JIHS
Japan Institute for Health Security

Modified siRNA against severe fever with thrombocytopenia syndrome virus (SFTSV) and methods for their delivery

Researcher Information

- Researchers: Masayoshi Fukasawa and Tomoharu Mizukami
- Affiliation: Biochemistry and Cell Biology, National Institute of Infectious Disease
- Collaborator: GenAhead Bio Inc.

Research Ideas and Technology Seeds

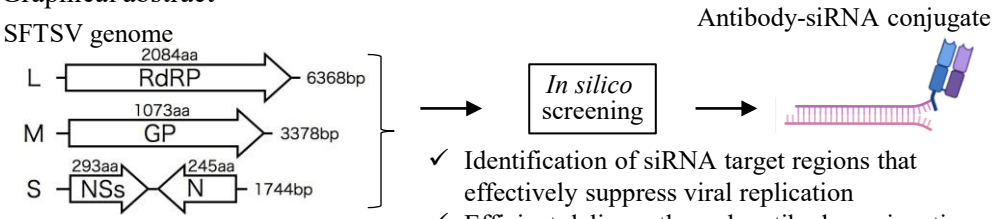
- Originality and advantages of our therapeutic candidate: Our therapeutic candidate uses siRNA incorporating chemically modified nucleic acids, a design intended to improve stability in the body, sustain its activity over time, and reduce undesirable activation of innate immune responses. In addition, the siRNA is conjugated to an antibody, allowing the antibody-siRNA conjugate to recycle between the intracellular and extracellular compartments. This design is intended to promote gradual intracellular release of siRNA, thereby enabling long-term, stable, and sustained suppression of viral replication. The antibody used in this molecule has also been shown to be suitable for efficient delivery to B cells, a major target cell type for SFTSV. Therefore, this therapeutic candidate may have potential not only as a post-infection treatment, but also as a prophylactic agent when administered in advance. The siRNA has been designed to target a conserved sequence across many SFTSV strains. Given that siRNA is a nucleic acid, its sequence can be rapidly redesigned to respond to mutations that emerge in SFTSV. Furthermore, by optimizing the linker between the siRNA and the antibody, or by changing the antibody used as the carrier, this platform may be adapted for broader applications, including more selective delivery to target organs or tissues.

Background and Unmet Needs

- Severe fever with thrombocytopenia syndrome (SFTS) is an emerging tick-borne viral infectious disease that was first reported in 2011. In Japan, SFTS cases were previously reported mainly in the western regions, but in recent years, the number of cases has also been increasing in eastern regions. SFTS is primarily transmitted through bites from virus-carrying ticks during outdoor activities. However, direct transmission from infected pets, such as dogs and cats, as well as from infected humans, has also been documented. SFTS has a high case fatality rate of approximately 30%. Although favipiravir was approved as a therapeutic agent in 2024, there remains an unmet need for treatments that can more effectively control severe disease progression. As one of Japan's priority infectious diseases, the development of new drugs is urgently needed.

Research Overview Diagram

Graphical abstract



- ✓ Identification of siRNA target regions that effectively suppress viral replication
- ✓ Efficient delivery through antibody conjugation

Future Plans

- We will evaluate prophylactic and therapeutic efficacy and safety of our antibodies through *in vivo* animal studies.
- Patent application filed for nucleic acids for the treatment of severe fever with thrombocytopenia syndrome virus (SFTSV) infection and their conjugation with targeting molecules (Japanese Patent Application No. 2024-133348).