THE 2024 MEDICINE NOBEL PRIZE

Bui Dac Chi MD
Saigon Medic Clinic

MicroRNA

-

The Nobel Assembly at the Karolinska Institutet has decided to award the 2024 Nobel Prize in Physiology or Medicine jointly to

VICTOR AMBROS
GARY RUVKUN

"for the discovery of microRNA and its role in post-transcriptional gene regulation"

fault Design English (U.S.)

Posttranscriptional Regulation of the Heterochronic Gene *lin-14* by *lin-4* Mediates Temporal Pattern Formation in C. elegans

Bruce Wightman,*† Iiho Ha,* and Gary Ruvkun
Department of Molecular Biology
Massachusetts General Hospital
Boston, Massachusetts 02114

Summary

During C. elegans development, the temporal pattern of many cell lineages is specified by graded activity of the heterochronic gene *Lin-14*. Here we demonstrate that a temporal gradient in Lin-14 protein is generated posttranscriptionally by multiple elements in the *lin-14* 3′UTR that are regulated by the heterochronic gene *Lin-4*. The *lin-14* 3′UTR is both necessary and sufficient to confer *lin-4*-mediated posttranscriptional temporal regulation. The function of the *lin-14* 3′UTR is conserved between C. elegans and C. briggsae. Among the conserved sequences are seven elements that are each complementary to the *lin-4* RNAs. A reporter gene bearing three of these elements shows partial temporal gradient activity. These data suggest a molecular

site phenotypes (Ambros and Horvitz, 1987). *li* alleles cause larvae stage 2 (L2) patterns of cell l in a variety of tissues to be executed precociously the L1 stage (Ambros and Horvitz, 1987). Two *lin* alleles cause the opposite transformation in tempo fate, reiterations of early cell fates at later stage instance, at the L2 stage, *lin-14(gf)* mutants repe terns of cell lineage appropriate for the L1 stage (A and Horvitz, 1984).

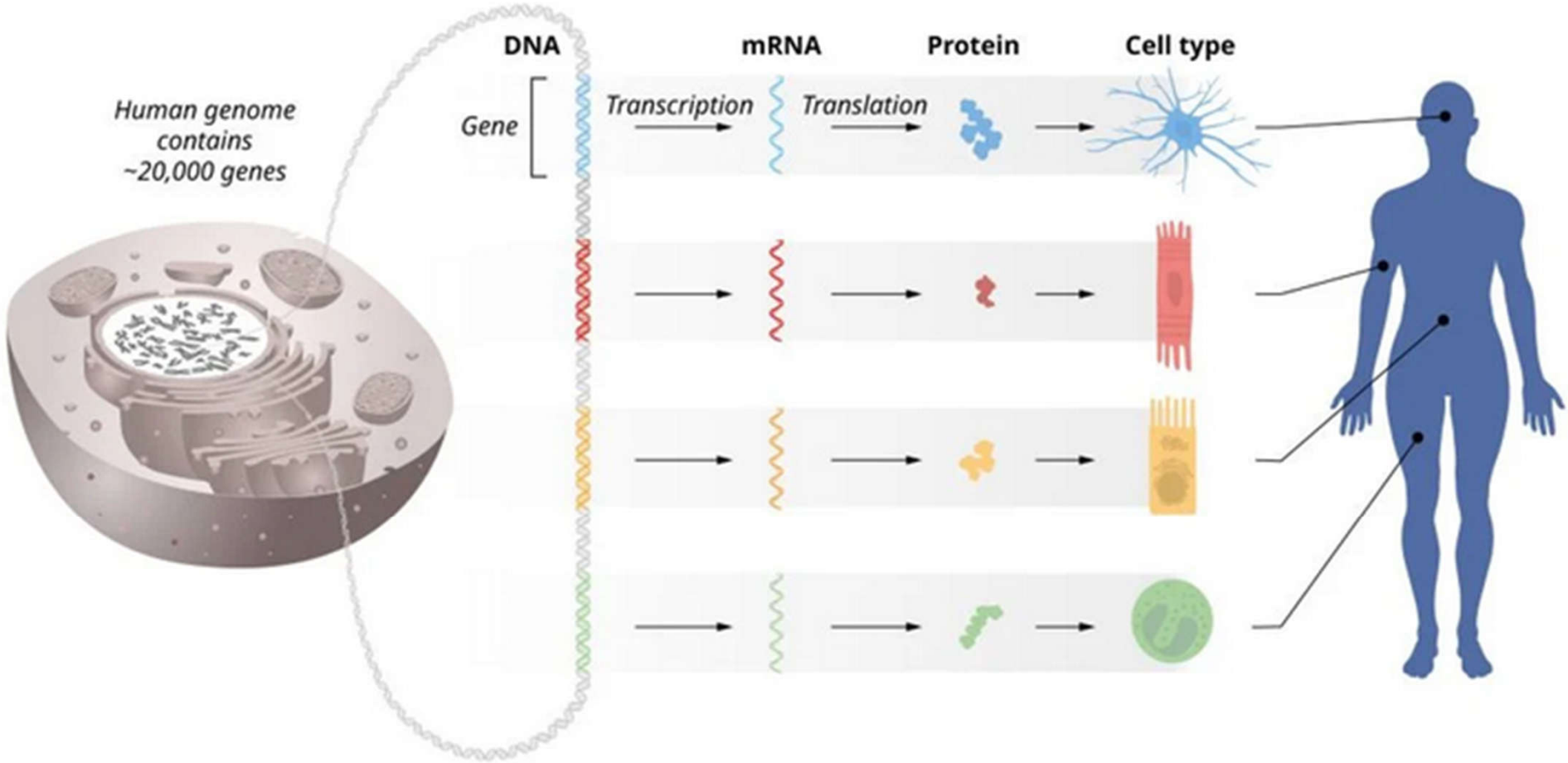
lin-14 controls these stage-specific cell lineages b erating a temporal gradient of Lin-14 nuclear prote 14p). Lin-14p levels are high during the L1 stage b faintly detectable by indirect immunofluorescence and later stages (Ruvkun and Giusto, 1989). The *lin* mutations interfere with *lin-14* temporal down-r tion, causing inappropriately high Lin-14p levels at p stages, which imposes L1 patterns of cell lineage o L1 blast cells (Ruvkun and Giusto, 1989). These mu delete sequences from the *lin-14* mRNA 3′ untrar region (3′UTR), suggesting that regulatory element 3′UTR normally are responsible for mediating the regulation of Lin-14p abundance at later larval

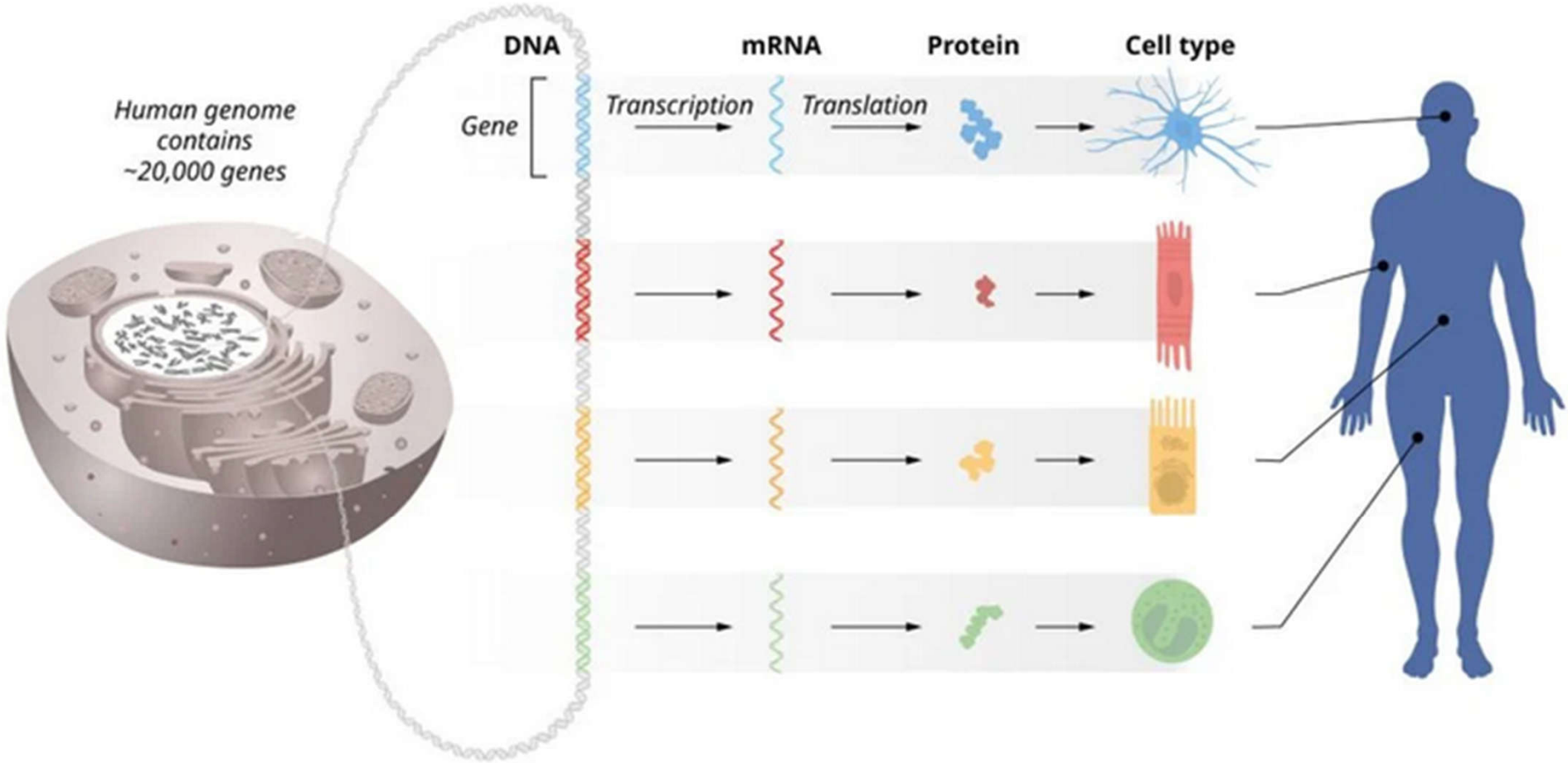
for the discovery of microRNA and its role in post-transcriptional gene regulation

This year's Nobel Prize honors two scientists for their discovery of a fundamental principle governing how gene activity is regulated.

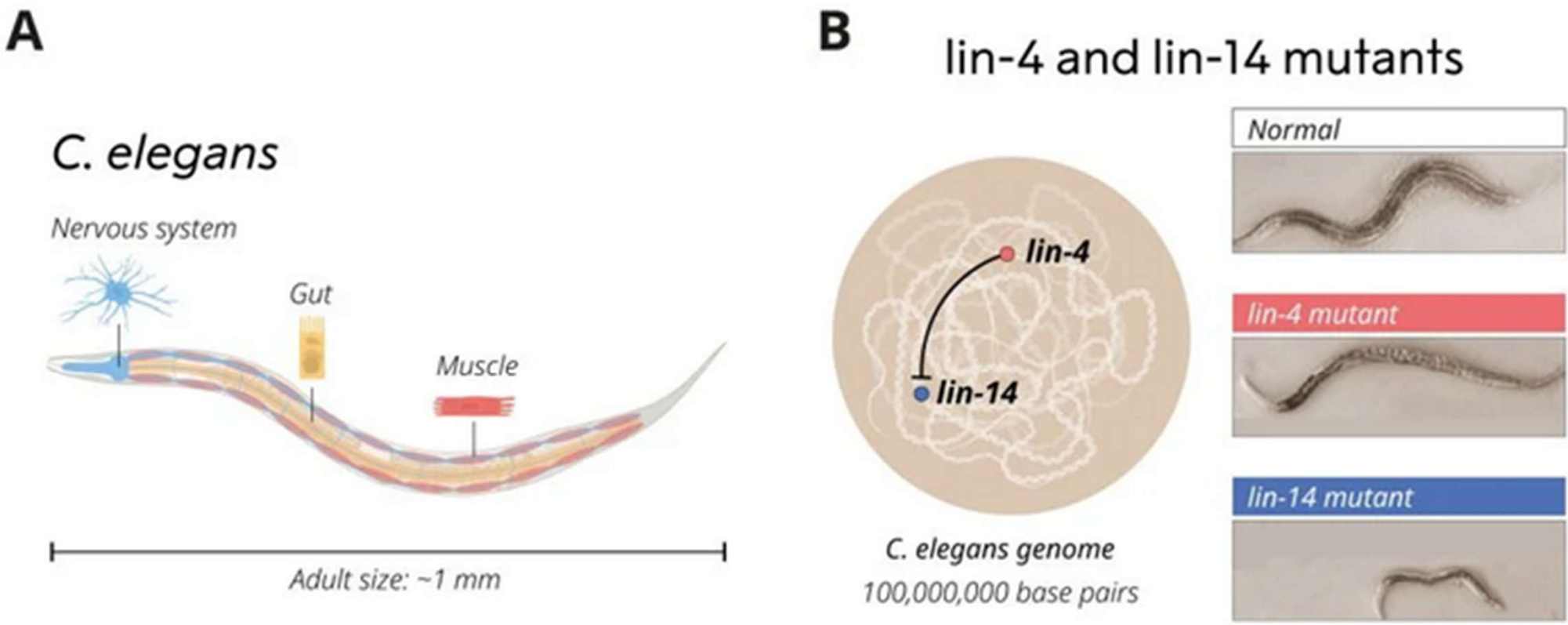
The information stored within our chromosomes can be likened to an instruction manual for all cells in our body. Every cell contains the same chromosomes, so every cell contains exactly the same set of genes and exactly the same set of instructions. Yet, different cell types, such as muscle and nerve cells, have very distinct characteristics. How do these differences arise? The answer lies in gene regulation, which allows each cell to select only the relevant instructions. This ensures that only the correct set of genes is active in each cell type.

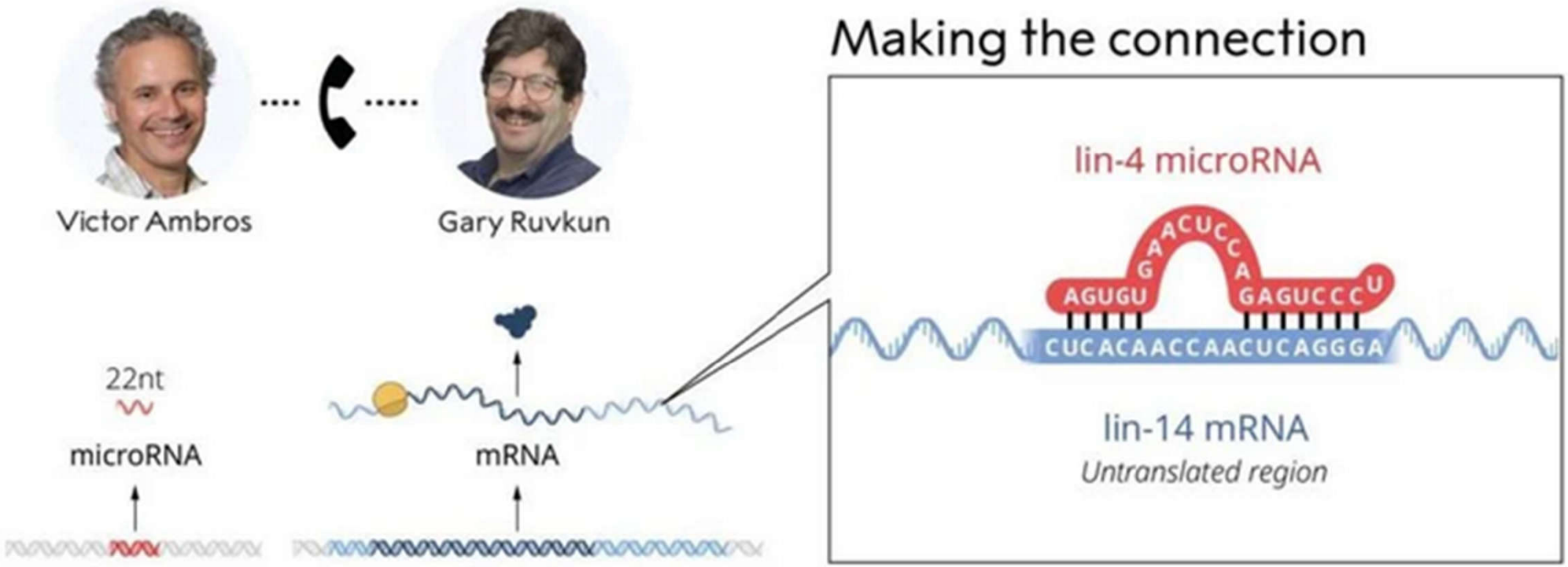
Victor Ambros and Gary Ruvkun were interested in how different cell types develop. They discovered microRNA, a new class of tiny RNA molecules that play a crucial role in gene regulation. Their groundbreaking discovery revealed a completely new principle of gene regulation that turned out to be essential for multicellular organisms, including humans. It is now known that the human genome codes for over one thousand microRNAs. Their surprising discovery revealed an entirely new dimension to gene regulation. MicroRNAs are proving to be


DNA
mRNA
Protein
Cell type
Human genome
contains
~20,000 genes
Gene
Transcription
Translation


DNA
mRNA
Protein
Cell type
Human genome
contains
~20,000 genes
Gene
Transcription
Translation

unknown. Ambros and Ruvkun were intrigued by these mutants and their potential relationship and set out to resolve these mysteries.




Victor Ambros
Gary Ruvkun
22nt
microRNA
mRNA
Making the connection
lin-4 microRNA
AGUGU
GAACUCCA
GAGUCCCU
CUCACAACCAACUCAGGGA
lin-14 mRNA
Untranslated region

PubMed®

Advanced

> Avicenna J Med Biotechnol. 2010 Oct;2(4):161-79.

The Role of MicroRNAs in Human Diseases

Ali M Ardekani [1], Mozhgan Moslemi Naeini

Affiliations + expand

PMID: 23407304 PMCID: PMC3558168

Abstract

MicroRNAs (miRNAs) are short RNA molecules which bind to target mRNAs, resultin repression and gene silencing and are found in all eukaryotic cells. Approximately 22 have been reported to exist in the mammalian genome, from which over 1000 belon genome. Many major cellular functions such as development, differentiation, growth are known to be regulated by miRNAs. Proximity to other genes in the genome and

o search

(6,797 unread) – buida
(6,797 unread) – buida
The Nobel Prize in Phy
(6,799 unread) – buida
https://pubmed.ncbi.nlm.nih.gov/23407304/

Avicenna J Med Biotechnol. 2010 Oct;2(4):161-79.

he Role of MicroRNAs in Human Diseases

i M Ardekani [1], Mozhgan Moslemi Naeini

filiations + expand

MID: 23407304 PMCID: PMC3558168

bstract

icroRNAs (miRNAs) are short RNA molecules which bind to target mRNAs, resulting in translational pression and gene silencing and are found in all eukaryotic cells. Approximately 2200 miRNA genes ve been reported to exist in the mammalian genome, from which over 1000 belong to the human nome. Many major cellular functions such as development, differentiation, growth, and metabolism e known to be regulated by miRNAs. Proximity to other genes in the genome and their locations in trons of coding genes, noncoding genes and exons have been reported to have a major influence on e level of gene expressions in eukaryotic cells. miRNAs are well conserved in eukaryotic system and e believed to be an essential and evolutionary ancient component of gene regulatory networks. erefore, in recent years miRNAs have been studied as a likely candidate for involvement in most ological processes and have been implicated in many human diseases.

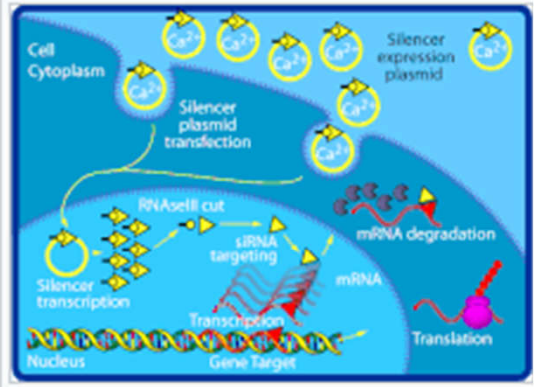
ywords: Disease; Human Genome; MicroRNAs; miRNA.

Small interfering RNA

From Wikipedia, the free encyclopedia

See also: RNA interference

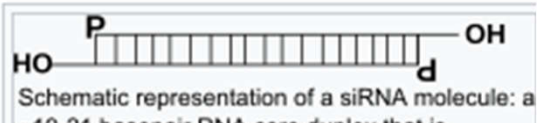
Small interfering RNA (**siRNA**), sometimes known as **short interfering RNA** or **silencing RNA**, is a class of double-stranded non-coding RNA molecules, typically 20–24 base pairs in length, similar to microRNA (miRNA), and operating within the RNA interference (RNAi) pathway. It interferes with the expression of specific genes with complementary nucleotide sequences by degrading messenger RNA (mRNA) after transcription, preventing translation.[1][2] It was discovered in 1998 by Andrew Fire at the Carnegie Institution for Science in Washington, D.C. and Craig Mello at the University of Massachusetts in Worcester.



Mediating RNA interference in cultured mammalian cells.

Structure [edit]

Naturally occurring siRNAs have a well-defined structure that is a short (usually 20 to 24-bp) double-stranded RNA (dsRNA) with phosphorylated 5' ends and hydroxylated 3' ends with two overhanging nucleotides. The Dicer enzyme catalyzes production of siRNAs from long dsRNAs and small hairpin RNAs.[3] siRNAs can also be introduced into cells by transfection. Since in principle any



Schematic representation of a siRNA molecule: a ~19-21 basepair RNA core duplex that is followed by a 2 nucelotide 3' overhang on each strand. OH: 3' hydroxyl; P: 5' Phosphate