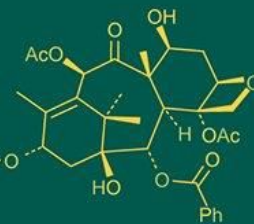
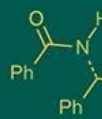
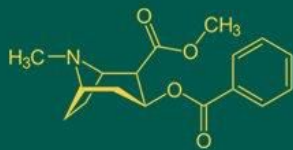


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6S RNA: A key player in transcriptional regulation

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Abstract

Transcription is a fundamental process in all biological systems and forms a major step in the central dogma of life. In prokaryotic cells, transcription is catalyzed by RNA polymerase (RNAP), which is subjected to a complex regulatory network. The activity of RNAP is controlled by a variety of molecules, including proteins, low-molecular compounds, and nucleic acids. Among these, bacterial 6S RNA is a prime example of transcriptional regulation through non-coding RNA. 6S RNA, a small RNA regulator of RNAP, is present throughout the bacterial kingdom. Studies in *Escherichia coli* revealed that 6S RNA forms a complex with RNAP, resulting in the regulation of transcription, and cells lacking 6S RNA exhibit altered survival phenotypes. 6S RNA functions by modulating protein activity or sequestration, directly impacting transcription. This article explores the discovery, structure, mechanism, and biological significance of 6S RNA, emphasizing its role as a global regulator in optimizing bacterial survival during nutrient limitation.

Keywords: Transcription, RNA polymerase (RNAP), 6S RNA

Introduction

Transcription, the synthesis of RNA from a DNA template, is a critical process in all living organisms. In prokaryotes, this process is catalyzed by RNA polymerase (RNAP), a multisubunit enzyme whose activity is finely regulated by various factors, including proteins, small molecules, and non-coding RNAs. Among the non-coding RNAs, bacterial 6S RNA has emerged as a crucial regulator of transcription. This regulatory RNA not only affects the transcription machinery but also plays a pivotal role in the cell's response to environmental changes.

Discovery and Initial Studies

6S RNA was first identified as a highly abundant and stable RNA in *Escherichia coli* over 50 years ago. However, its functional significance remained unclear until more than 30 years later, when it was discovered that 6S RNA forms a complex with RNAP, particularly with the housekeeping holoenzyme (Eσ70) form of RNAP (Kim *et al.*, 2004) [2]. This interaction suggested that 6S RNA could directly influence transcriptional activity by sequestering the RNAP holoenzyme, thus preventing it from transcribing certain genes.

The significance of 6S RNA was further highlighted by studies showing that cells lacking 6S RNA exhibited altered survival phenotypes, particularly under nutrient-limiting conditions. These findings indicated that 6S RNA plays a role in the cell's ability to adapt to environmental stresses.

Structure of 6S RNA

The structure of 6S RNA is characterized by three conserved domains: the closing stem, the central bubble, and the terminal loop.

- Closing Stem:** The closing stem is composed of several base pairs and bulged nucleotides, which are highly conserved. This domain is crucial for the stability of the 6S RNA molecule and its interaction with RNAP.
- Central Bubble:** The central bubble is a large single-stranded region in the center of the molecule. This region is essential for the function of 6S RNA, as it mimics an open promoter DNA structure, allowing it to bind RNAP.
- Terminal Loop:** The terminal loop shows lineage-specific variations in length and bulge loops. This domain may play a role in the specificity and regulation of 6S RNA function in different bacterial species.

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Mechanism of Action

6S RNA regulates transcription by interacting with the housekeeping holoenzyme form of RNAP (E σ 70). This interaction sequesters RNAP, thereby downregulating transcription during nutrient limitation. Specifically, 6S RNA binds to RNAP in a manner that mimics the DNA template, effectively blocking the transcription of certain genes. When nutrient conditions improve, 6S RNA can act as a template for the synthesis of product RNA (pRNA), which facilitates the dissociation of the RNAP-6S RNA complex and allows normal transcription to resume.

This sequestration mechanism ensures that the cell conserves resources during times of nutrient scarcity by downregulating the transcription of genes that are not immediately necessary for survival. Additionally, the synthesis of pRNA from 6S RNA under favorable conditions highlights a unique aspect of its regulatory function, enabling a rapid response to changing environmental conditions.

Biological Significance: The role of 6S RNA as a global regulator has been well-documented. Expression studies

have shown that 6S RNA directs changes in the expression of numerous genes, including many high-level regulators (Cavanagh *et al.*, 2014) [1]. In *E. coli*, 6S RNA dampens aspects of the stress response, conserving resources and optimizing survival during nutrient limitation. This role in survival is a common theme among different bacterial species, although the specifics may vary.

Ecological and Evolutionary Implications

The conservation of 6S RNA across diverse bacterial species suggests that it provides a significant adaptive advantage. By modulating the activity of RNAP and thus the transcriptional profile of the cell, 6S RNA allows bacteria to quickly adjust to fluctuating environmental conditions. This ability to rapidly switch between different transcriptional states is likely crucial for survival in habitats where nutrient availability and other conditions can change rapidly.

Furthermore, the ability of 6S RNA to act as a template for pRNA synthesis represents an elegant example of molecular mimicry and regulatory versatility. This feature may provide insights into the evolution of regulatory RNAs and their integration into complex cellular networks.

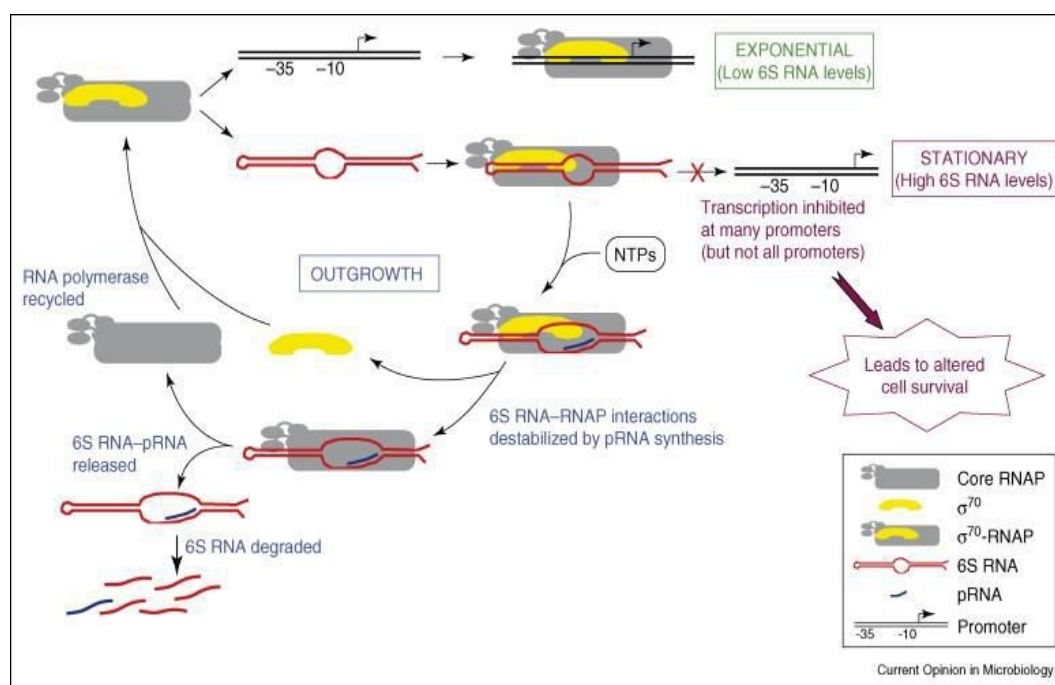


Fig 1: 6S RNA: A small RNA regulator of transcription

Conclusion

6S RNA is a key player in the regulation of transcription in bacteria. Its ability to interact with RNAP and modulate transcription in response to nutrient conditions highlights its importance in bacterial physiology. Understanding the mechanisms and functions of 6S RNA not only provides insight into bacterial transcriptional regulation but also offers potential avenues for developing new antimicrobial strategies. As research continues to uncover the intricacies of 6S RNA function and regulation, it may reveal further applications in biotechnology and medicine.

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