This article appeared in a journal published by Elsevier. The attached copy is furnished to the author for internal non-commercial research and education use, including for instruction at the authors institution and sharing with colleagues.

Other uses, including reproduction and distribution, or selling or licensing copies, or posting to personal, institutional or third party websites are prohibited.

In most cases authors are permitted to post their version of the article (e.g. in Word or Tex form) to their personal website or institutional repository. Authors requiring further information regarding Elsevier’s archiving and manuscript policies are encouraged to visit:

http://www.elsevier.com/copyright
Maggot microRNA: A new inhibitory pathway to bacterial infection

Shouyu Wang, Zhen Zhang

Department of Orthopedic Surgery, First Affiliated Hospital, Dalian Medical University, Dalian 116011, Liaoning Province, China

Introduction

Nowadays with the indiscriminate use or abuse of antibiotics, more and more multi-drug resistance bacterial have come across, which pose a significant problem to us [1]. Maggot, the larvae of the green-bottle fly lucilia sericata, a kind of insect, has been widely used to resist methicillin-resistant S aureus (MRSA) or Pseudomonas aeruginosa in chronic infected wounds including diabetes foot ulcers and pressure ulcers for a long time [2–5]. Our group also performed a successful debridement of an infected wound after forearm replantation using maggot therapy [6]. Additionally, the previous study in our laboratory have proved that when the homogenate product of maggot and bacterial was co-cultured in vitro, the growth of bacterial was inhibited [7]. The anti-bacterial effect of maggots can partly be attributed to its secretion of so called anti-bacterial peptide [2,3]. However its anti-bacterial mechanisms are not fully understood. MicroRNA, first discovered in Caenorhabditis elegans, are endogenous small non-coding RNAs that can bind to the 3'-untranslated regions (UTR) of the messenger RNA of the target genes [8]. The binding by imperfect base pairing leads to post-transcriptional gene silencing, so that the expression of target gene is down-regulated.

Summary

Refractory bacterial infectious diseases are clinically common and troublesome in the treatment. The traditional antibiotics could not be used to control bacterial infection with the indiscriminate use or abuse of drugs. Maggot therapy is a simple and highly successful method for healing of drug-resistant bacterial infected and necrotic wounds. It has been proved maggot can reduce the bacterial load within wounds effectively. However, the anti-bacterial mechanism of maggot is not clear. So far, most previous researches only focus on the anti-bacterial peptides from maggot, ignoring other possible anti-bacterial molecules such as nucleotides. MicroRNAs are endogenous small non-coding RNAs that can bind to the 3'-untranslated regions of the messenger RNA of the target genes. The binding by imperfect base pairing leads to post-transcriptional gene silencing, so that the expression of target gene is down-regulated. Combined understand of maggot and microRNA theory may give us a new method inhibiting bacteria growth and treating infectious diseases. It is hypothesized that finding an effective microRNA from maggot to down-regulate expression of bacteria pathogenic protein may open a new window to cure clinical infectious diseases.

The Theory of the hypotheses

As we all know, bacteria have specific properties that contribute to pathogenicity, the ability to cause disease in a host [11,12]. This kind of specific properties require a serial of proteins including (1) proteins on both the bacterial surface and fimbriae to attach themselves to the host epithelial cells; (2) extracellular enzymes and related substance such as leukocidin, hemolysin, coagulase, bacterial kinase, hyaluronidase, et al. to break host cell open, dissolve materials between cells, and form or dissolve blood clots, among other functions; (3) toxin consisting of exotoxin producing by gram-positive and endotoxin produced by gram-negative bacterial to damage directly to host cells. Many traditional anti-bacterial drugs inhibit above key proteins to either kill bacterial directly (bactericidal) or simply prevent them from growing (bacteriostatic) by affecting prokaryotic 70S ribosomes. But after the drugs were used indiscriminately, bacteria became resistant to antimicrobials in a number of different ways, for example, resistance to tetracycline is usually related to cellular changes that decrease the cell’s intake of the drug. So inhibiting these pathogenic proteins expression of bacterial in another way is certainly promising.
MicroRNAs are small non-coding RNAs (usually 21–23 nucleotides) that can target to the 3′-untranslated regions (UTR) of the messenger RNA of the genes by imperfect base pairing, thus to regulate gene expression at the post-transcriptional level. Recently, the key roles of microRNA in biological functions of cells have been discovered in mammal animals and plants, including their participation in invasion, migration and apoptosis of cancer cells [13–16]. In addition to regulating developmental processes and providing a powerful approach for creating gene-specific phenocopies of loss-of-function mutations, microRNA may also play an important biological role in protecting the genome against instability caused by the accumulation of transposons and repetitive sequences [17]. MicroRNA in animals may also represent a traditional antiviral response, which is the same as post-transcriptional gene silencing. microRNA biogenesis pathways in Drosophila. RNA 2010;16:506–15.

Evaluation of the hypotheses

Under the direction of theory of the hypotheses, we can take the following steps to create new drug treating infectious disease: (1) screen and search genes coding the key pathogenic proteins of bacteria, look for possible microRNA in the maggot; (2) compare the microRNA with the screened genes to make sure the role of MicroRNA for pathogenic proteins; (3) after finding the effective microRNA, apply polymerase chain reaction to amplify the microRNA; (4) use related effective vector to deliver the microRNA to the focus of bacterial infection, achieving a personalized treatment purposes. Of course, we may face problems and difficulties at any steps, but this novel method will indeed contribute to overcome the challenge of bacterial infection.

Conflict of interest statement

The authors declare that there are no competing interests.

Acknowledgement

The hypothesis is based on the present study in our laboratory that is supported by National Natural Science Foundation of China (Nos. 30873336 and 30901950).

References


