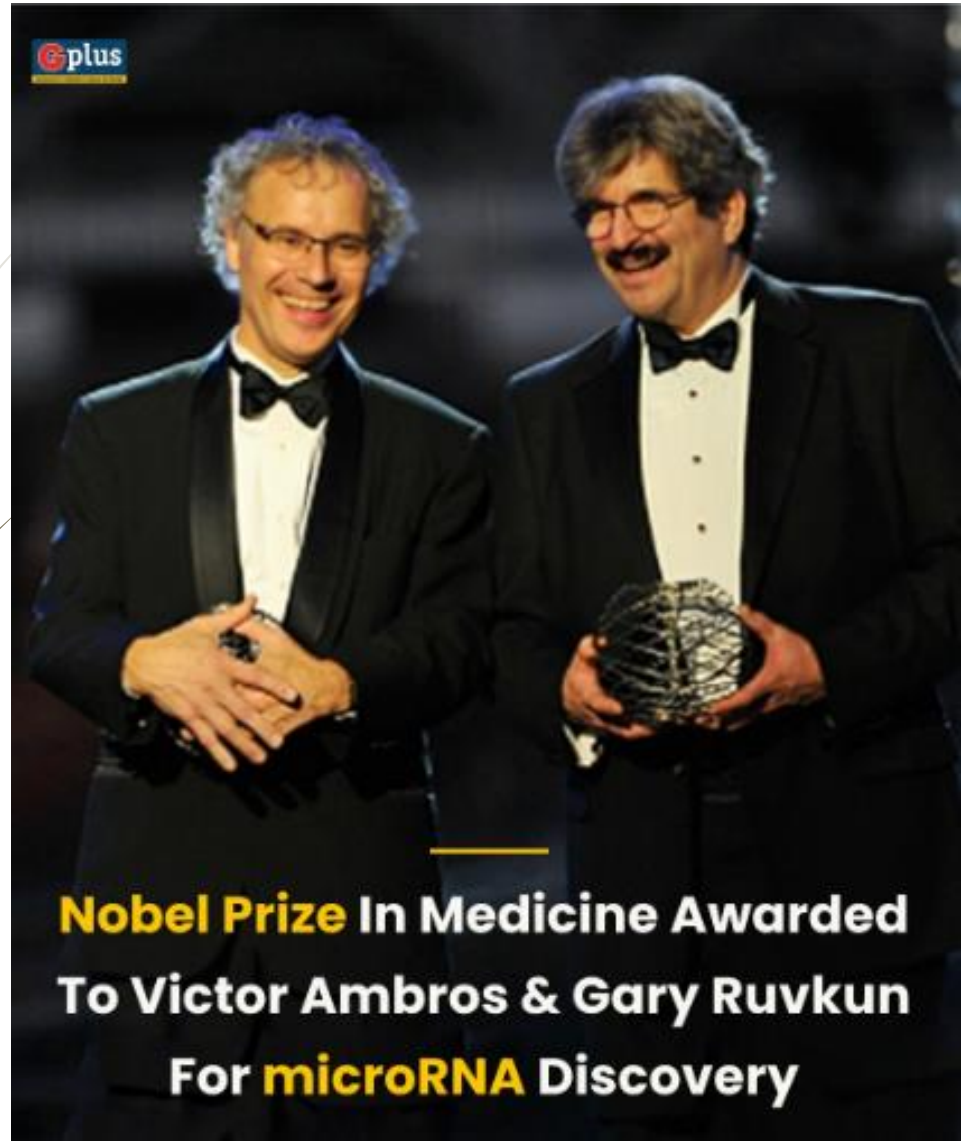
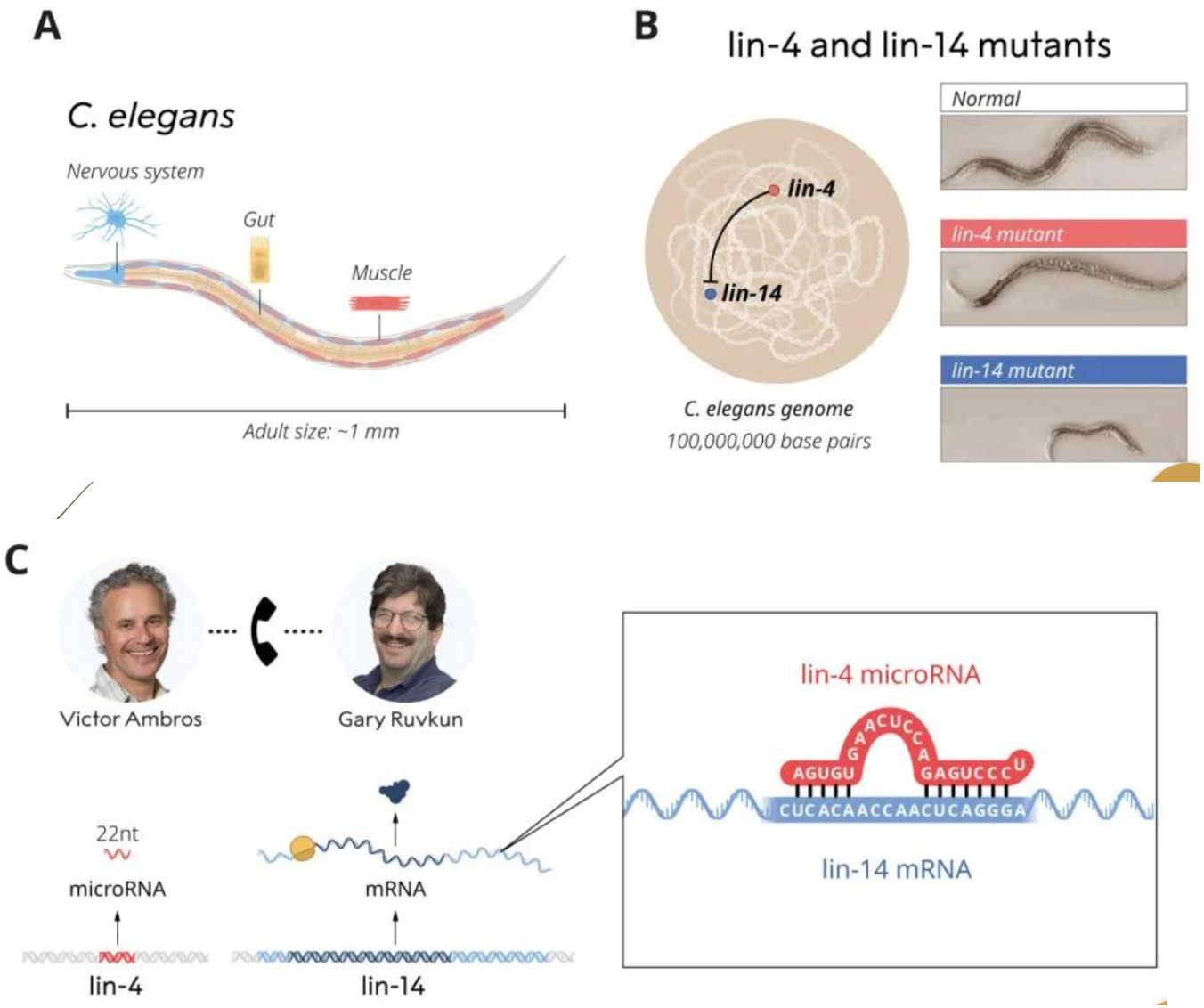
miRNA-Nobel Prize 2024

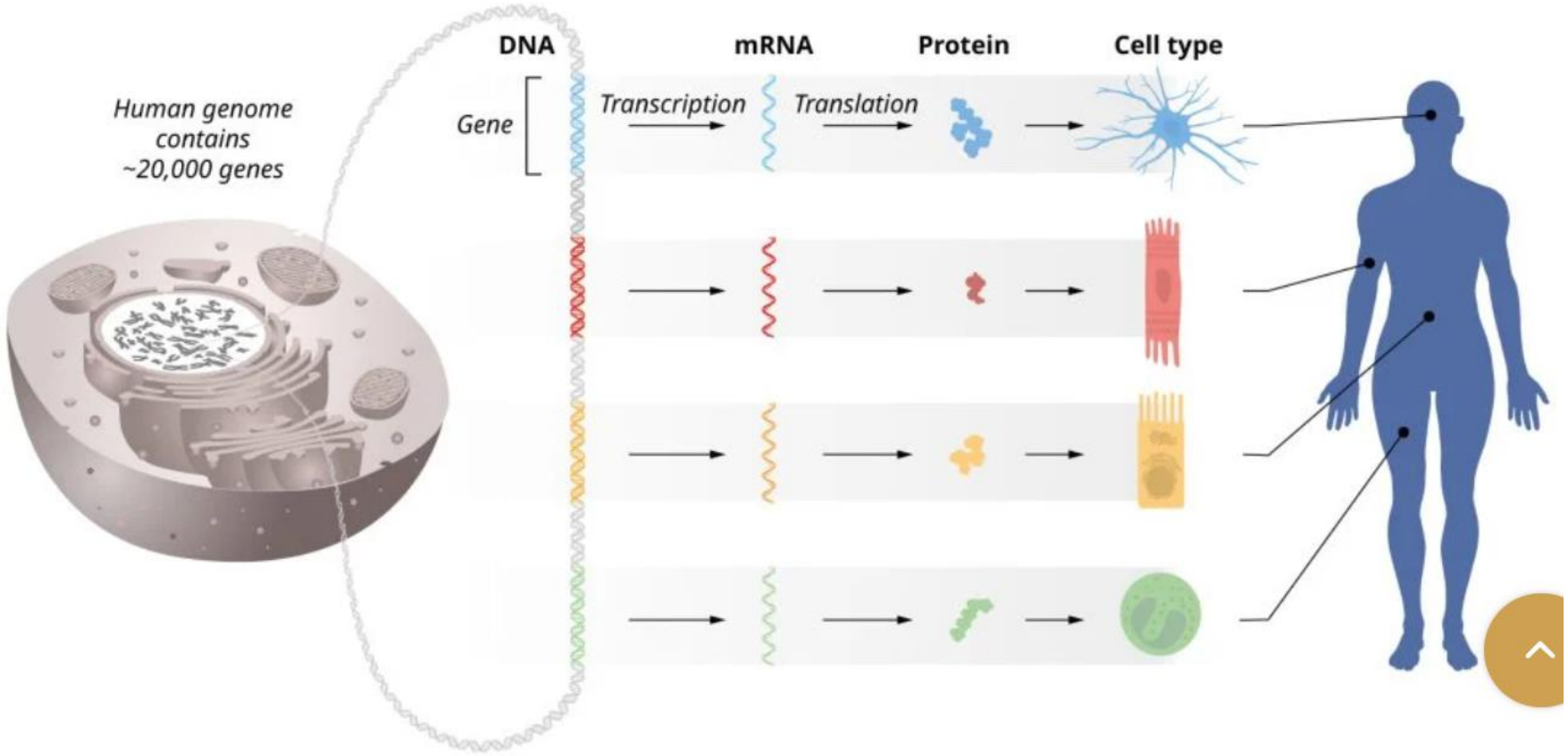


In the late 1980s, Victor Ambros and Gary Ruvkun were postdoctoral fellows in the laboratory of Robert Horvitz, who was awarded the Nobel Prize in 2002, alongside Sydney Brenner and John Sulston. In Horvitz's laboratory, they studied a relatively unassuming 1 mm long roundworm, *C. elegans*.

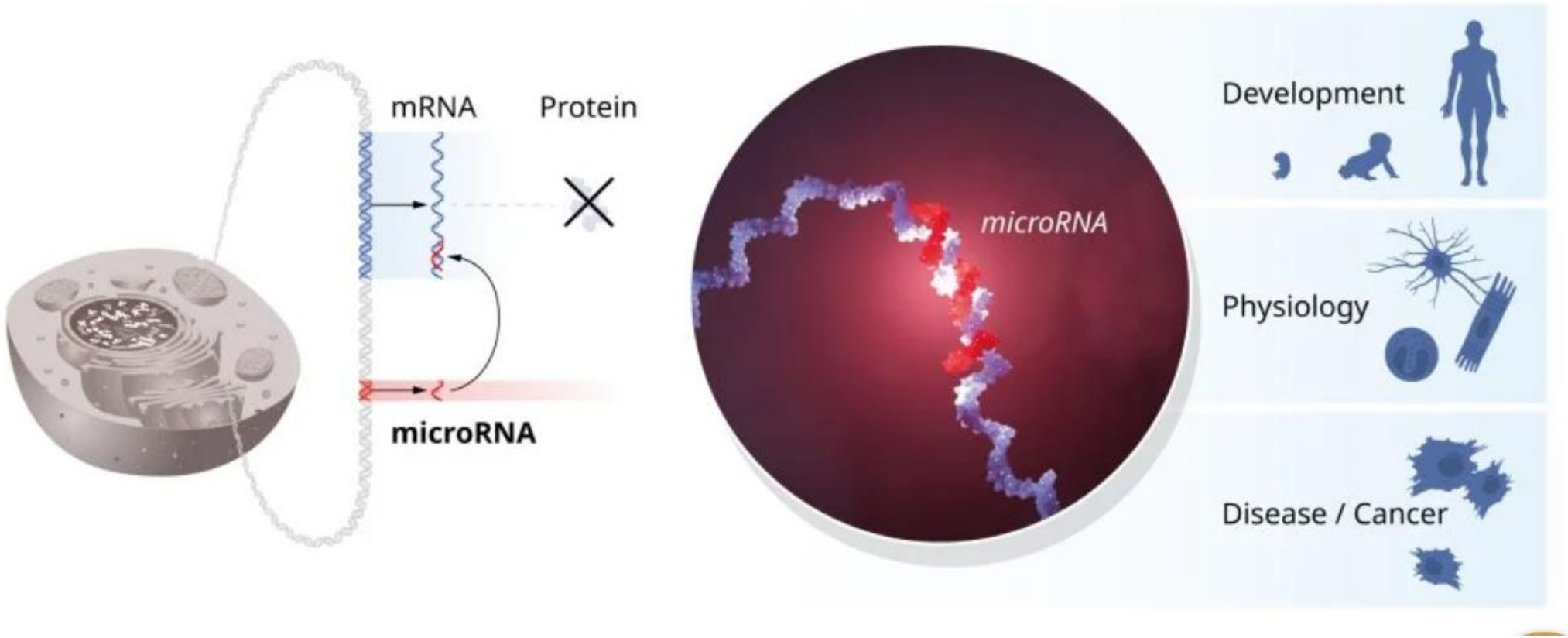
- Despite its small size, *C. elegans* possesses many specialized cell types such as nerve and muscle cells also found in larger, more complex animals, making it a useful model for investigating how tissues develop and mature in multicellular organisms.
- Ambros and Ruvkun were interested in genes that control the timing of activation of different genetic programs, ensuring that various cell types develop at the right time.
- They studied two mutant strains of worms, lin-4 and lin-14, that displayed defects in the timing of activation of genetic programs during development. The laureates wanted to identify the mutated genes and understand their function.
- Ambros had previously shown that the lin-4 gene appeared to be a negative regulator of the lin-14 gene. However, how the lin-14 activity was blocked was unknown. Ambros and Ruvkun were intrigued by these mutants and their potential relationship and set out to resolve these mysteries.



(A) *C. elegans* is a useful model organism for understanding how different cell types develop. **(B)** Ambros and Ruvkun studied the lin-4 and lin-14 mutants. Ambros had shown that lin-4 appeared to be a negative regulator of lin-14. **(C)** Ambros discovered that the lin-4 gene encoded a tiny RNA, microRNA, that did not code for a protein. Ruvkun cloned the lin-14 gene, and the two scientists realized that the lin-4 microRNA sequence matched a complementary sequence in the lin-14 mRNA.



The flow of genetic information from DNA to mRNA to proteins. The identical genetic information is stored in DNA of all cells in our bodies. This requires precise regulation of gene activity so that only the correct set of genes is active in each specific cell type. © The Nobel Committee for Physiology or Medicine. Ill. Mattias Karlén



The seminal discovery of microRNAs was unexpected and revealed a new dimension of gene regulation. © The Nobel Committee for Physiology or Medicine. Ill. Mattias Karlén

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The C. elegans heterochronic gene lin-4 encodes small RNAs with antisense complementarity to lin-14

R C Lee [1], R L Feinbaum, V Ambros

Affiliations + expand

PMID: 8252621 DOI: 10.1016/0092-8674(93)90529-y

Comparative Study > Cell. 1993 Dec 3;75(5):855-62. doi: 10.1016/0092-8674(93)90530-4.

Posttranscriptional regulation of the heterochronic gene lin-14 by lin-4 mediates temporal pattern formation in C. elegans

B Wightman [1], I Ha, G Ruvkun

Affiliations + expand

PMID: 8252622 DOI: 10.1016/0092-8674(93)90530-4

Conservation of the sequence and temporal expression of *let-7* heterochronic regulatory RNA

Amy E. Pasquinelli, Brenda J. Reinhart, Frank Slack, Mark Q. Martindale, Mitzi I. Kuroda, Betsy Maller, David C. Hayward, Eldon E. Ball, Bernard Degnan, Peter Müller, Jürg Spring, Ashok Srinivasan, Mark Fishman, John Finnerty, Joseph Corbo, Michael Levine, Patrick Leahy, Eric Davidson & Gary Ruvkun

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