Non Patent Literature 7: Deer JR. and Allison DS., Biotechnol. Prog. 20: 880-889, 2004
Non Patent Literature 8: Hoeksema F. et al., Biotechnology Research International, Volume 2011, Article ID 492875, 11 pages

Summary

[0007a] In one aspect, provided herein is a polynucleotide that is a Chinese hamster-derived gene promoter, the polynucleotide comprising a nucleotide sequence that is selected from SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13 and SEQ ID NO: 14, or has 85% or higher sequence identity to each of the sequences, or a partial sequence of the nucleotide sequence.

[0007b] In another aspect, provided herein is a polynucleotide that is a mouse-derived gene promoter, the polynucleotide comprising a nucleotide sequence that is selected from SEQ ID NO: 2, SEQ ID NO: 17 and SEQ ID NO: 16, or has 85% or higher sequence identity to each of the sequences, or a partial sequence of the nucleotide sequence.

[0007c] In another aspect, provided herein is a polynucleotide comprising a nucleotide sequence having 90% or higher sequence identity to the nucleotide sequence of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 2, SEQ ID NO: 17 or SEQ ID NO:

16 according to the disclosure, or a partial sequence of the nucleotide sequence, the polynucleotide having promoter activity.

[0007d] In another aspect, provided herein is a polynucleotide comprising a nucleotide sequence having 95% or higher sequence identity to the nucleotide sequence of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 2, SEQ ID NO: 17 or SEQ ID NO: 16 according to the disclosure, or a partial sequence of the nucleotide sequence, the polynucleotide having promoter activity.

[0007e] In another aspect, provided herein is a polynucleotide that hybridizes under stringent conditions to a polynucleotide consisting of a nucleotide sequence complementary to the nucleotide sequence of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 2, SEQ ID NO: 17 or SEQ ID NO: 16 according to the disclosure, the polynucleotide having promoter activity.

[0007f] In another aspect, provided herein is a foreign gene expression unit comprising the polynucleotide according to the disclosure and a foreign gene.

[0007g] In another aspect, provided herein is a foreign gene expression vector comprising the foreign gene expression unit according to the disclosure.

[0007h] In another aspect, provided herein is a foreign gene expression vector comprising the foreign gene

expression unit according to the disclosure, and one or more polynucleotides selected from the following (a) to (e):

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO: 5, or a partial sequence thereof;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO: 6, or a partial sequence thereof;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO: 7, or a partial sequence thereof;

(d) a polynucleotide comprising a nucleotide sequence having 80% or higher sequence identity to the nucleotide sequence of SEQ ID NO: 5, SEQ ID NO: 6 or SEQ ID NO: 7, or a partial sequence of the nucleotide sequence, the polynucleotide having foreign gene expression-enhancing activity; and

(e) a polynucleotide comprising a nucleotide sequence having 85% or higher sequence identity to the nucleotide sequence of SEQ ID NO: 5, SEQ ID NO: 6 or SEQ ID NO: 7, or a partial sequence of the nucleotide sequence, the polynucleotide having foreign gene expression-enhancing activity.

[0007i] In another aspect, provided herein is a transfected cell into which the foreign gene expression vector according to the disclosure has been introduced.

[0007j] In another aspect, provided herein is a method for producing a foreign gene-derived protein, comprising culturing the transfected cell according to the

disclosure, and obtaining the foreign gene-derived protein from the culture.

[0007k] In another aspect, provided herein is a use of the polynucleotide according to the disclosure for expressing a foreign gene in a transfected cell *ex vivo*.

[0007l] In another aspect, provided herein is a use of the foreign gene expression vector according to the disclosure for expressing a foreign gene in a transfected cell *ex vivo*.

Technical Problem

[0008]

An object of the present invention is to provide a promoter having high foreign gene expression-enhancing activity in host cells such as cultured mammalian cells, and to provide an approach to enhancing the amount of a foreign protein, which serves as a protein-based pharmaceutical product, produced using the promoter.

Solution to Problem

[0009]

For solving the above-described problems, the present invention provides the following [1] to [34].

[1] A polynucleotide that is a Chinese hamster-derived gene promoter, the polynucleotide comprising a nucleotide sequence that is selected from SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13 and SEQ ID NO: 14, or has 85% or higher

sequence identity to each of the sequences, or a partial sequence of the nucleotide sequence.

Claims

[Claim 1]

A polynucleotide that is a Chinese hamster-derived gene promoter, the polynucleotide comprising a nucleotide sequence that is selected from SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13 and SEQ ID NO: 14, or has 85% or higher sequence identity to each of the sequences, or a partial sequence of the nucleotide sequence.

[Claim 2]

The polynucleotide according to claim 1, which comprises a nucleotide sequence that is selected from SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 10, SEQ ID NO: 11 and SEQ ID NO: 12, or has 85% or higher sequence identity to each of the sequences, or a partial sequence of the nucleotide sequence.

[Claim 3]

The polynucleotide according to claim 1, which consists of a nucleotide sequence having 99% or higher sequence identity to the nucleotide sequence of SEQ ID NO: 1.

[Claim 4]

The polynucleotide according to claim 1, which consists of a nucleotide sequence having 99% or higher sequence identity to the nucleotide sequence of SEQ ID NO: 3.

[Claim 5]

The polynucleotide according to claim 1, which consists of a nucleotide sequence having 99% or higher sequence identity to the nucleotide sequence of SEQ ID NO: 4.

[Claim 6]

The polynucleotide according to claim 1, which consists of a nucleotide sequence having 99% or higher sequence identity to the nucleotide sequence of SEQ ID NO: 10.

[Claim 7]

The polynucleotide according to claim 1, which consists of a nucleotide sequence having 99% or higher sequence identity to the nucleotide sequence of SEQ ID NO: 11.

[Claim 8]

The polynucleotide according to claim 1, which consists of a nucleotide sequence having 99% or higher sequence identity to the nucleotide sequence of SEQ ID NO: 12.

[Claim 9]

The polynucleotide according to claim 1, which consists of a nucleotide sequence having 99% or higher sequence identity to the nucleotide sequence of SEQ ID NO: 13.

[Claim 10]

The polynucleotide according to claim 1, which consists of a nucleotide sequence having 99% or higher

sequence identity to the nucleotide sequence of SEQ ID NO: 14.

[Claim 11]

A polynucleotide that is a mouse-derived gene promoter, the polynucleotide comprising a nucleotide sequence that is selected from SEQ ID NO: 2, SEQ ID NO: 17 and SEQ ID NO: 16, or has 85% or higher sequence identity to each of the sequences, or a partial sequence of the nucleotide sequence.

[Claim 12]

The polynucleotide according to claim 11, which consists of a nucleotide sequence having 99% or higher sequence identity to the nucleotide sequence of SEQ ID NO: 2.

[Claim 13]

The polynucleotide according to claim 11, which consists of a nucleotide sequence having 99% or higher sequence identity to the nucleotide sequence of SEQ ID NO: 17.

[Claim 14]

The polynucleotide according to claim 11, which consists of a nucleotide sequence having 99% or higher sequence identity to the nucleotide sequence of SEQ ID NO: 16.

[Claim 15]

A polynucleotide comprising a nucleotide sequence having 90% or higher sequence identity to the nucleotide sequence of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ

ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 2, SEQ ID NO: 17 or SEQ ID NO: 16 according to claim 1 or 11, or a partial sequence of the nucleotide sequence, the polynucleotide having promoter activity.

[Claim 16]

A polynucleotide comprising a nucleotide sequence having 95% or higher sequence identity to the nucleotide sequence of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 2, SEQ ID NO: 17 or SEQ ID NO: 16 according to claim 1 or 11, or a partial sequence of the nucleotide sequence, the polynucleotide having promoter activity.

[Claim 17]

A polynucleotide that hybridizes under stringent conditions to a polynucleotide consisting of a nucleotide sequence complementary to the nucleotide sequence of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 2, SEQ ID NO: 17 or SEQ ID NO: 16 according to claim 1 or 11, the polynucleotide having promoter activity.

[Claim 18]

The polynucleotide according to claim 17, which is a Chinese hamster-derived gene promoter and comprises a nucleotide sequence of SEQ ID NO: 18, or a nucleotide

sequence having 85% or higher sequence identity to the sequence.

[Claim 19]

A foreign gene expression unit comprising the polynucleotide according to any one of claims 1 to 18 and a foreign gene.

[Claim 20]

The foreign gene expression unit according to claim 19, wherein the foreign gene is a gene encoding a protein.

[Claim 21]

The foreign gene expression unit according to claim 20, wherein the foreign gene is a gene encoding a heteromultimeric protein.

[Claim 22]

The foreign gene expression unit according to claim 21, wherein the foreign gene is a gene encoding an antibody or an antigen-binding fragment thereof.

[Claim 23]

A foreign gene expression vector comprising the foreign gene expression unit according to any one of claims 19 to 22.

[Claim 24]

A foreign gene expression vector comprising the foreign gene expression unit according to any one of claims 19 to 22, and one or more polynucleotides selected from the following (a) to (e):

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO: 5, or a partial sequence thereof;
(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO: 6, or a partial sequence thereof;
(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO: 7, or a partial sequence thereof;
(d) a polynucleotide comprising a nucleotide sequence having 80% or higher sequence identity to the nucleotide sequence of SEQ ID NO: 5, SEQ ID NO: 6 or SEQ ID NO: 7, or a partial sequence of the nucleotide sequence, the polynucleotide having foreign gene expression-enhancing activity; and
(e) a polynucleotide comprising a nucleotide sequence having 85% or higher sequence identity to the nucleotide sequence of SEQ ID NO: 5, SEQ ID NO: 6 or SEQ ID NO: 7, or a partial sequence of the nucleotide sequence, the polynucleotide having foreign gene expression-enhancing activity.

[Claim 25]

A transfected cell into which the foreign gene expression vector according to claim 23 or 24 has been introduced.

[Claim 26]

The transfected cell according to claim 25, wherein the cell is a cultured cell derived from a mammal.

[Claim 27]

The transfected cell according to claim 26, wherein the cell is a COS-1 cell, a 293 cell, or a CHO cell.

[Claim 28]

A method for producing a foreign gene-derived protein, comprising culturing the transfected cell according to any one of claims 25 to 27, and obtaining the foreign gene-derived protein from the culture.

[Claim 29]

The production method according to claim 28, wherein the foreign gene-derived protein is a monomeric protein or a multimeric protein.

[Claim 30]

The production method according to claim 29, wherein the multimeric protein is a heteromultimeric protein.

[Claim 31]

The production method according to claim 30, wherein the heteromultimeric protein is an antibody protein.

[Claim 32]

Use of the polynucleotide according to any one of claims 1 to 18 for expressing a foreign gene in a transfected cell *ex vivo*.

[Claim 33]

Use of the foreign gene expression vector according to claim 23 or 24 for expressing a foreign gene in a transfected cell *ex vivo*.