

Commentary

Small RNAs may be Transported through the Meridians

Yun Zhang*

College of Information Engineering, Guizhou University of Traditional Chinese Medicine, Guiyang, China

Abstract

The discovery of small RNAs has transformed life sciences by supporting the “RNA world” theory and highlighting their role in diseases like cancers and viral infections. Some small RNAs in Traditional Chinese Medicine (TCM) herbs show stability and therapeutic effects, such as tumor suppression and antiviral activity against viruses like SARS-CoV-2. TCM's meridians, believed to regulate body fluids and energy, might transport small RNAs, suggesting a mechanism for their therapeutic effects. Historically linked to antiviral properties, meridians could facilitate small RNA movement, possibly through pore proteins on cell membranes, explaining their elusive presence in anatomical studies. This hypothesis may shed light on meridians' role in disease resistance and organ connectivity, offering new insights into TCM and small RNA functions, with significant implications for medical science.

Introduction

The discovery of small RNAs stands as one of the most thrilling advancements in life sciences in recent years, providing substantial support for the “RNA world” theory. Recent studies have shown that various complex diseases, including cancers, viral infections, metabolic disorders, cardiovascular diseases, neurological disorders, and autoimmune diseases, are closely associated with small RNAs [1]. Intriguingly, some small RNAs found in herbs used in Traditional Chinese Medicine (TCM) exhibit resistance to gastrointestinal RNase digestion and remain stable under harsh conditions such as boiling, extreme pH levels, extended storage, and freeze-thaw cycles. These small RNAs may not only inhibit tumor growth by targeting crucial human gene transcripts but also impede viral replication by targeting

***Corresponding author:** Yun Zhang, College of Information Engineering, Guizhou University of Traditional Chinese Medicine, Guiyang, China, Tel No: +86 851 88233004; E-mail: zhangyun016@gzy.edu.cn

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key gene transcripts of various viruses, such as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), influenza A viruses, varicella-zoster virus, and enterovirus 71 [2-6] (Figure 1).



Figure 1: Delving deeply into the ancient culture of traditional Chinese medicine from the perspective of modern science.

For millennia, meridians have been considered the core regulatory system in TCM. According to TCM, meridians facilitate the flow of body fluids and an energy known as qi within them, resist external evil, and connect internal organs [7]. Regarding the facilitation of body fluids flow, while meridians have not been observed in anatomical studies, experiments using isotope tracing and other methods have demonstrated the presence of slow liquid flow along meridian pathways [7,8]. Recent research suggests that these flow channels might be pore proteins on cell membranes, explaining why they have not been detected in anatomical studies [9].

In terms of resisting external evil, the focus is primarily on antiviral properties. Modern medicine has not yet discovered natural antiviral molecules analogous to antibiotics that counteract bacteria. TCM, however, relies on classical prescriptions based on the differentiation of the six meridians (three yang meridians and three yin meridians) outlined by the TCM sage Zhang Zhongjing in the “Treatise

on Cold Damage.” The classical prescriptions in this treatise, especially those related to the three yang meridians, are predominantly associated with antiviral effects and have laid the foundation for subsequent generations of prescriptions. In modern classical prescription research, there are three main schools of thought: the School of Pattern Identification represented by Juquan Ye and Huang Huang, the School of Pathogenesis represented by Xishu Hu, and the School of Organs and Meridians represented by Duzhou Liu. Duzhou Liu, regarded by the Japanese TCM community as the “foremost expert in treating cold damage in China”, believed that Zhang Zhongjing was a staunch advocate of meridian studies and insisted that studying cold damage must be approached from a meridian perspective [10]. Renowned TCM master Yuansu Zhang also proposed the meridian tropism theory of herbs. According to this theory, in modern times, some TCM practitioners use meridian injection to administer antiviral medications extracted from herbs in the “Treatise on Cold Damage” into the meridians, often achieving better therapeutic effects than oral administration. Previous research has also shown that some herbal extracts from TCM antiviral herbs, such as *Bupleurum chinense* DC. and *Notopterygium incisum* Ting ex H. T. Chang, can diffuse along the meridians after being injected [11]. Some small RNAs are natural antiviral molecules that have been discovered by humans in recent years. In 1928, the phenomenon of RNA interference caused by small RNAs was also first discovered in tobacco antiviral experiments [12]. Current research indicates that after certain plants are consumed by insects, their small RNAs are absorbed into the insects’ bodies through the SID pore proteins on the insect gut cell membranes. Mammals and humans also possess homologous genes of the SID protein gene. Recent studies have confirmed that humans can absorb small RNAs from food through a homologous protein pore of the SID protein in the stomach [13]. Previous research on the effective components of medicinal plants has primarily focused on secondary metabolites, which are mostly large molecules and unlikely to enter pore proteins. Small RNAs, being among the smallest biological molecules discovered to date, are transported between plant cells through plasmodesmata and vascular bundles and can be transported through pore proteins between animal cells [14]. If these pore proteins are located near meridian pathways, it could better explain the role of meridians in resisting external evil, as well as the theories of the Six Meridians in TCM diagnosis and the guiding of herbal medicines. For instance, certain medicinal plant small RNAs absorbed by the human body and small RNAs produced by the human body might be transported through these pores to combat viruses.

Finally, regarding the connection with internal organs, the flow of substances within the meridians plays a pivotal role in the formation and maintenance of visceral organs [8]. Small RNAs can traverse long distances across organs in both animals and plants, contributing significantly to the formation and maintenance of various tissues and organs [15]. If substantiated, the transport of small RNAs through the meridians could partially elucidate the meridians’ involvement in connecting internal organs. For example, through the transmission of information via small RNAs, they could effectively coordinate the developmental processes of diverse tissues and organs.

Building upon these insights, this article posits a daring hypothesis: small RNAs may be transported through the meridians. Subsequent research into this phenomenon holds the promise of yielding profound implications for the medical field.

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