Strange and Unexpected Genetics

RNA interference

http://www.pbs.org/wgbh/nova/sciencenow/3210/02.html

http://www.hhmi.org/biointeractive/rna/rnai/index.html

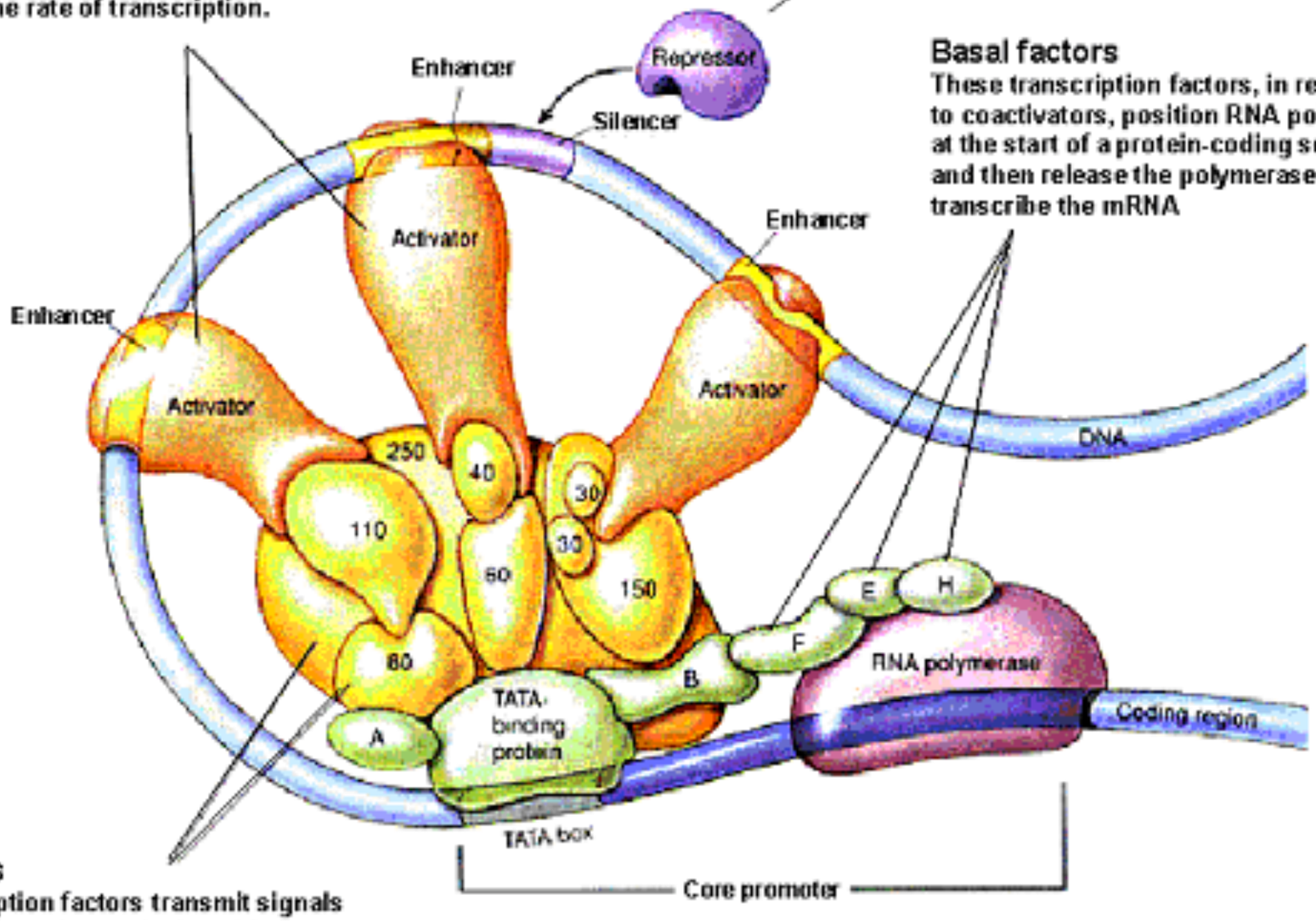
Review Session:
Wed May 14 this room, 1-2 PM
YOU provide the questions

This is true, but.....

Activators
The regulatory proteins bind to DNA at distant sites known as enhancers. When DNA folds so that the enhancer is brought into proximity with the transcription complex, the activator proteins interact with the complex to increase the rate of transcription.

Repressors
These regulatory proteins bind to "silencer sites" on the DNA preventing the binding of activator to nearby enhancers and so slowing transcription.

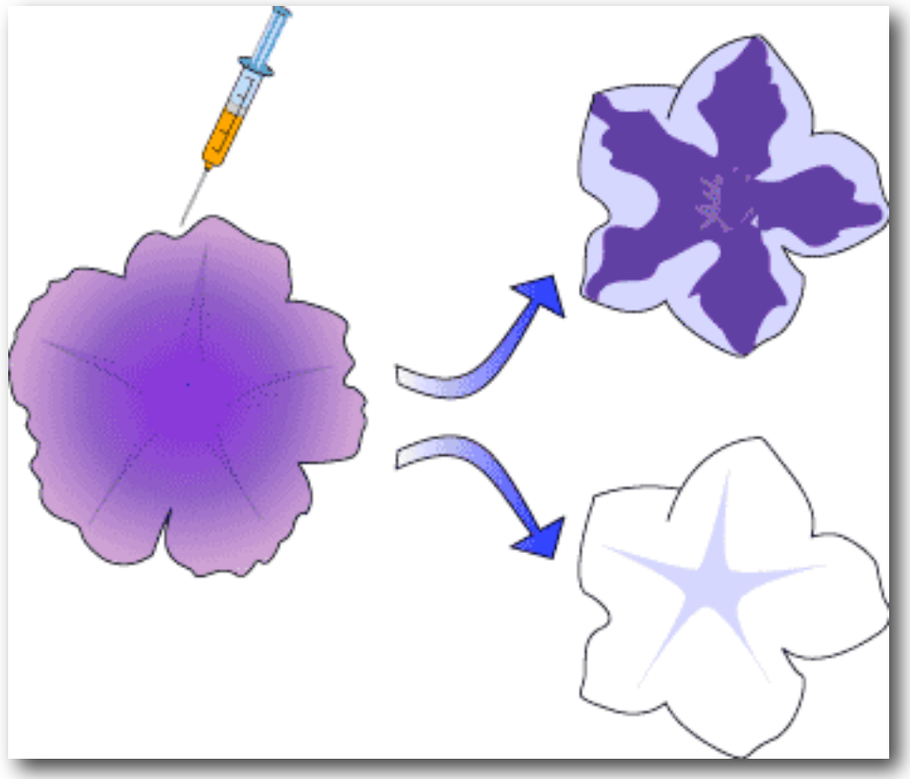
Basal factors
These transcription factors, in response to coactivators, position RNA polymerase at the start of a protein-coding sequence, and then release the polymerase to transcribe the mRNA



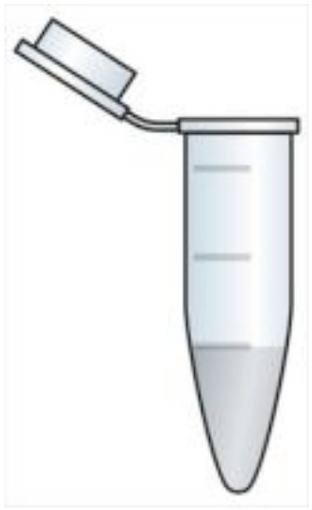
Coactivators
These transcription factors transmit signals from activator proteins to the basal factors.

Petunia

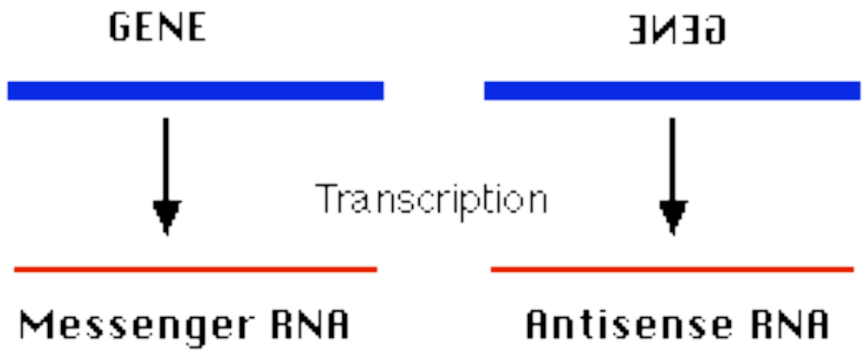
The Petunia Mystery



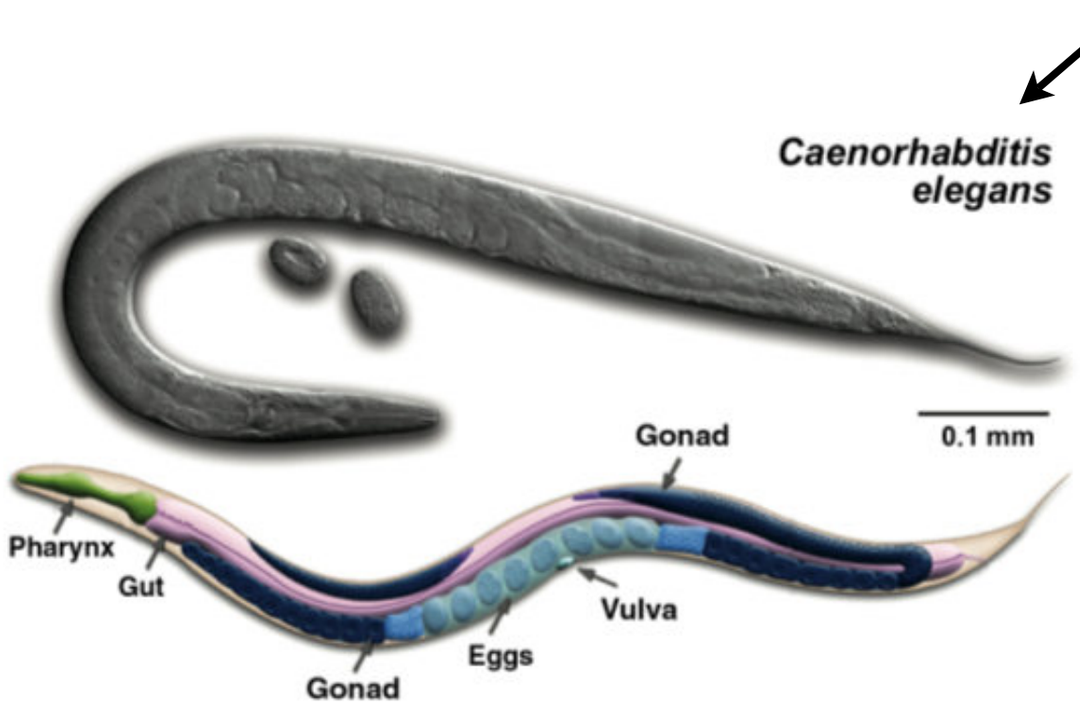
Co-Suppression: The transgene inhibits both the expression of the transgene AND the endogenous gene



Make antisense RNA
of your favorite gene

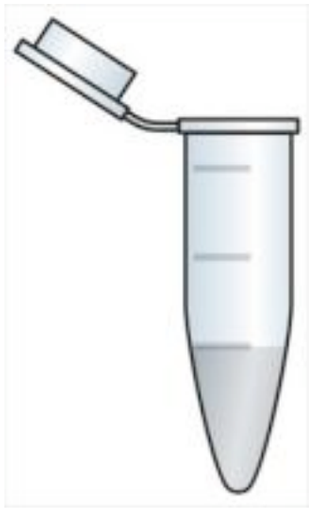


Inject

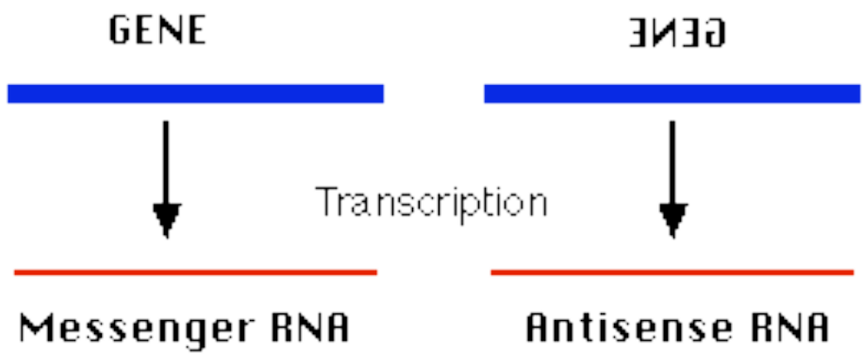


Mutant
Phenotype

No translation????



Make sense RNA of your favorite gene



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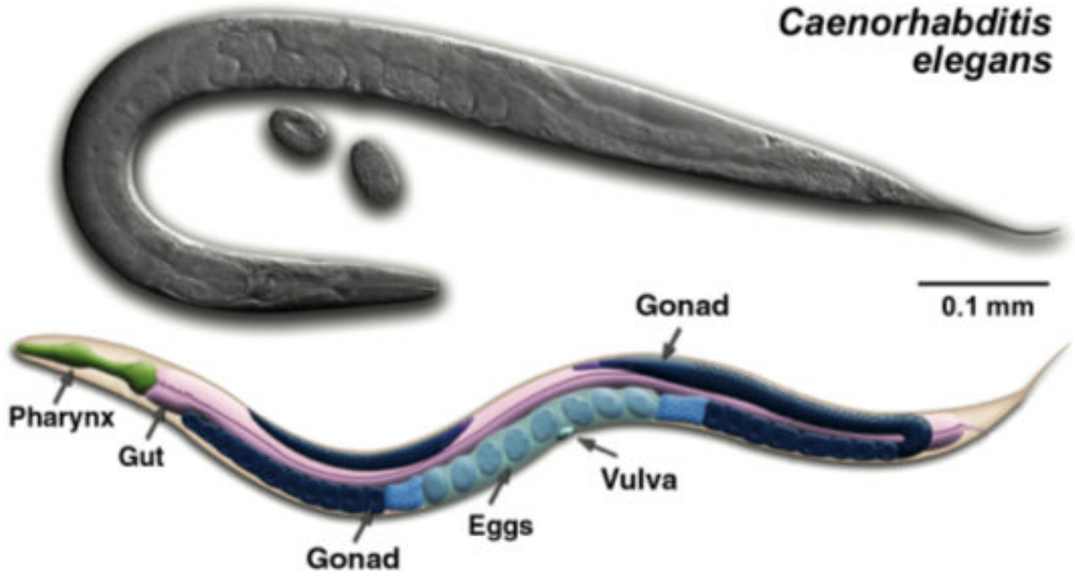
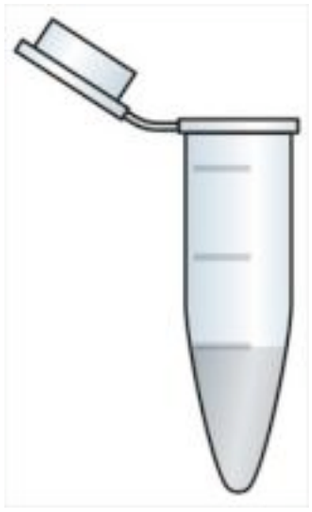


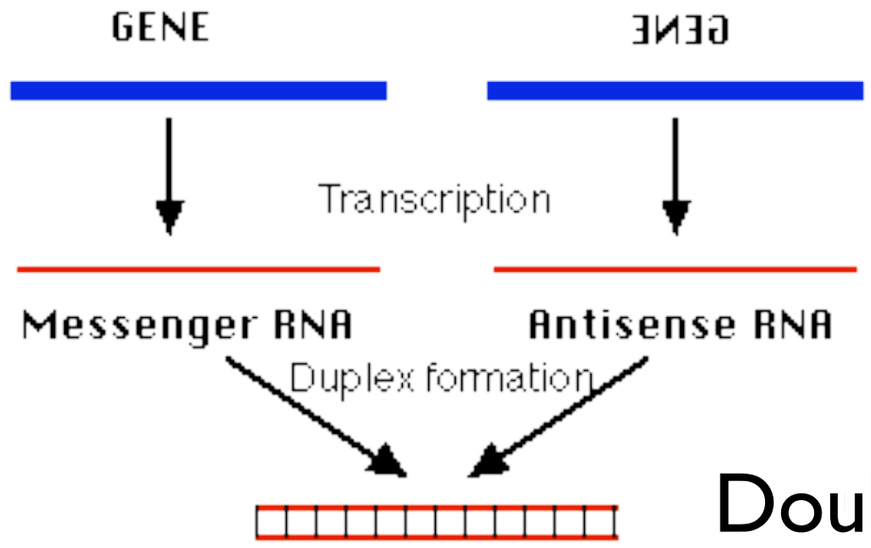
Mutant Phenotype ←

HOW?



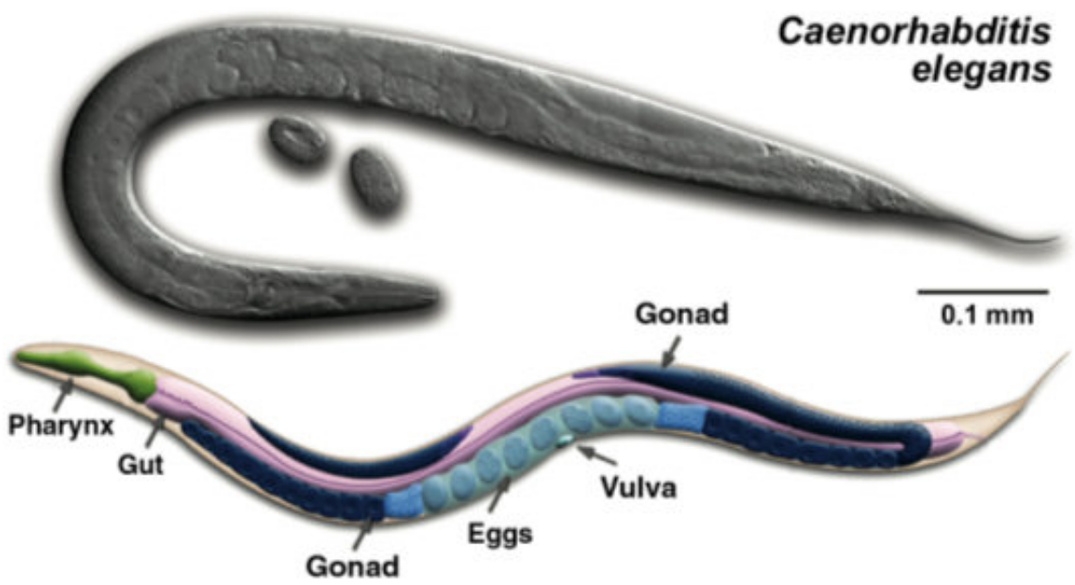
Make sense RNA of your favorite gene

Make antisense RNA of your favorite gene



Double Stranded RNA

Inject ↓



← Mutant Phenotype

RNA Interference is a Biological System that Recognizes dsRNA and Inactivates Corresponding mRNAs in a Sequence Specific Manner.

ALARM!!!!

dsRNA

"Dice" into Small Pieces

Dicer

22 nt

Small Inhibiting RNA (siRNAs)

Assemble into RISC Complex

Perfect Base-pairing to mRNA

AAAAAA

mRNA Cleavage and Destruction

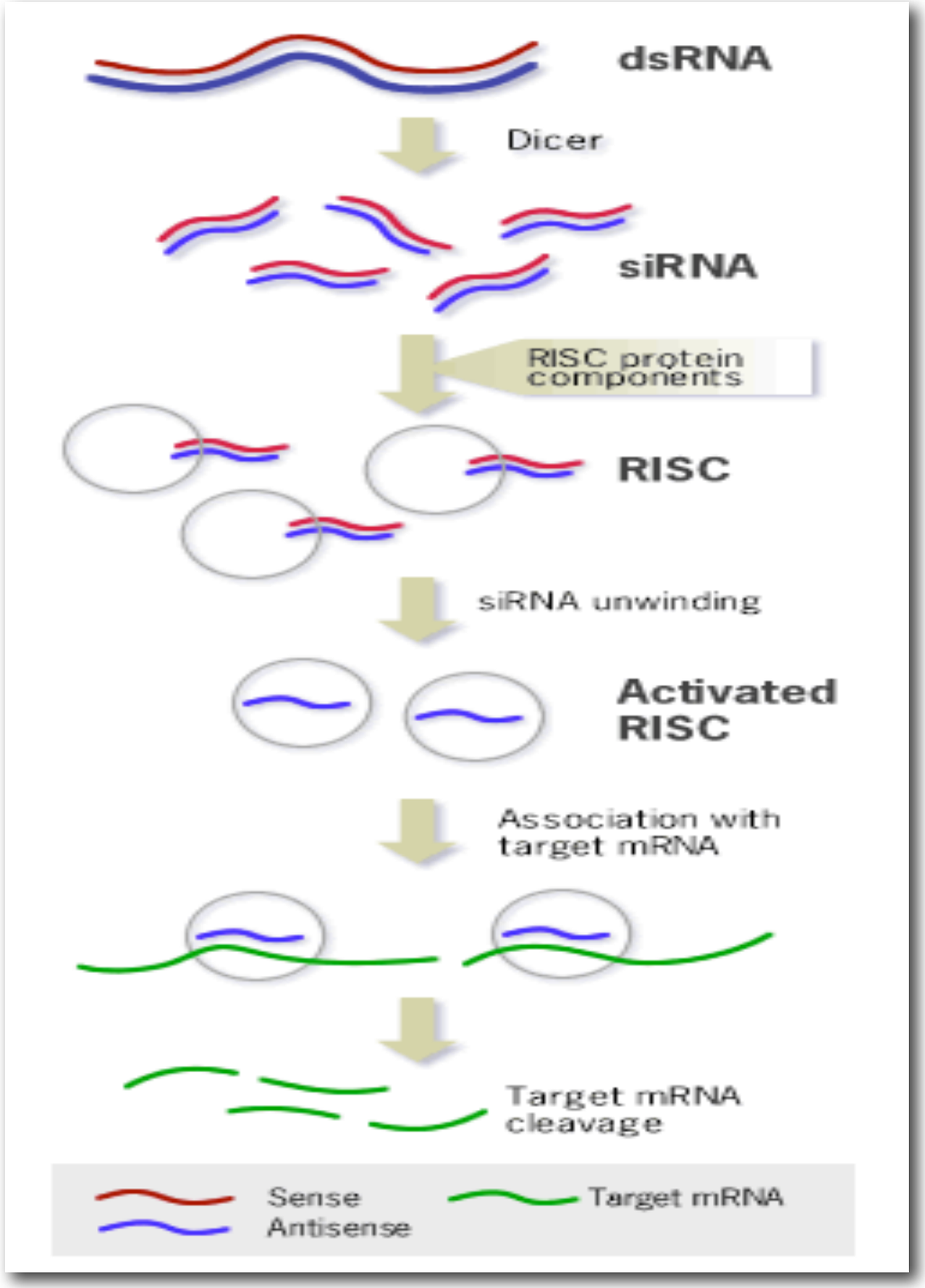
Andrew Z. Fire

Craig C. Mello

2006 Nobel

A WHOLE NEW WAY OF GENE REGULATION

Why is it there?



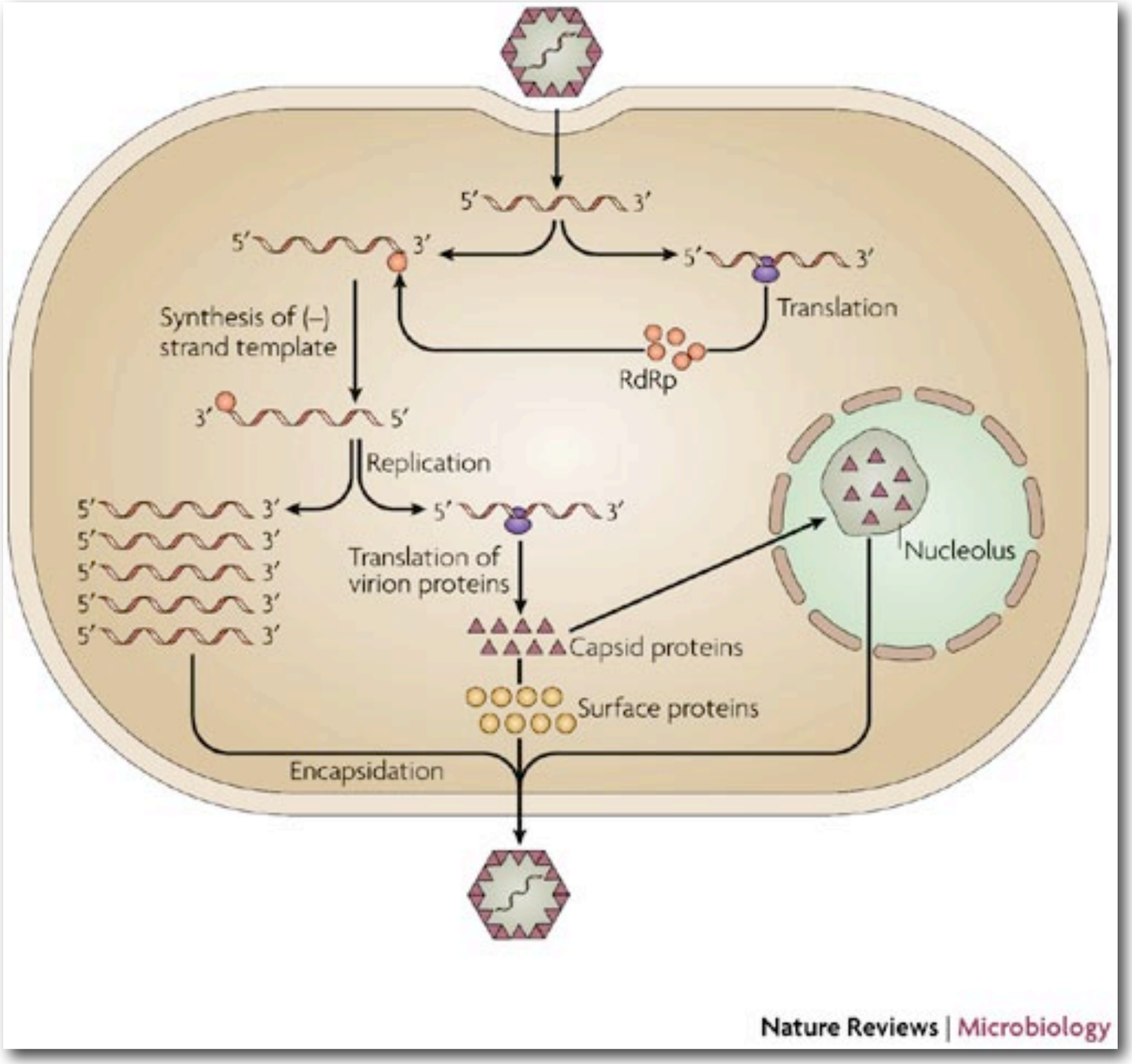
A Protection against RNA viruses

Dicer

Activated RISC

Viral RNA breakdown

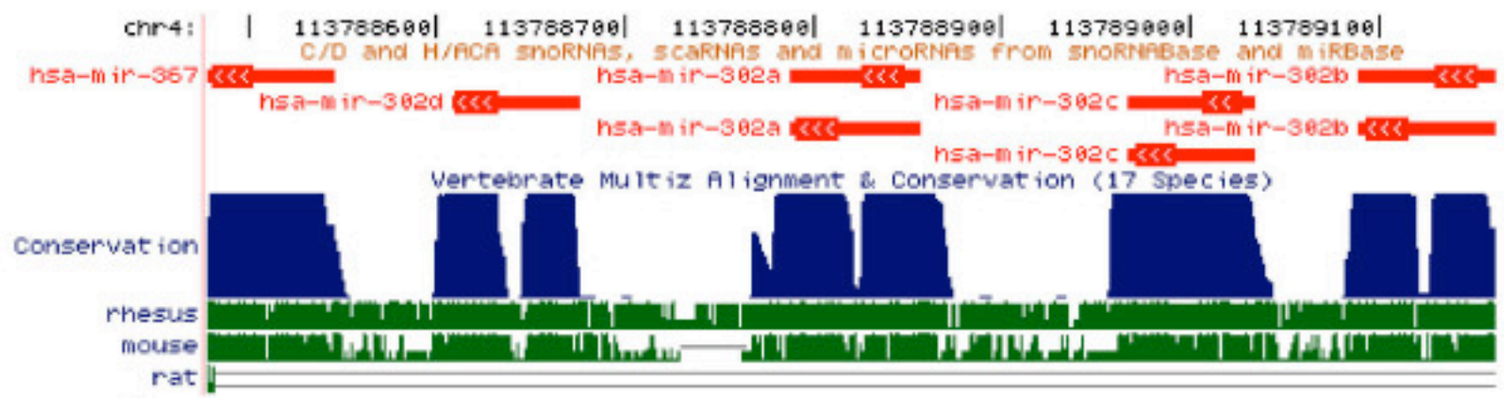
Less Virus



A.


chr19:
58983000
58983500
C/D and H/ACA snoRNAs, scaRNAs and microRNAs from snoRNABase and miRBase
hsa-mir-371
hsa-mir-372
hsa-mir-373
hsa-mir-373
Vertebrate Multiz Alignment & Conservation (17 Species)
Conservation
rhesus
mouse
rat

B.


chr4:
113788600
113788700
113788800
113788900
113789000
113789100
C/D and H/ACA snoRNAs, scaRNAs and microRNAs from snoRNABase and miRBase
hsa-mir-367
hsa-mir-302d
hsa-mir-302a
hsa-mir-302a
hsa-mir-302c
hsa-mir-302b
hsa-mir-302c
hsa-mir-302b
Vertebrate Multiz Alignment & Conservation (17 Species)
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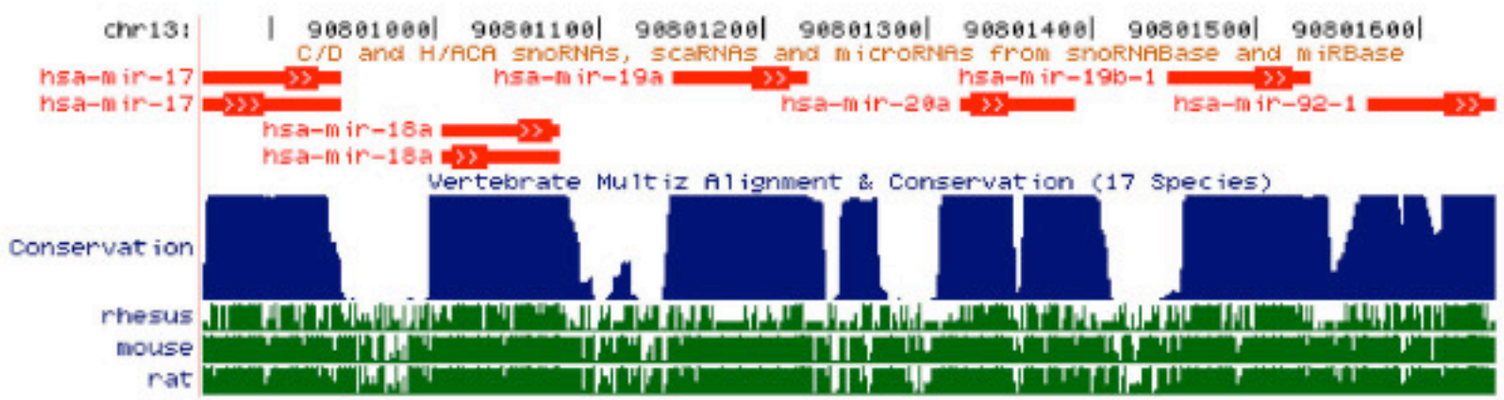
C:


chr13:
90801000
90801100
90801200
90801300
90801400
90801500
90801600
C/D and H/ACA snoRNAs, scaRNAs and microRNAs from snoRNABase and miRBase
hsa-mir-17
hsa-mir-17
hsa-mir-19a
hsa-mir-20a
hsa-mir-19b-1
hsa-mir-92-1
hsa-mir-18a
hsa-mir-18a
Vertebrate Multiz Alignment & Conservation (17 Species)
Conservation
rhesus
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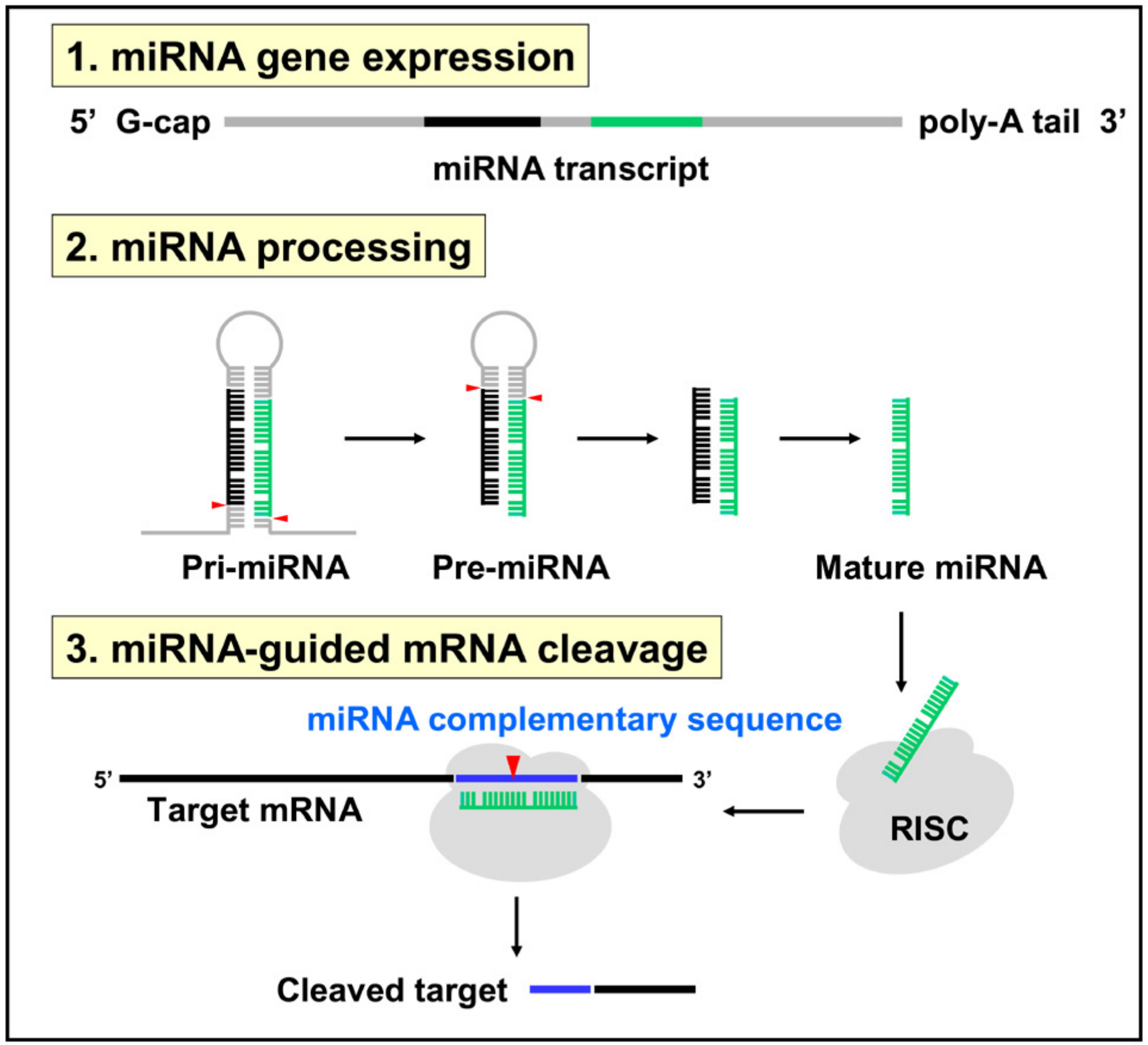
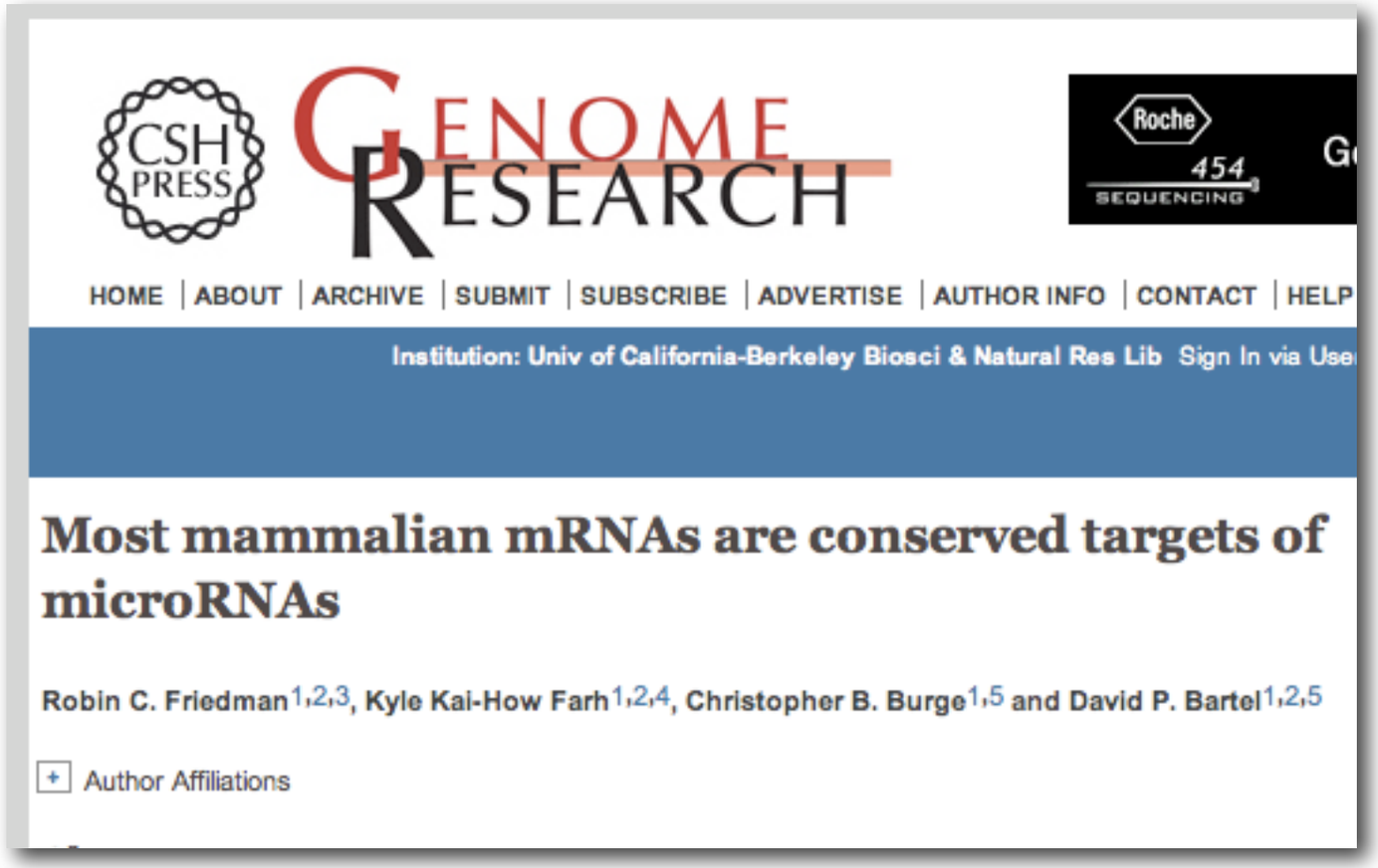
II Regulation of "normal" gene function

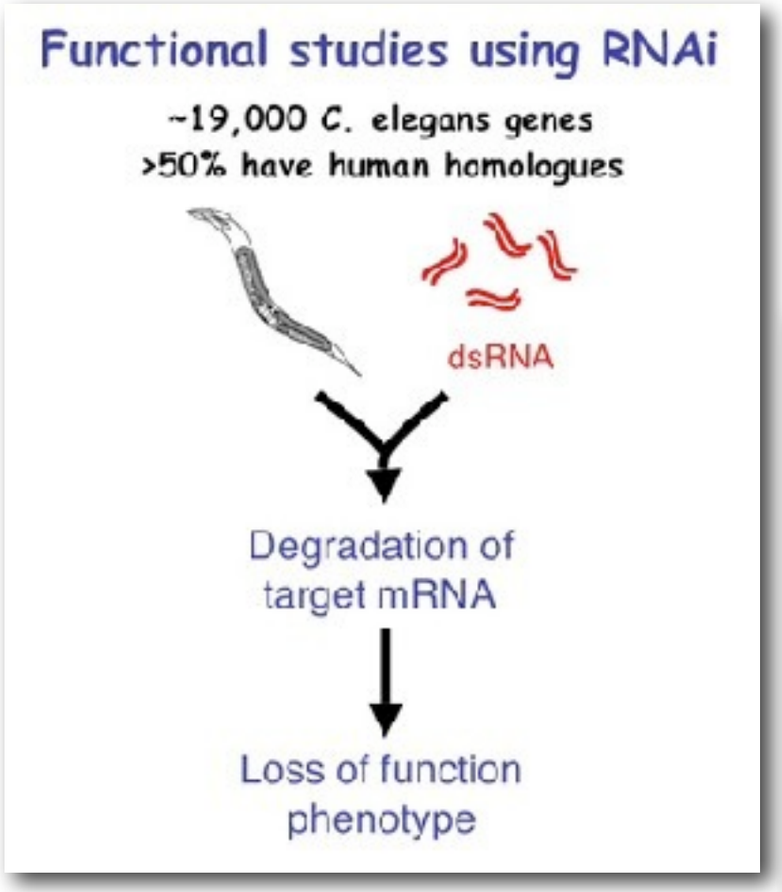


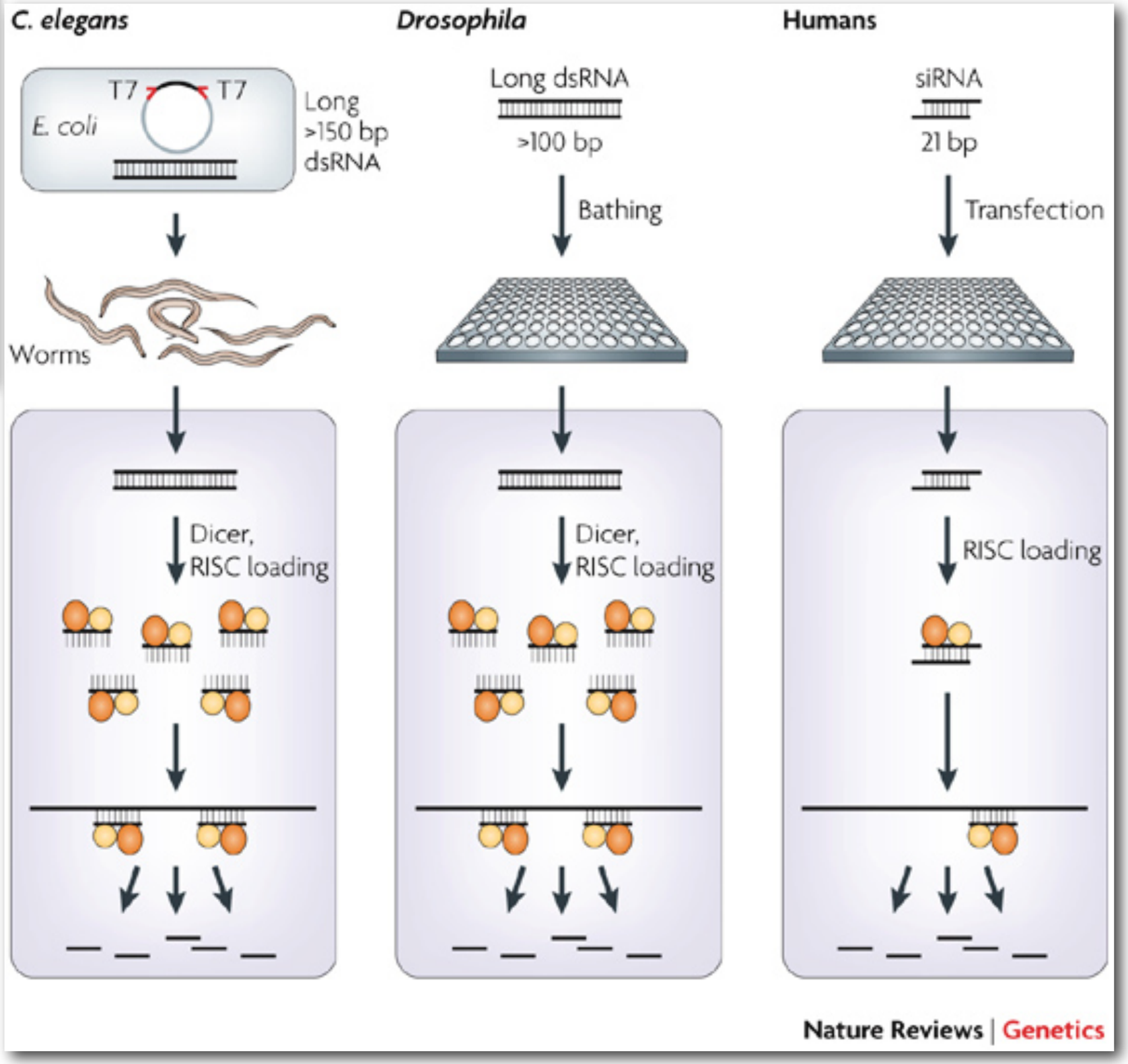
The human genome contains about 250 miRNA genes, and perhaps most mRNAs could be a target



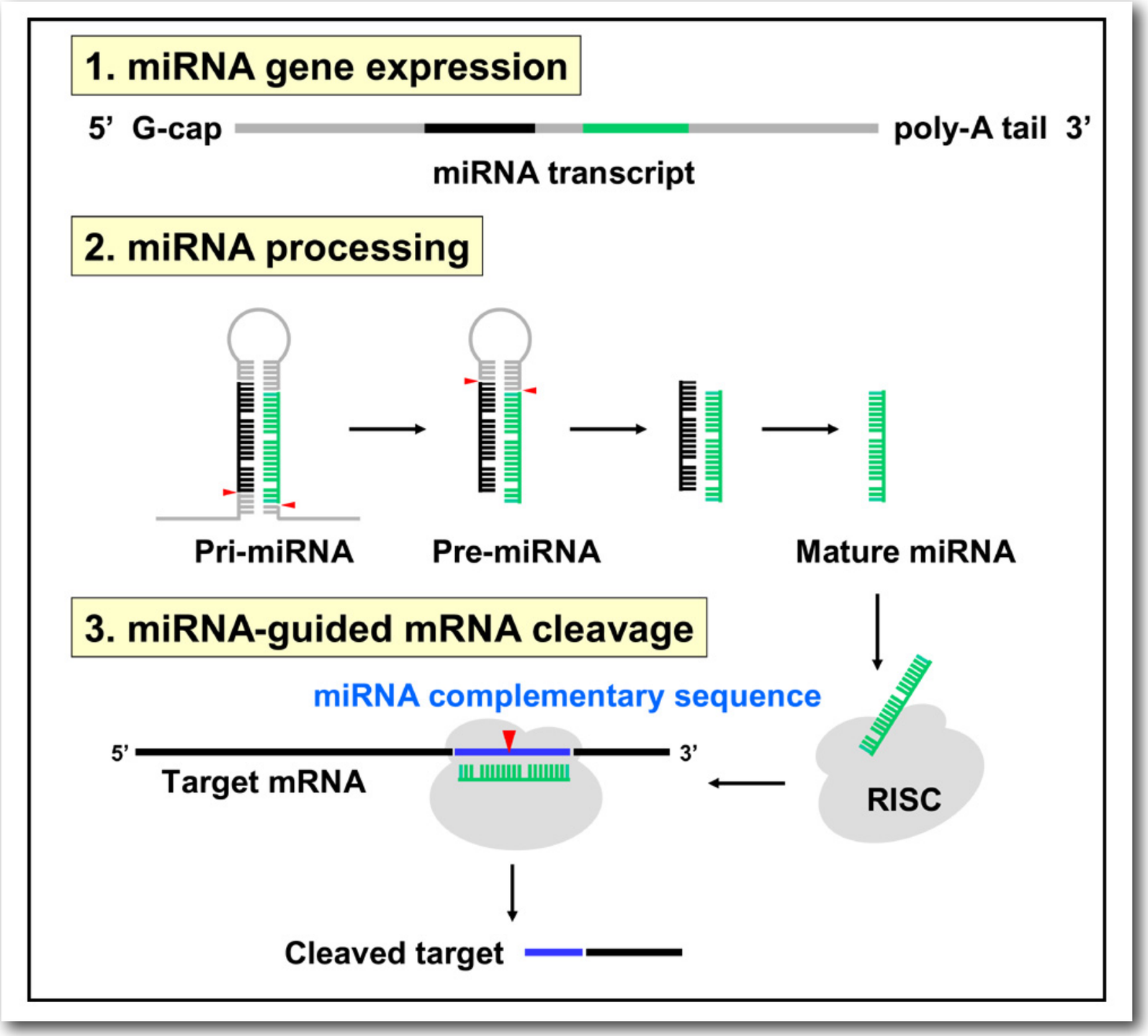
Lots of people are trying to figure out all the relationships between miRNA expression and protein expression from other mRNAs. Major implications for cancer, development and stem cell biology

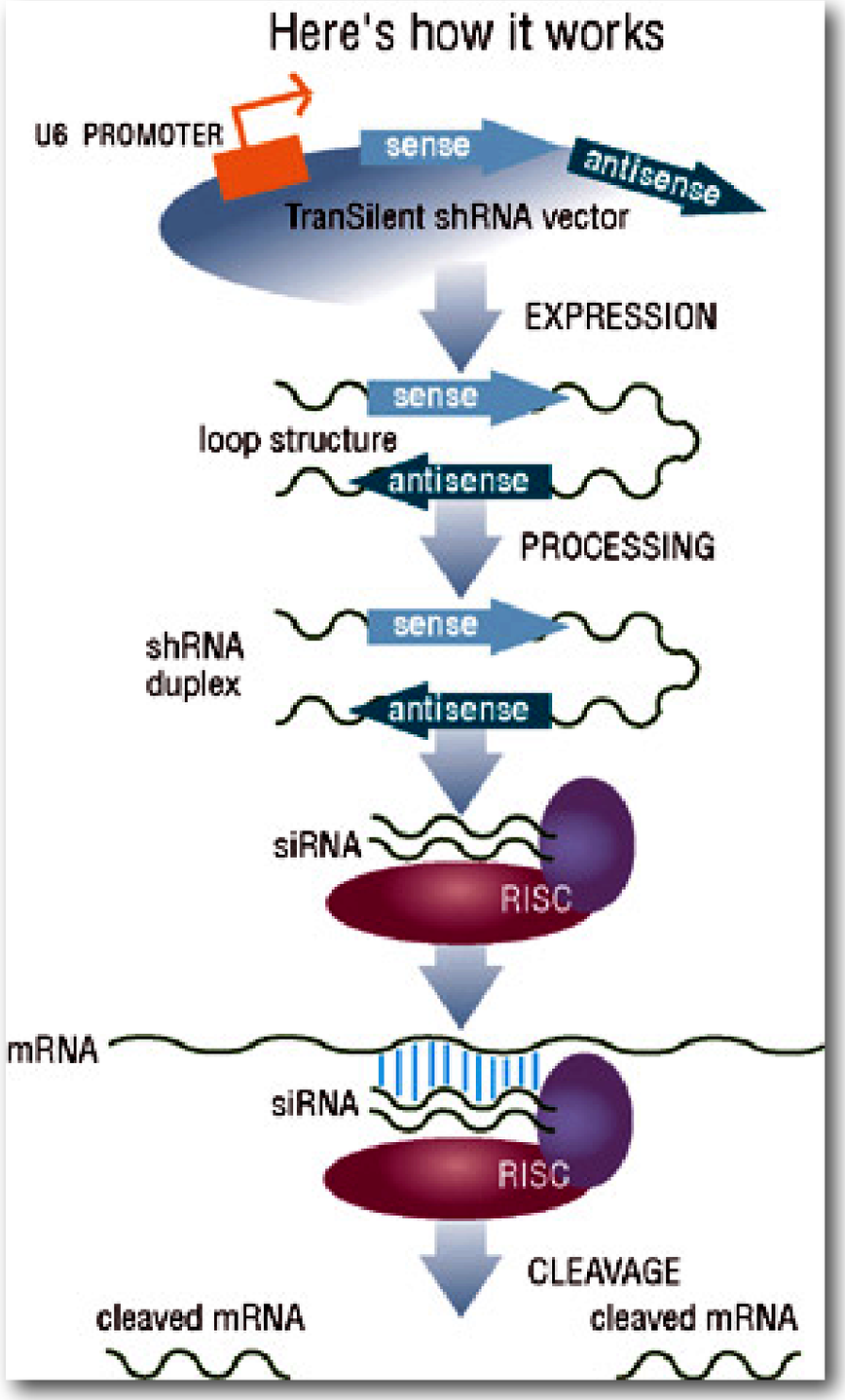
Genome wide screens of gene function





Inhibit your favorite mRNA from your favorite organism





Future?

Cancer treatment:
Break down the mRNA for the GO signal or telomerase

AIDS treatment:
Break down viral RNA

Cosmetic treatment:
Get blue eyes, lighter skin
Block fat production

The take-home message