

Therapeutic Application of siRNAs for Hepatic Viral Diseases

RNA interference-based therapeutics targeting HBV and HCV

Summary

Indication:

Anti-viral therapeutics for HBV and HCV

Development Stage:

Research

Intellectual Property:

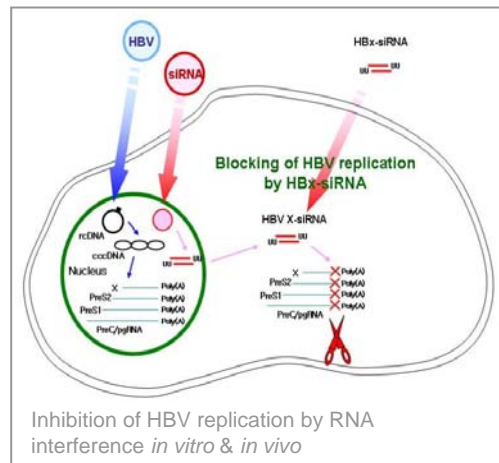
Patents applied in US and KR.

Partnering Interests:

Co-development (with a company specializing in siRNA delivery) & Licensing out

Introduction

RNA interference (RNAi) is a cytoplasmic gene-silencing mechanism induced by small interfering RNAs (siRNAs) for sequence-specific degradation of a target mRNA, and now widely accepted to be a highly promising therapeutic approach for pathogenic viruses, such as hepatitis virus and HIV.



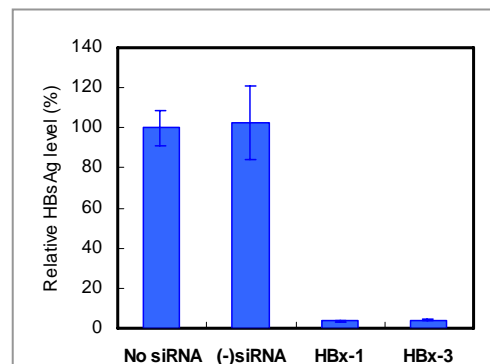
Hepatitis B Virus

HBV is a prototype for liver-specific pathogens in which the failure of the immune system to mount an effective response leads to chronic infection. Our data demonstrated that a synthetic siRNA HBx-1 showed a profound reduction of the HBsAg expression levels by over 90% with an extremely low level of the treated siRNA, which has potentially significant advantages over previous data. The results to date suggest that two siRNAs, HBx-1 and HBx-3, significantly and efficiently inhibit viral protein expression and RNA transcription, and thereby block the viral replication. Experiments with adult mice further confirmed the sequence-specific antiviral activity.

Hepatitis C Virus

To develop an antiviral drug with RNAi activity against HCV, we generated various HCV-specific siRNAs which were

transcribed from DNA-based siRNA expression vectors. Among those siRNAs, we have selected 9 candidates which significantly inhibit viral RNA replication and protein synthesis in mammalian cells stably replicating HCV full-length replicon. Upon transfection under hydrodynamic conditions, a synthetic siRNA directed against HCV core coding region harbored the efficient RNAi activity and down-regulated core protein expression below the detection limit in adult mice. The results to date assure us that siRNAs screened systematically by using a plasmid-based expression system have a great potential for treatment of chronic HCV infections.



In vivo potencies of the siRNAs against HBV X region, 0.5 nmole of siRNAs were co-delivered with 10 μ g of HBV1.3 DNA via hydrodynamic injection.

Potential Benefits

- Highly potent antiviral activity of the selected siRNA candidates *in vitro* and *in vivo*
- Great potential for use alone or in combination with conventional therapies to eliminate the hepatitis viruses from chronic viral hepatitis
- Applicable to a potential drug for the treatment of acute viral hepatitis or for liver transplantation in combination with antibodies
- Applicable to use for the treatment of virus-induced hepatocellular carcinoma in combination with chemical drugs

Interested in this technology?
Ask for more information.

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