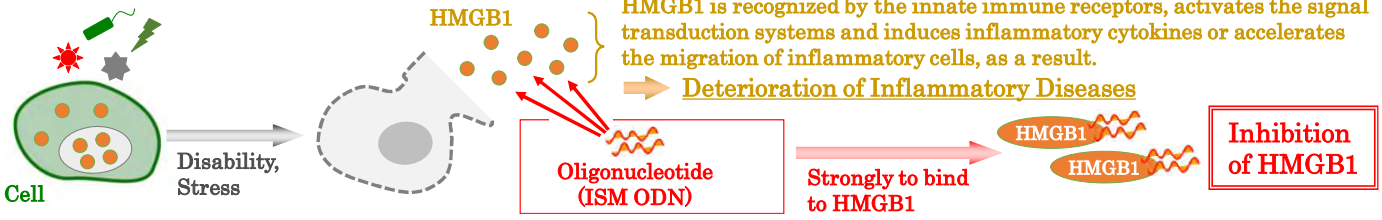
Oligonucleotide to inhibit HMGB1

~ Inhibition of Inflammatory Diseases using ISM ODN ~

Department of Intellectual Property Management

KEY INVENTION

A novel oligonucleotide (ISM ODN) to strongly bind to HMGB1 (High Mobility Group Box 1) has been developed to inhibit inflammatory diseases.



HMGB1 is recognized by the innate immune receptors, activates the signal transduction systems and induces inflammatory cytokines or accelerates the migration of inflammatory cells, as a result.

→ Deterioration of Inflammatory Diseases

SUMMARY of INVENTION

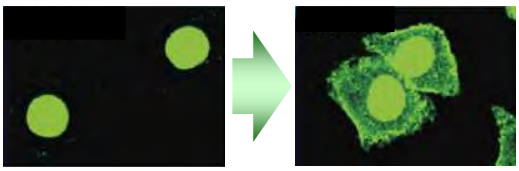
HMGB1 is a protein mainly in the nucleus and involved with stabilization of chromatin structure, transcription of genes, etc.

↓ Released outside the cell by disability or stress.

HMGB1 is recognized by the innate immune receptors, activates the signal transduction systems and induces inflammatory cytokines or accelerates the migration of inflammatory cells, as a result.

→ *Deterioration of Inflammatory Diseases*

Re-Localization of HMGB1



HMGB1 is in the nucleus under no stimulation.

HMGB1 spreads inside or outside the cell under a stress condition.

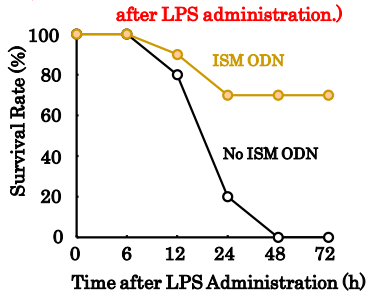
ISM ODN is a non-immunogenic oligonucleotide (phosphorothioate oligonucleotide; TCCATGAGGTTCCTGATGCT)

- strongly binds to HMGB1.
- inhibits the function of HMGB1.

→ inhibits the inflammatory diseases caused by HMGB1.

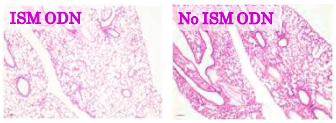
EFFECT of INVENTION

[Inhibition of Sepsis]
- LPS-induced Sepsis Model
Survival Rate of Mice
(ISM ODN was administered after LPS administration.)



The survival rate of mice after LPS administration was improved.

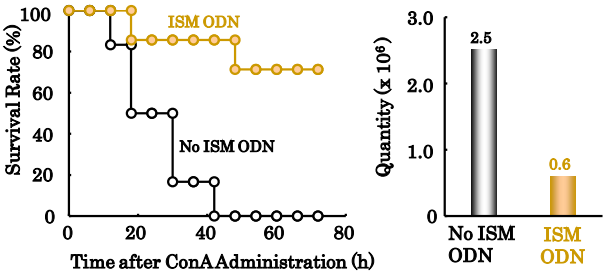
[Inhibition of Lung Disorders]
- LPS-induced ARDS Model
Lung in 3 days after LPS Administration (HE Staining)



The inhibition of the lung cell thickening and the neutrophil infiltration were observed.

The LPS-induced lung disorders was inhibited.

[Inhibition of Neutrophil Infiltration]
- ConA-induced Hepatitis Model
Survival Rate of Mice **Number of Neutrophil**
(ISM ODN was administered after ConA administration)



The survival rate of mice was improved and the number of neutrophil was decreased after ConA administration.

cf. LPS: Lipopolysuccaride (Septic shock by high dose), ARDS : Acute Respiratory Distress Syndrome, ConA: Concanavalin A (Fulminant hepatitis by high dose)

APPLICATION expected

- ◎ Development of the therapeutic methods for inflammatory or autoimmune diseases by targeting HMGB1
- ◎ Development of the methods to analyze the roles or functions of HMGB1 as inflammatory cytokines
- ◎ Elucidation of the biodefense mechanism of HMGB1 in cytoplasm, including the relevance to autophagy

Representative Inventor: Tadatsugu Taniguchi (University of Tokyo, Honorary Professor)
Co-Inventor: Hideyuki Yanai (The University of Tokyo, Associate Professor)

Licensable Patent

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Contact:
IP Management & Licensing Group,
Department of Intellectual Property Management, JST
TEL) +81-3-5214-8486 email) license@jst.go.jp
URL) www.jst.go.jp/chizai/