

**The Double Life of RNA**  
**1995 Holiday Lectures on Science**  
**Chapter List**

Lecture One

Catalysis, Chemical and Biochemical

Thomas R. Cech, Ph.D.

1. Start of Lecture One
2. Introduction by HHMI President Purnell Choppin
3. Video introduction of Dr. Thomas Cech
4. Molecular biology and its relation to chemistry
5. Demonstration: Determining the gas in three balloons
6. Demonstration: Testing the hypothesis
7. The chemistry of hydrogen combustion
8. Chemical versus biochemical reactions
9. RNA as an information carrier and an enzyme
10. Protein as a biochemical catalyst
11. DNA is suited to storing information
12. RNA can take many shapes
13. Demonstration: Mr. Lincoln glows
14. Chemistry of Mr. Lincoln glows
15. Principles of catalysis
16. Demonstration: Catalyzed oxidation of tartrate
17. Chemistry of tartrate oxidation
18. RNA acting as a catalyst
19. Summary
20. Q&A: Why did you go into molecular biology?
21. Q&A: Why did you decide to research RNA?
22. Q&A: What are examples of RNA as a catalyst?
23. Q&A: Drawbacks of molecular biology research?
24. Q&A: Why did you heat the sodium tartrate?
25. Q&A: What is the catalyst in DNA purification?
26. Q&A: Does DNA have catalytic properties?
27. Q&A: What allows RNA to form different structures?
28. Closing remarks by HHMI President Choppin

## Lecture Two

### RNA as an Enzyme: Discovery, Origins of Life, and Medical Possibilities

Thomas R. Cech, Ph.D.

1. Start of Lecture Two
2. Introduction by HHMI President Dr. Purnell Choppin
3. Review of RNA's dual nature
4. Properties of protein enzymes
5. RNA catalysts are folded RNAs
6. How scientific discoveries are made
7. Why study the protozoan *Tetrahymena*?
8. DNA transcription and RNA splicing
9. RNA splicing can occur in a test tube
10. RNA splicing occurs without cellular extract
11. In search of the RNA-splicing protein enzyme
12. Recombinant *E. coli* shows RNA can splice itself
13. RNA enzymes and the origin of life
14. Simulating the origin of life in a test tube
15. Looking for molecular fossils from the origin of life
16. Possible uses of ribozymes to fight diseases
17. Designing ribozymes to attack specific RNAs
18. Fighting retroviruses with ribozymes
19. Correcting mutant RNAs with ribozymes
20. Summary
21. Closing remarks by HHMI President Choppin

## Lecture Three

How to Accelerate a Reaction 100,000,000,000 Times Using Only RNA

Thomas R. Cech, Ph.D.

1. Start of Lecture Three
2. Introduction by HHMI Vice President Dr. Joseph Perpich
3. Interview with Dr. Thomas Cech
4. Outline of the lecture
5. Biochemical mechanism of RNA splicing
6. Transesterification reaction
7. The system used for studying the nature of catalysis
8. Structural basis of catalysis
9. Laboratory data showing RNA cleavage
10. Estimating the affinity of an enzyme for its substrate
11. Single atom substitution causes reaction failure
12. Metal ions are important in the catalytic reaction
13. How do you build the active site with RNA?
14. Using electron microscopy to see RNA structures
15. Extending molecules to study ribozyme structure
16. Crystallizing ribozymes to study molecular structure
17. Q&A: Inhibitors that compete with the active site?
18. Q&A: Do pH and temperature affect ribozymes?
19. Q&A: Which base pairs to use for arm extension?
20. Q&A: Can ribozymes keep going?
21. Q&A: Is Mg the most effective metal ion cofactor?
22. Q&A: Do RNA catalysts handle specific cell functions?
23. Closing remarks by HHMI Vice President Dr. Joseph Perpich

## Lecture Four

### Life at the End of the Chromosome: Another RNA Machine

Thomas R. Cech, Ph.D.

1. Start of Lecture Four
2. Introduction by HHMI Vice President Dr. Joseph Perpich
3. Human chromosomes and their replication
4. What happens at the end of the chromosomes?
5. Functions of telomeres
6. DNA sequences of telomeres in different species
7. *Oxytricha* as a source of telomere proteins
8. How do the telomere proteins interact with DNA?
9. The 3D structure of telomere proteins
10. Replication problems at the ends of the DNA strand
11. Telomerase solves the end-replication problem
12. Using PCR to clone telomerase RNA genes
13. Telomerase RNA is similar across different species
14. Using antibodies to tag proteins in a cell
15. Alpha/beta telomere protein location in the nucleus
16. Using an RNA probe to tag telomerase RNA
17. Location of telomerase suggests its replication role
18. Summary
19. Cech lab personnel and path of scientific training
20. Q&A: What are telomerases doing in 'storage'?
21. Closing remarks by HHMI President Choppin