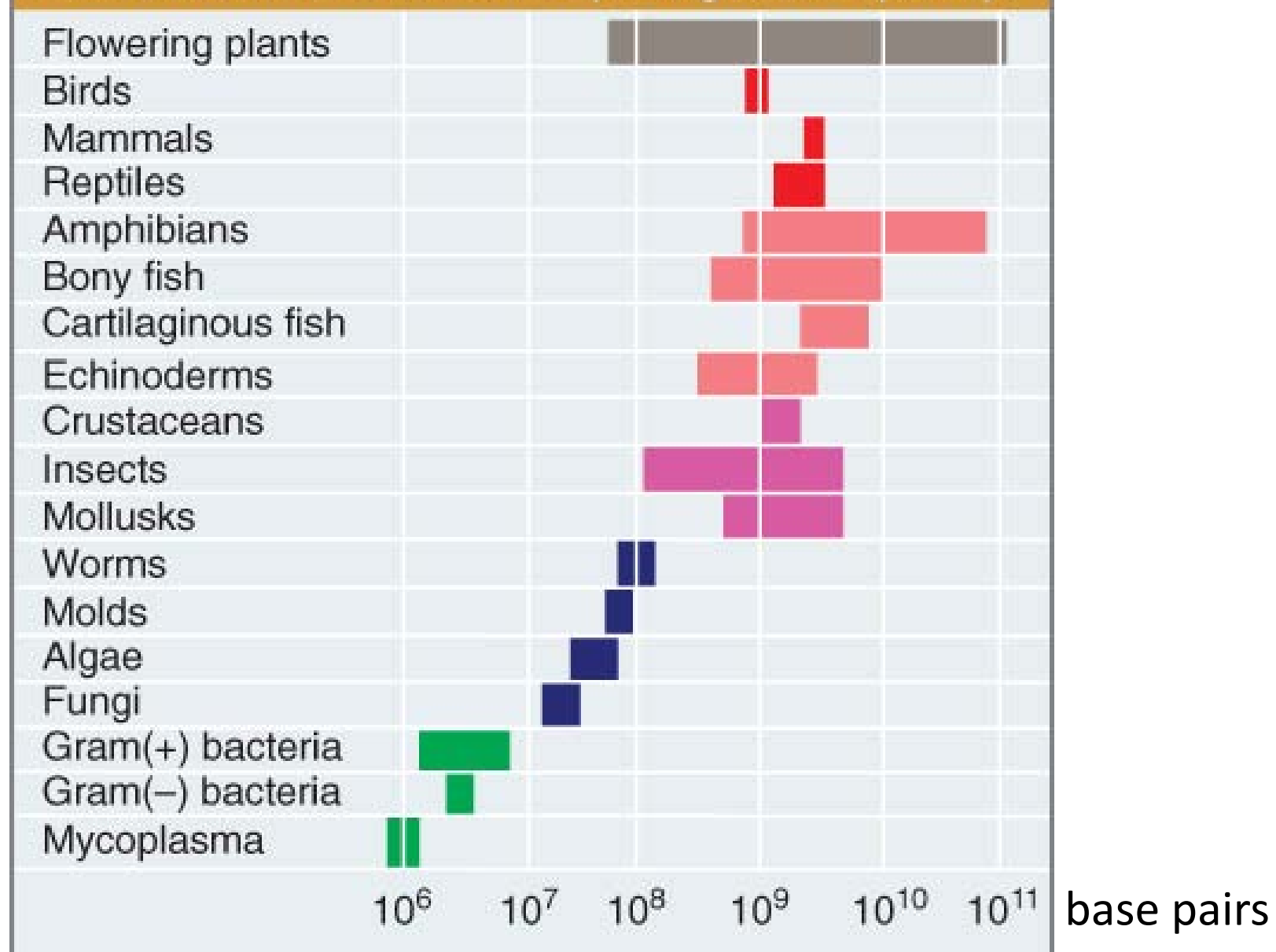
**What is the relationship between transcriptome size and organismal complexity?**

**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

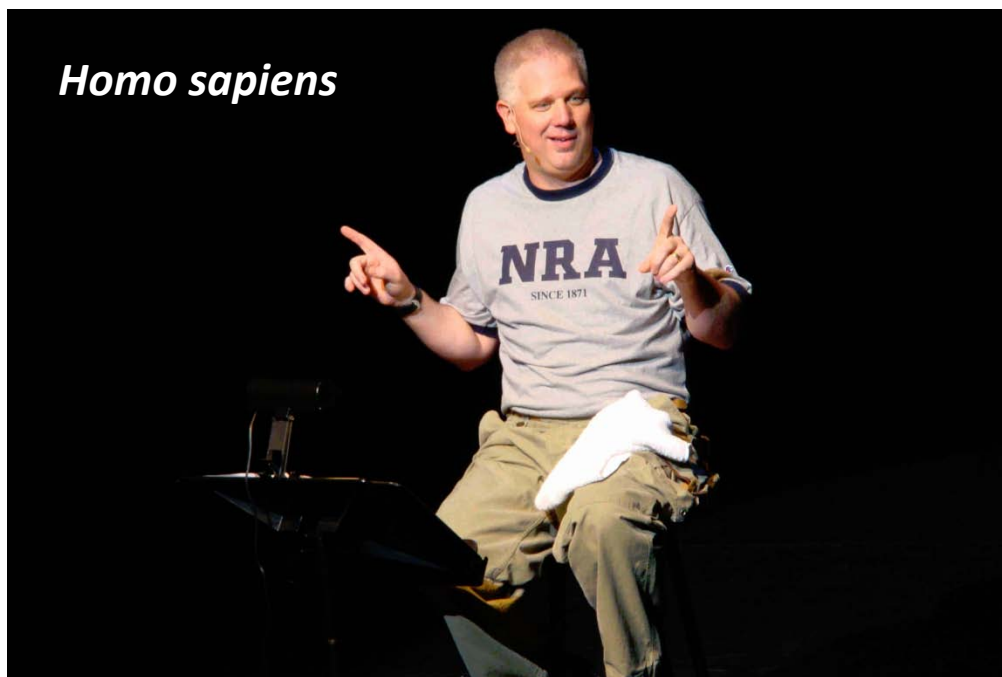
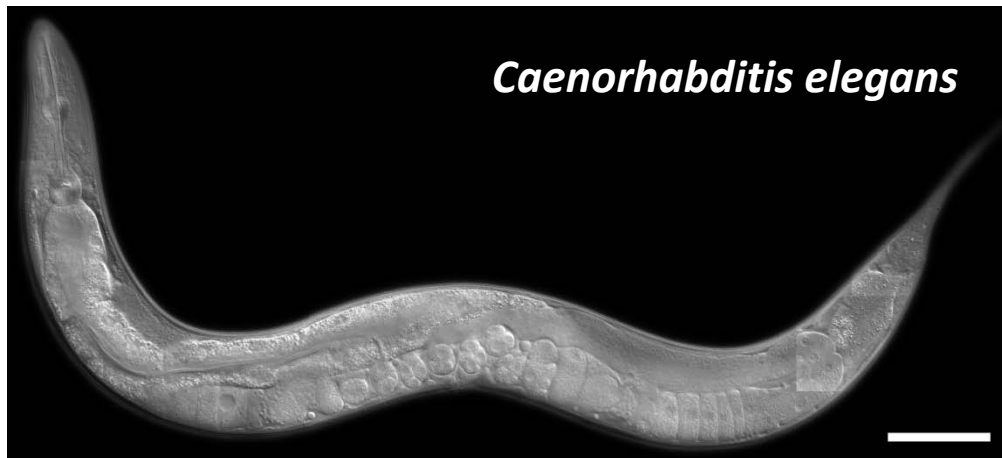


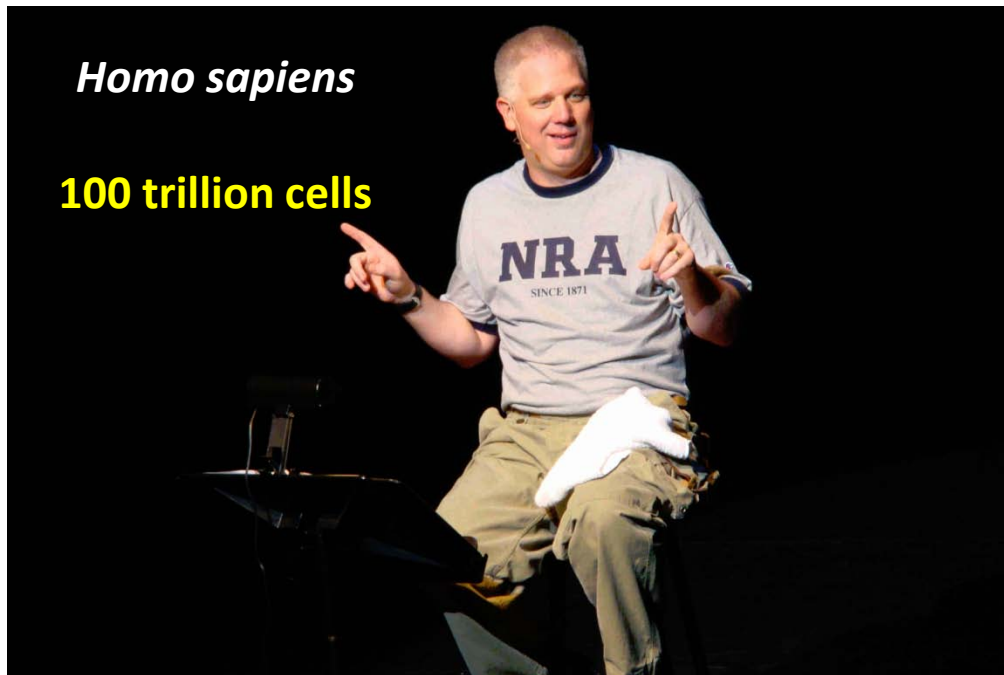
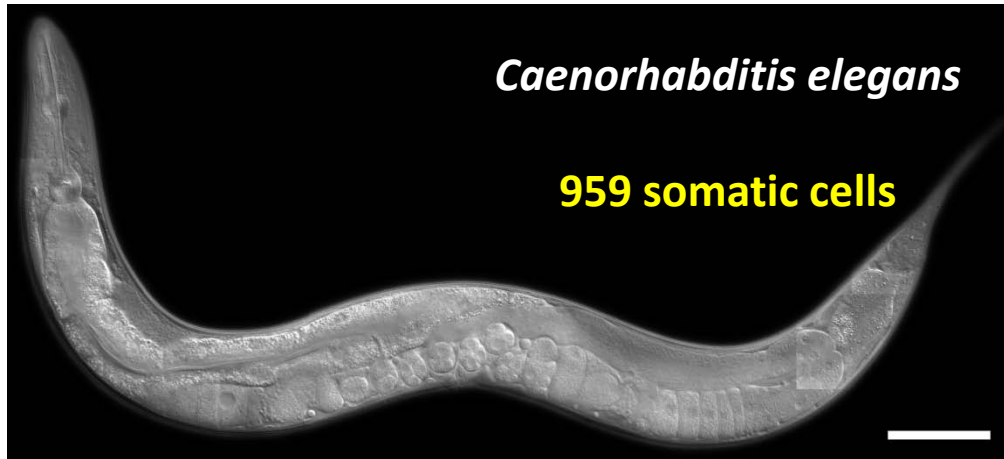
**22,000 genes**

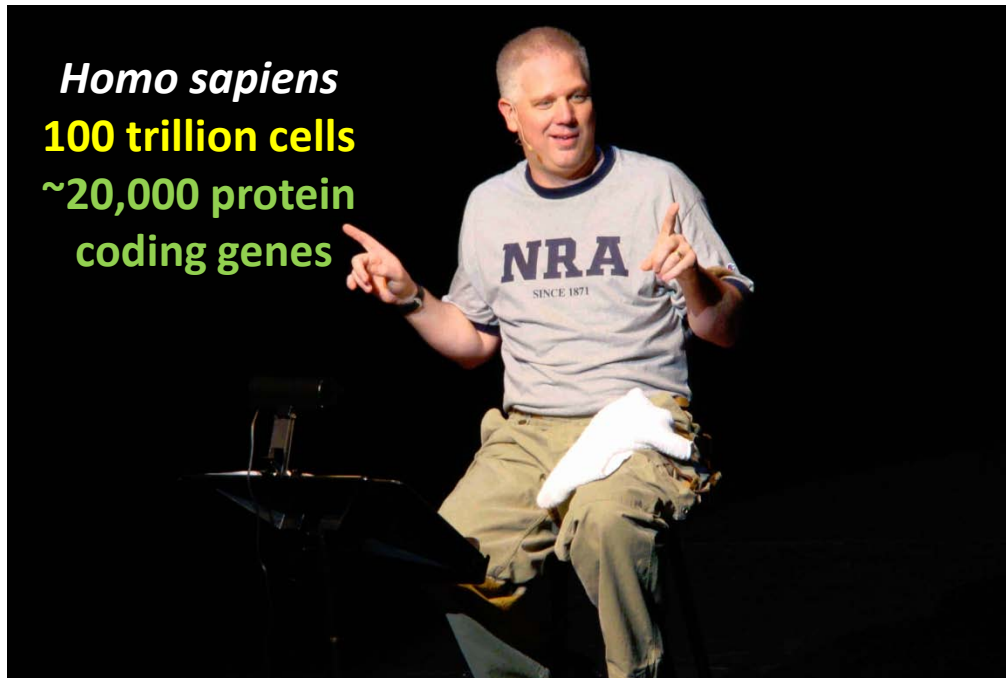
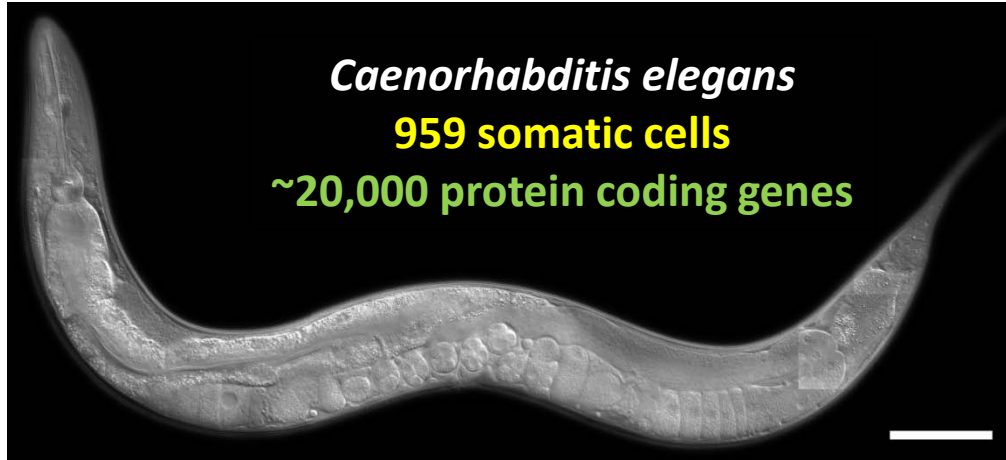
Mammals



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







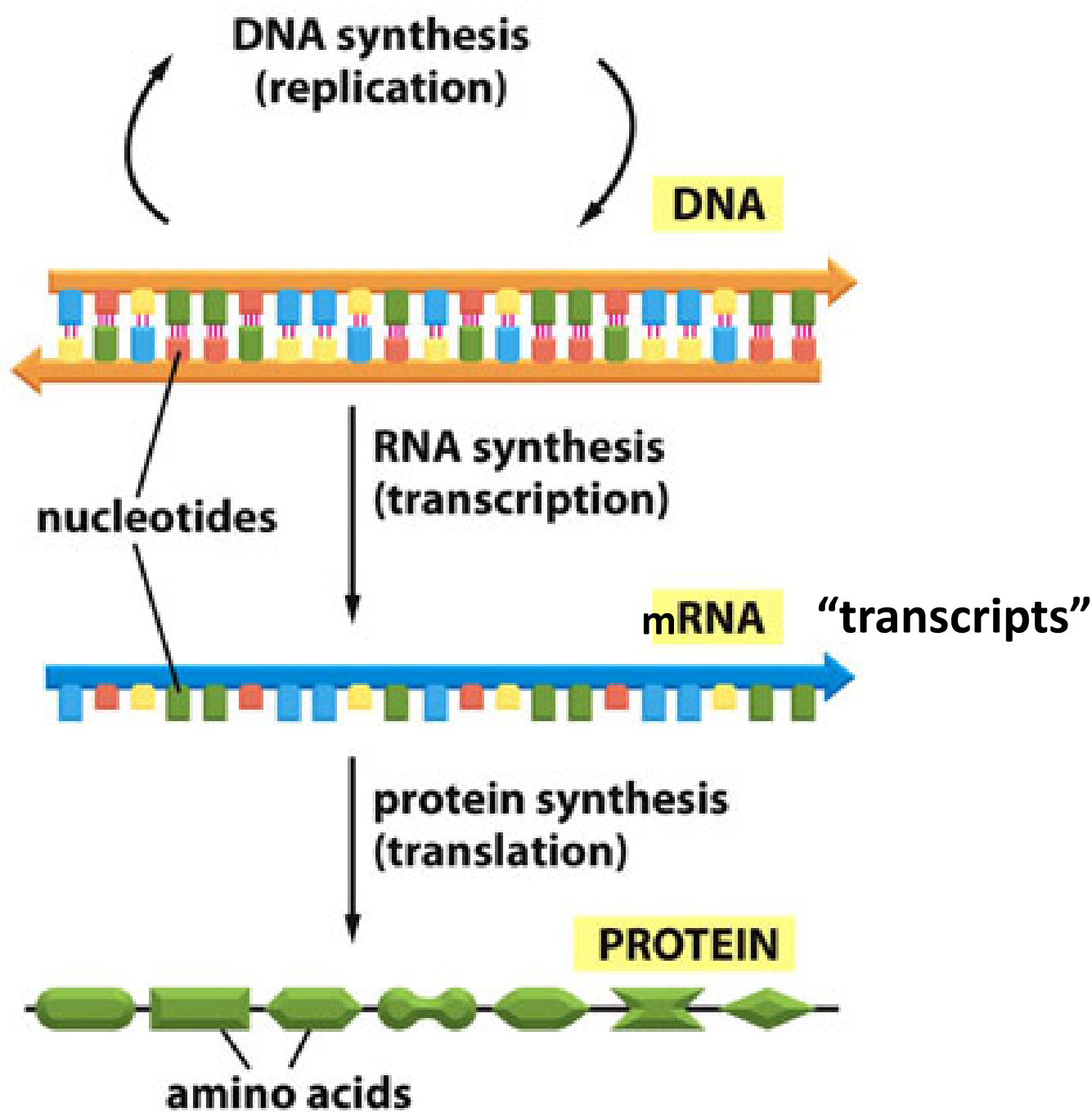
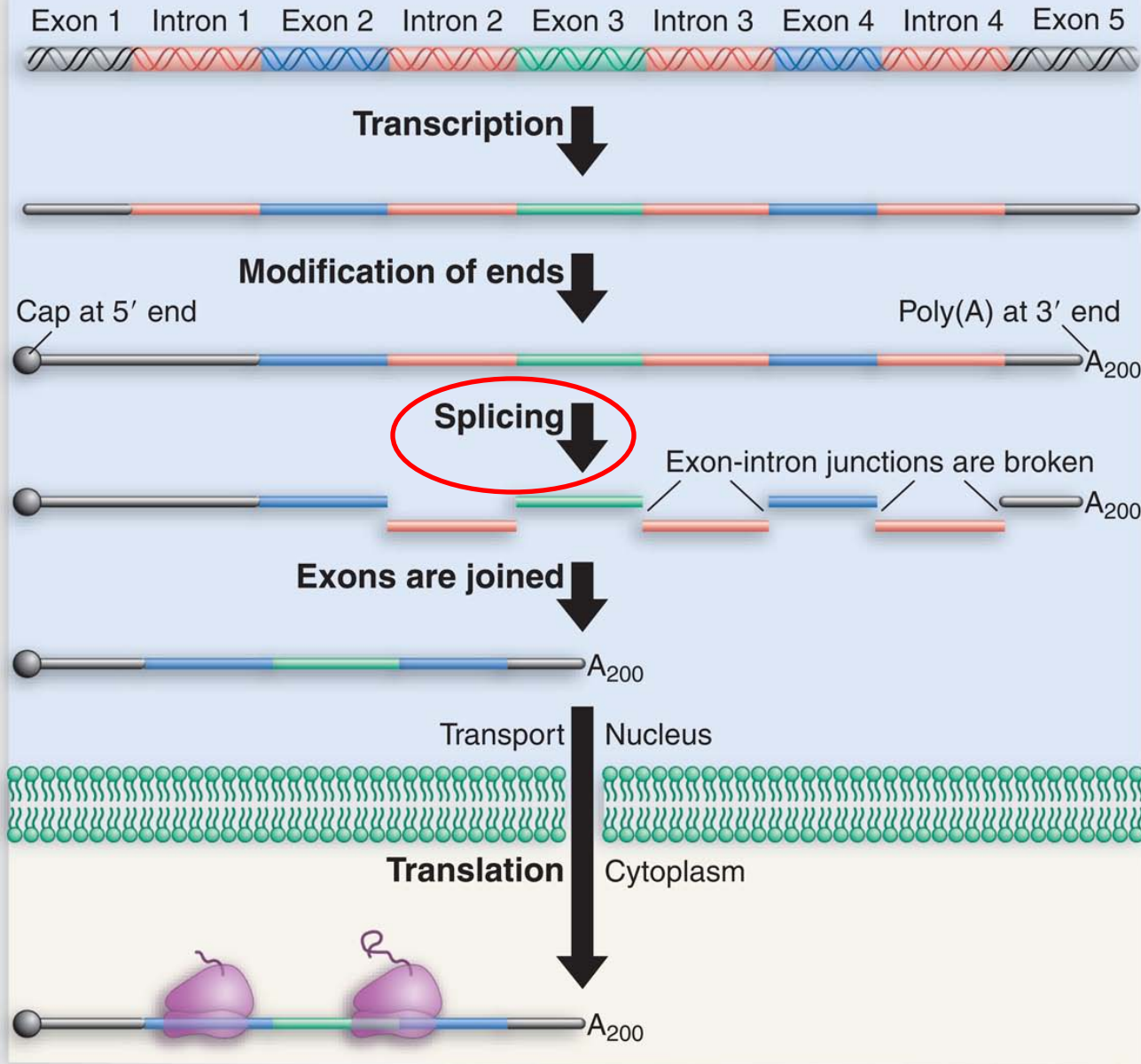


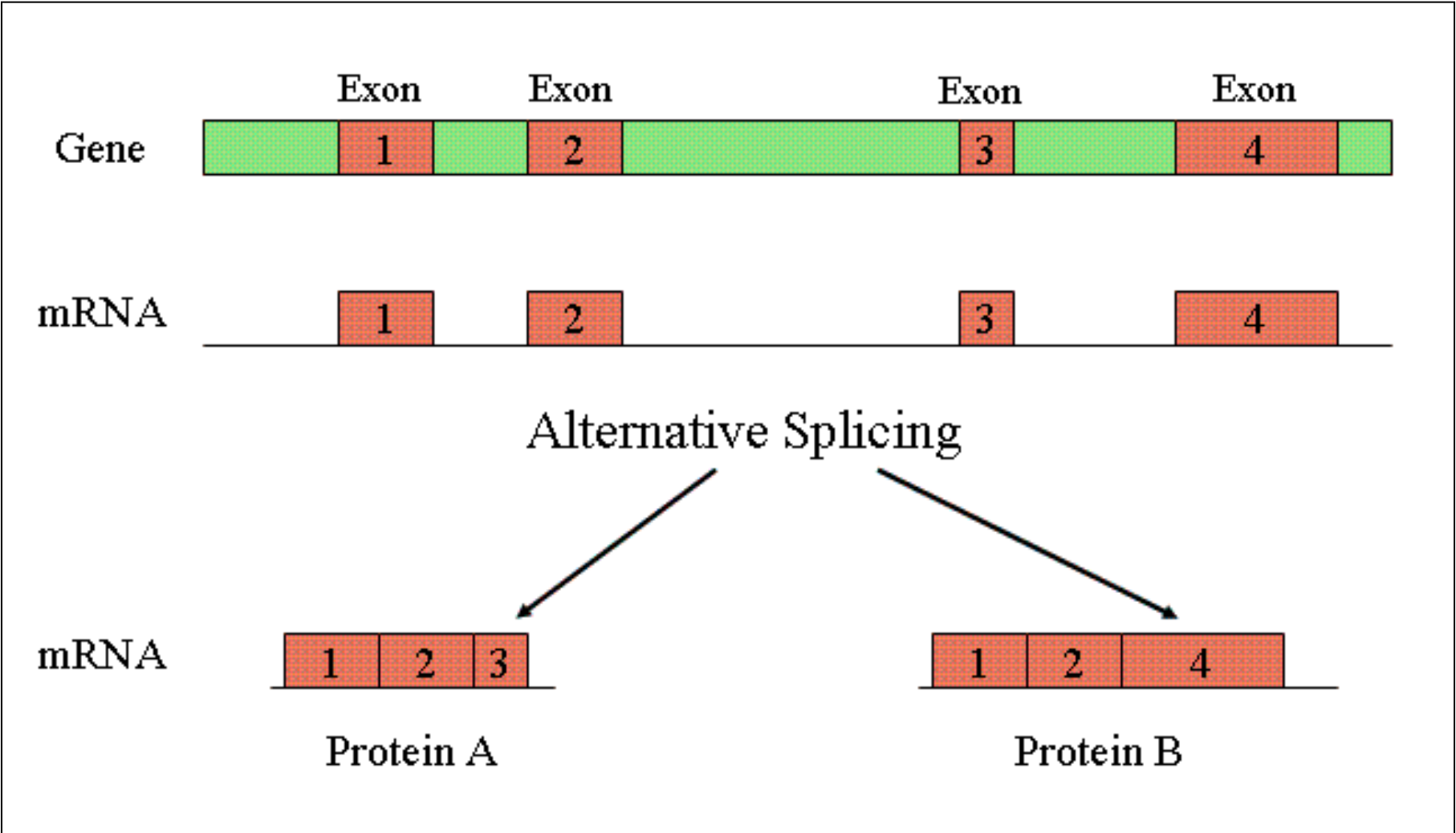
Figure 1-2 Essential Cell Biology 3/e (© Garland Science 2010)



# Eukaryotic mRNA is modified, processed, and transported

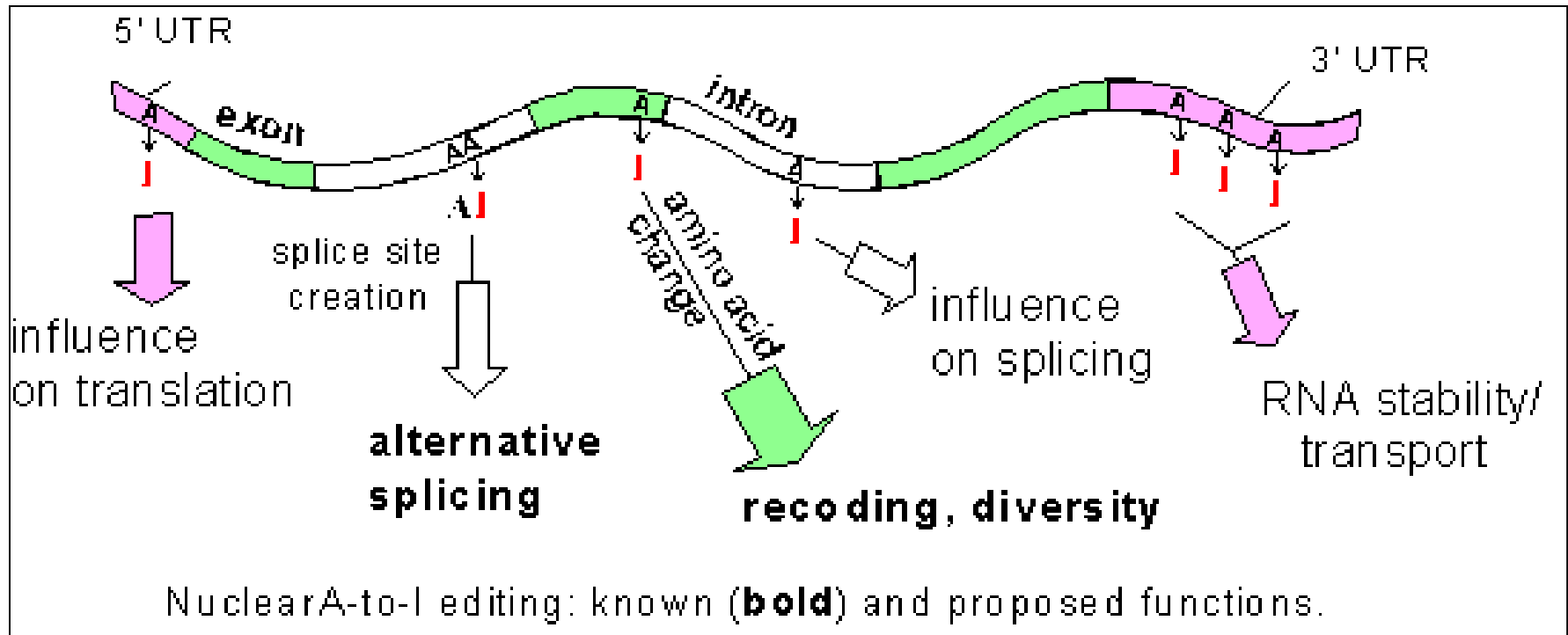


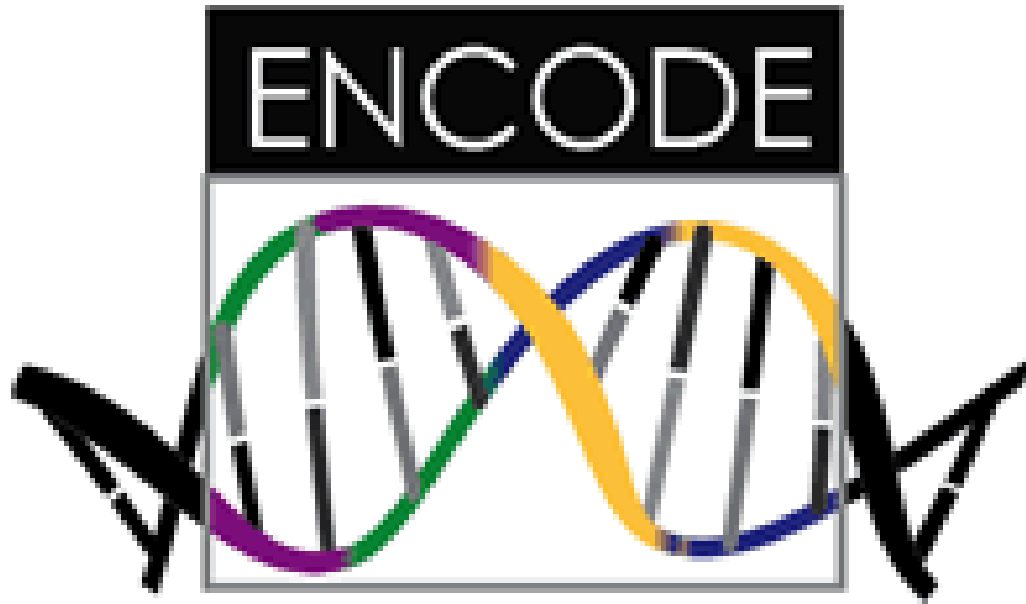
# Alternative splicing adds to the size (complexity) of the transcriptome.



From: [ncbi.nlm.nih.gov](http://ncbi.nlm.nih.gov)

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

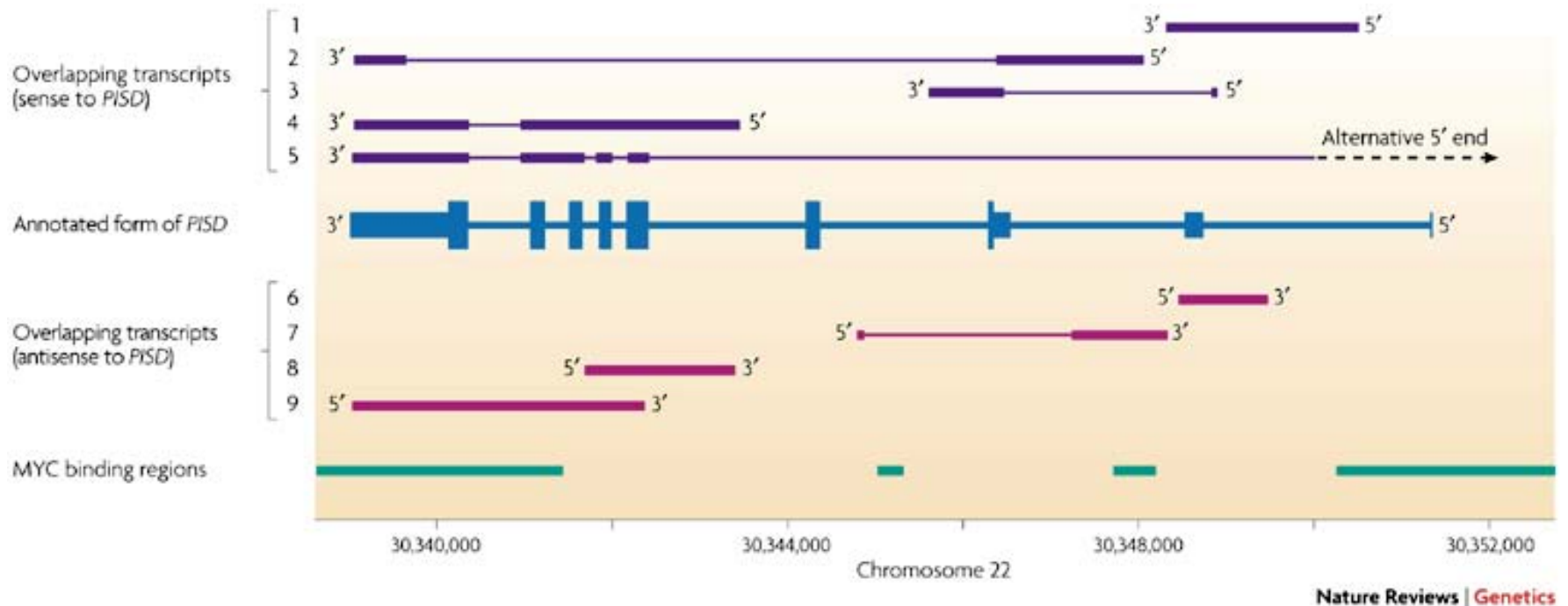




The National Human Genome Research Institute (NHGRI) launched a public research consortium named **ENCODE**, the **Encyclopedia Of DNA Elements**, in September 2003, to carry out a project **to identify all functional elements in the human genome sequence**. The project started with two components -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

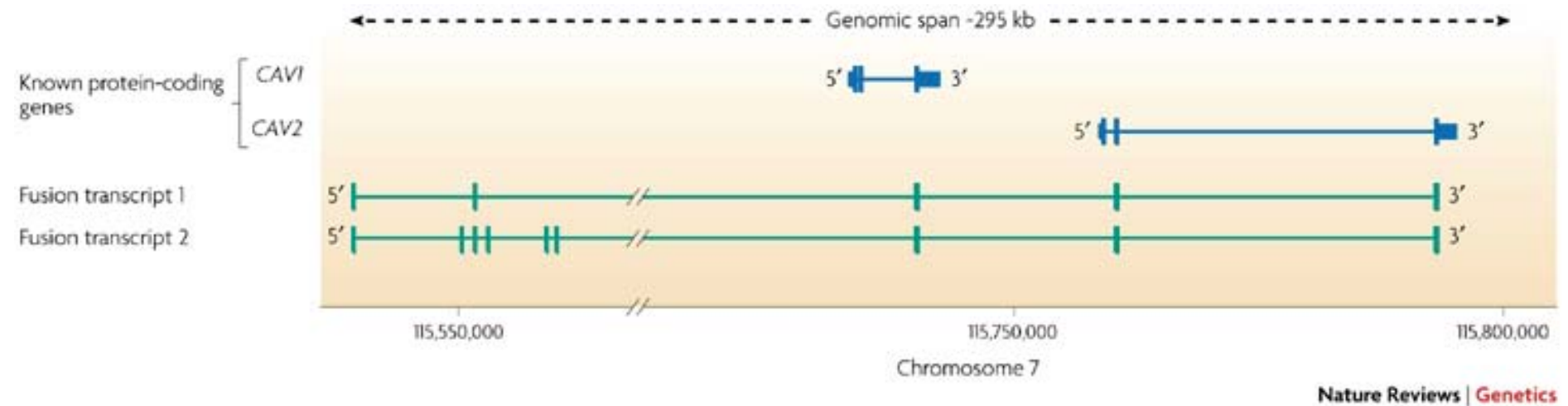
The **pilot phase** tested and compared existing methods to rigorously analyze a defined portion of the human genome sequence. **1 percent (30 Mb)** of the human genome was selected as the target for the pilot project.

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



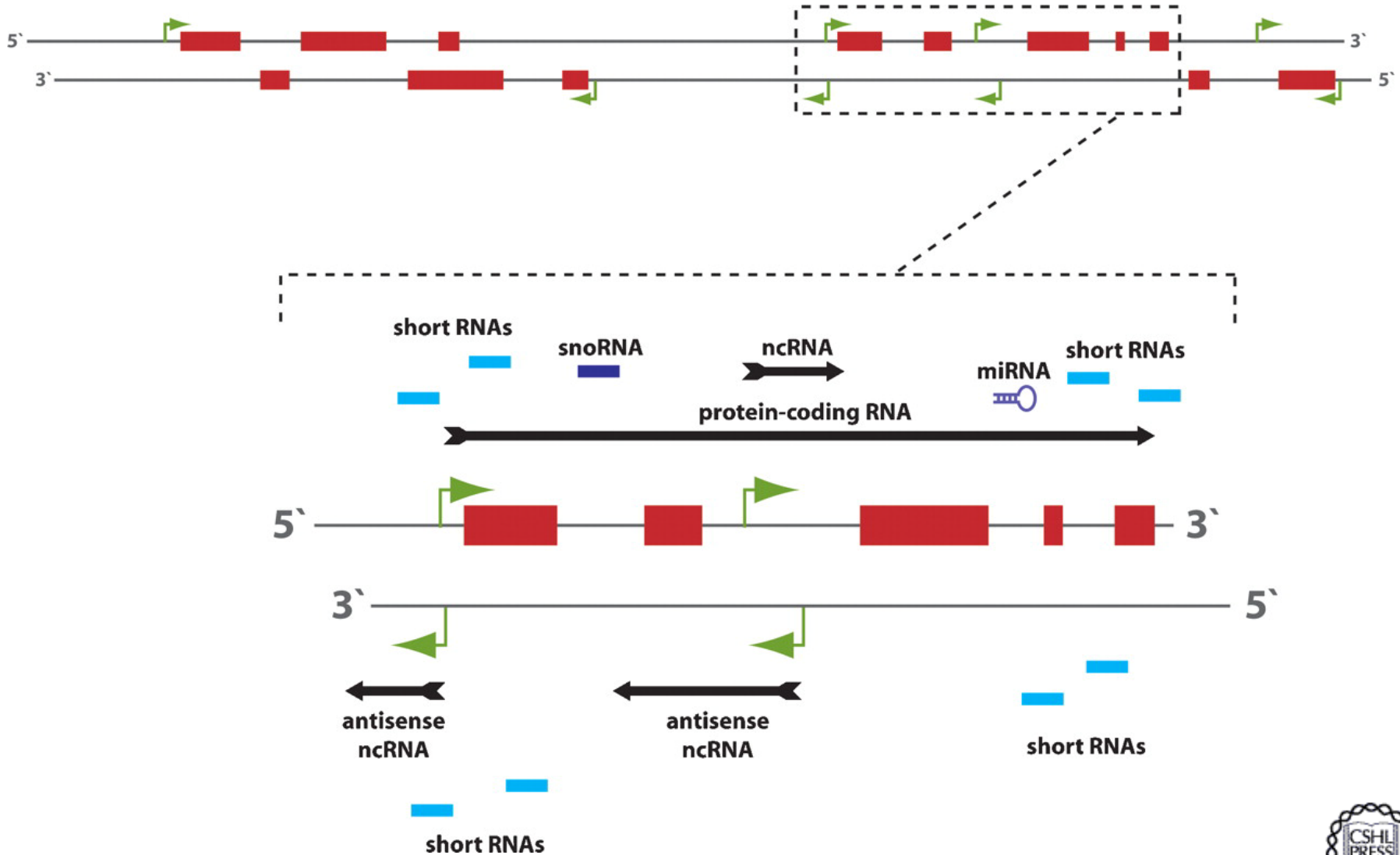
**From: Kapranov *et al.* (2007) *Nature Reviews Genetics*, 8: 413 – 423.**

**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

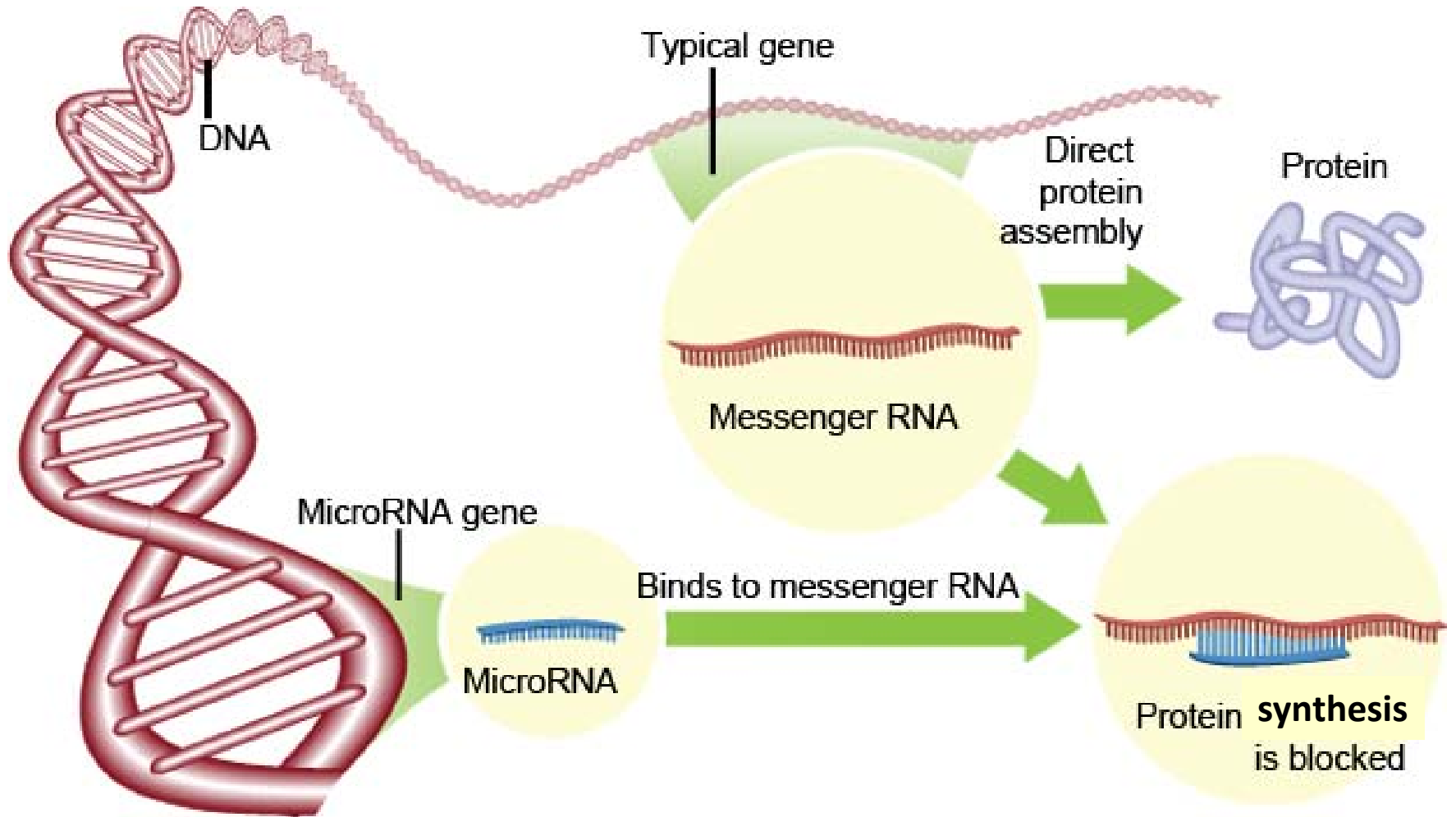
sRNAs

lincRNAs

tasRNAs

casiRNAs

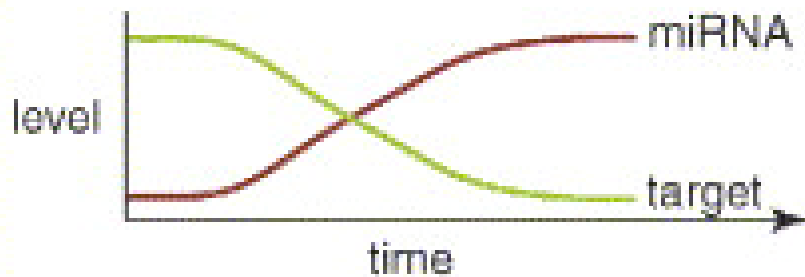
**microRNAs** are FUNCTIONAL gene products 21 – 22 nucleotides long .



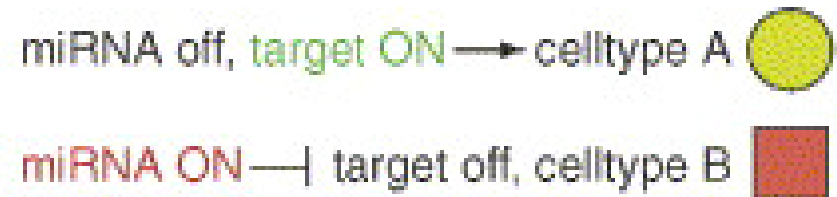
From: [discovermagazine.com](http://discovermagazine.com)

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

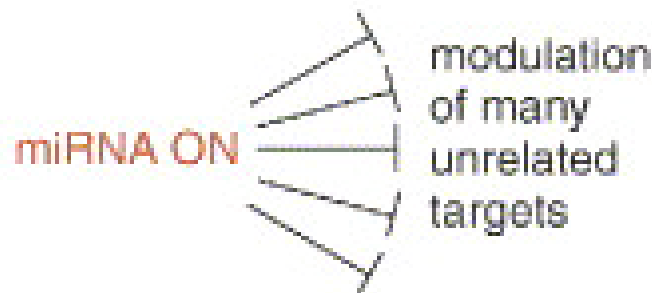
**A Temporal switch (*lin-4, let-7*)**



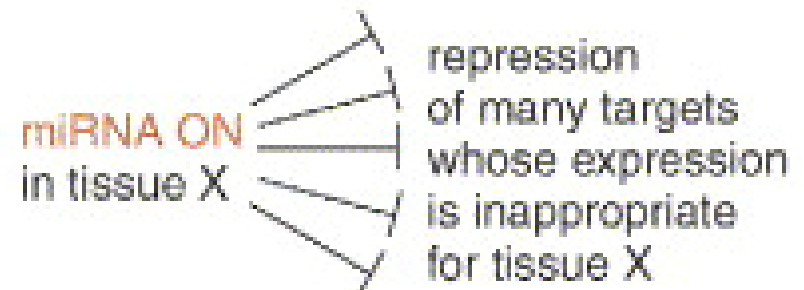
**B Spatial switch (*miR-273, lsy-6*)**



**C Fine-tuning expression**



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



**microRNAs** are mis-regulated in human cancers.

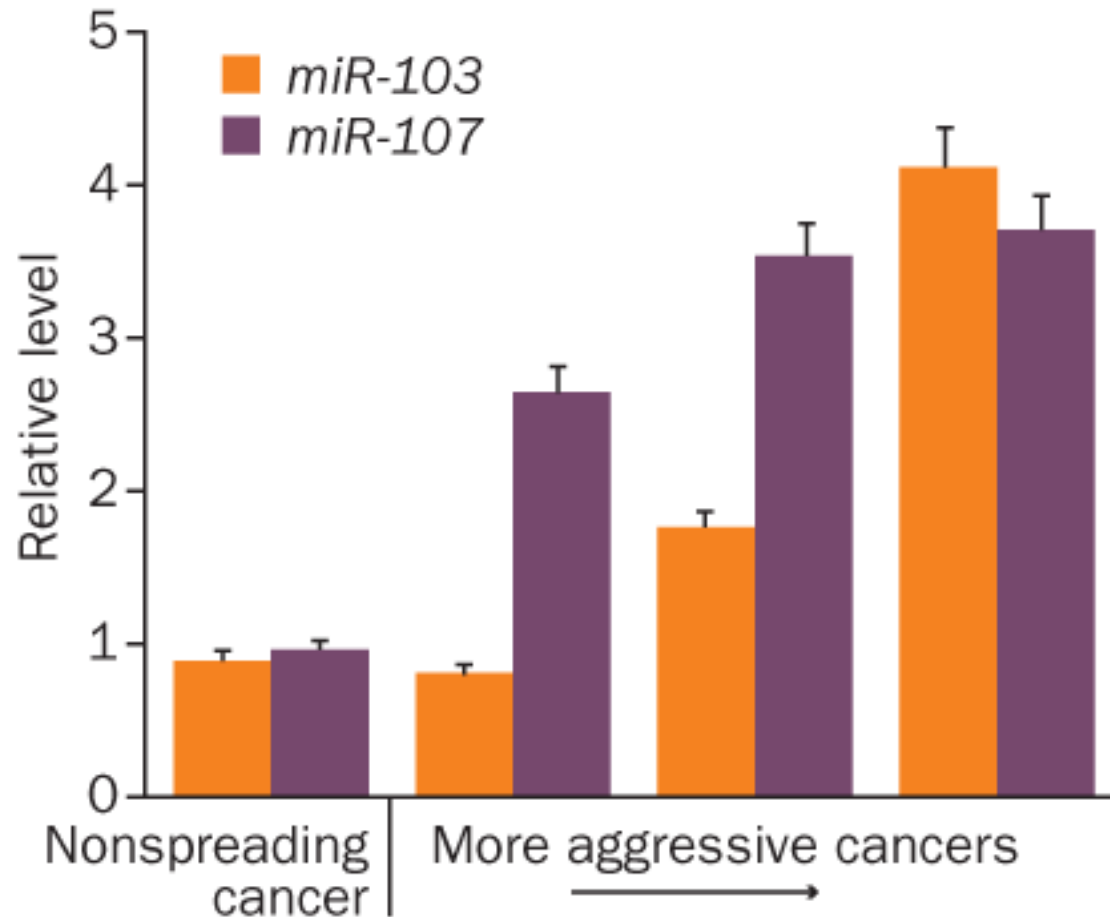
**Variations in microRNA genes linked to cancers**

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.**

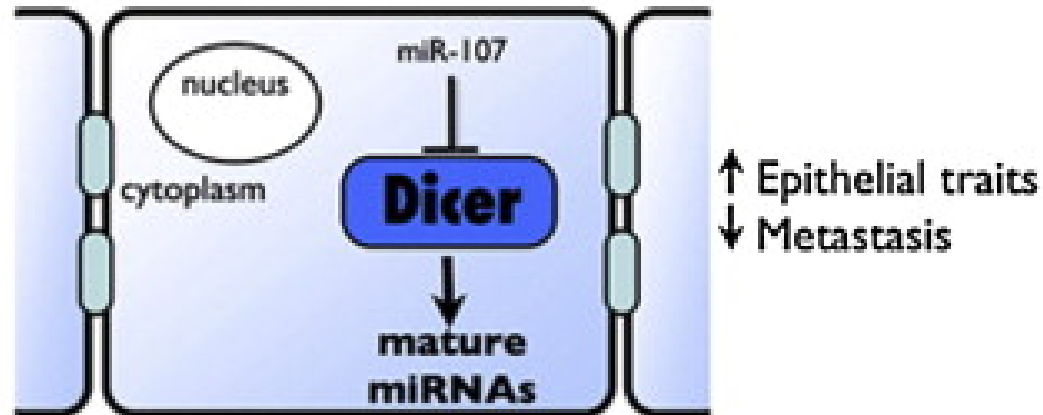
**microRNAs** are involved in cancer metastasis.

### MicroRNA levels and cancer aggressiveness

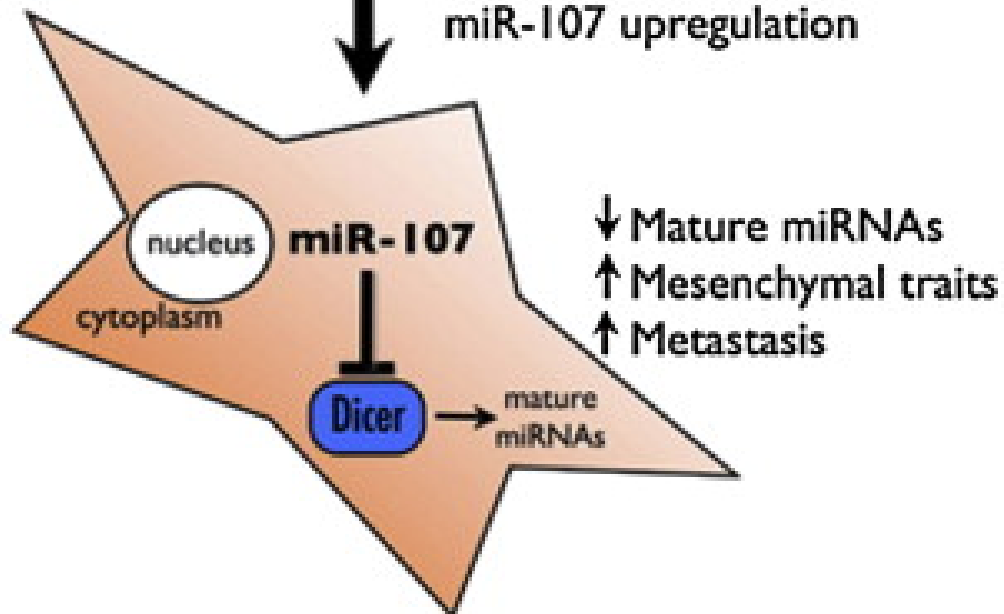


**From:** Martello *et al.* (2010) *Cell*, 141: 1195 – 1207.

**microRNAs** are involved in cancer metastasis.

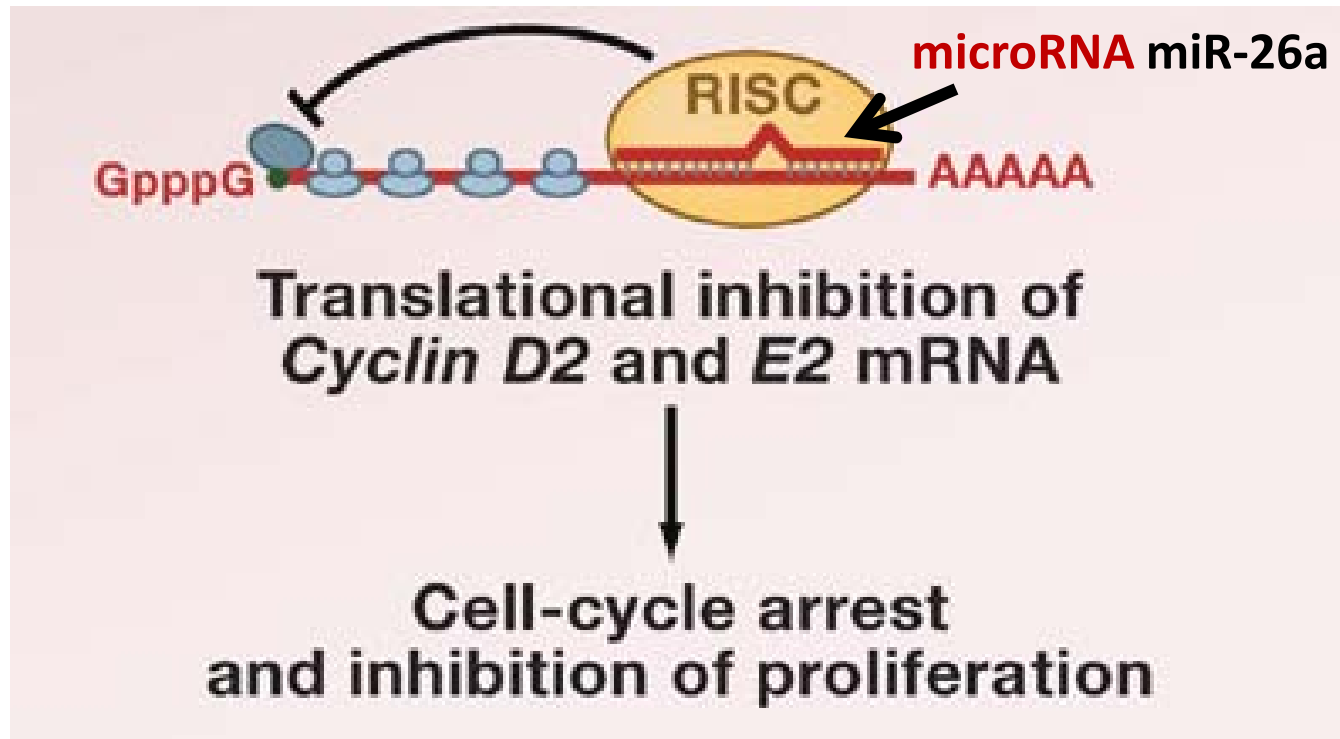


miR-107 upregulation



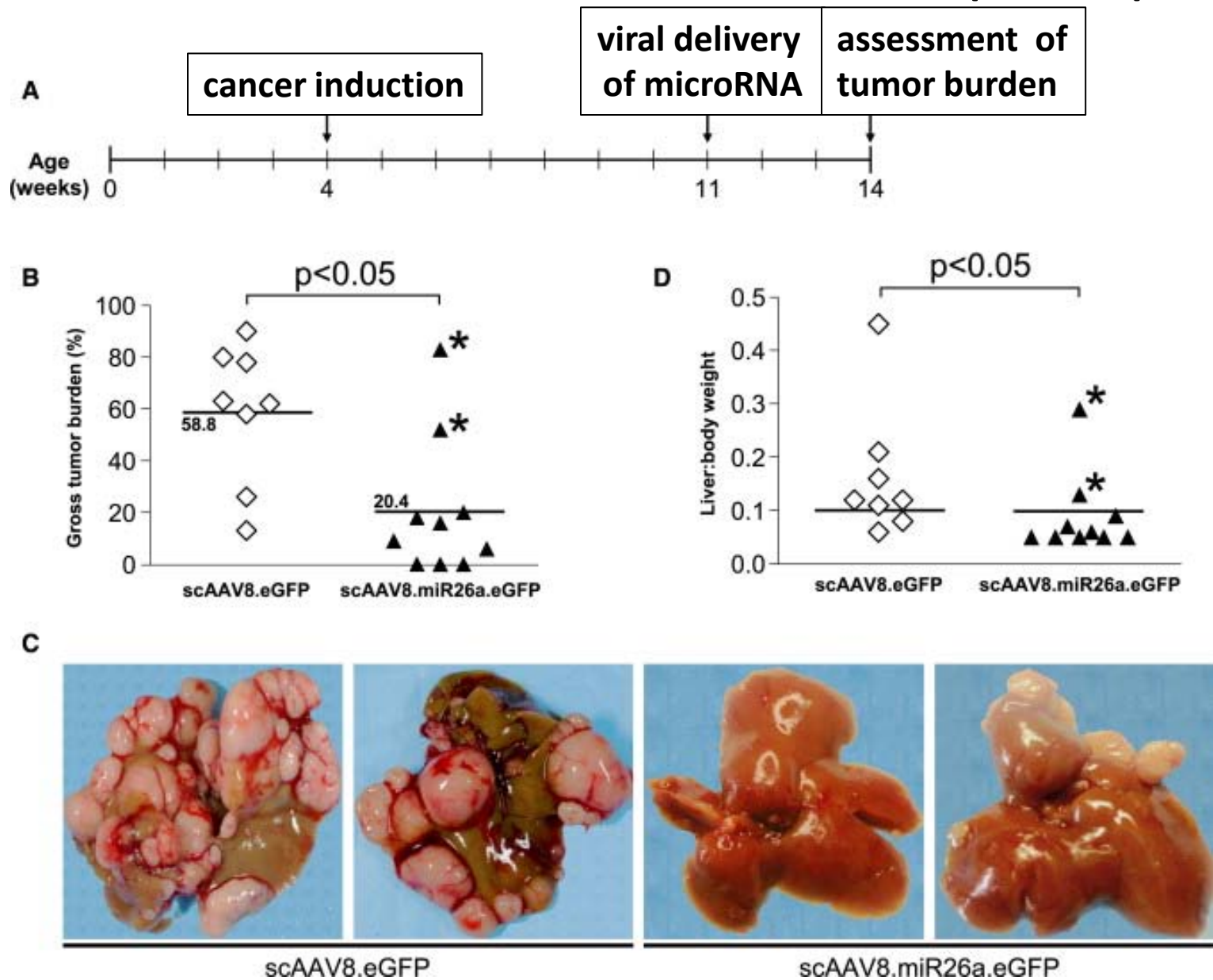
From: Martello *et al.* (2010) *Cell*, 141: 1195 – 1207.

**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?

