PATENT ASSIGNMENT COVER SHEET

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SUBMISSION TYPE:	NEW ASSIGNMENT
NATURE OF CONVEYANCE:	ASSIGNMENT

CONVEYING PARTY DATA

Name	Execution Date
CARGILL FRANCE	10/25/2012

RECEIVING PARTY DATA

Name:	DSM IP ASSETS B.V.
Street Address:	HET OVERLOON 1
City:	TE HEERLEN
State/Country:	NETHERLANDS
Postal Code:	6411

PROPERTY NUMBERS Total: 2

Property Type	Number
Patent Number:	5712150
Patent Number:	5658770

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NAME OF SUBMITTER:	RACHEL A BERGENDAHL
Signature:	/Rachel A. Bergendahl/
Date:	02/21/2014

Total Attachments: 26

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DEED OF ASSIGNMENT

THIS DEED OF ASSIGNMENT is made the 6th day of December 2012 **BETWEEN**

Cargill France SAS, a French *société par actions simplifiée* with a share capital of € 103,422,065, having its registered office at 18/20 rue des Gaudines 78100 Saint Germain en Laye, France, registered with the Trade and Companies Register under number 572 099 695 RCS Versailles, represented by Mr. Stefan HORN (the **Assignor**); and

DSM IP ASSETS B.V. whose registered office is at Het Overloon 1, 6411 TE, Heerlen, the Netherlands (the **Assignee**).

WHEREAS the Assignor is the proprietor of the trade mark registrations detailed in the Schedule to this Deed (the **Trade Marks**).

WHEREAS pursuant to the Master Sale of Business Agreement relating to the sale of the Cargill cultures, culture media and enzymes business between CARGILL, INCORPORATED, CARGILL FRANCE SAS and DSM FOOD SPECIALTIES CULTURES USA, INC., DSM FOOD SPECIALTIES CULTURES SAS, DSM IP ASSETS B.V., DSM FOOD SPECIALTIES B.V. dated October 25th, 2012 (the **MSPA**) the Assignor has agreed to assign, and the Assignee has agreed to accept the assignment of, the Trade Marks on the terms of this Deed.

NOW THEREFORE, the parties hereby agree as follows:

1. ASSIGNMENT OF TRADE MARKS

The Assignor hereby assigns to the Assignee and the Assignee hereby accepts the assignment of all rights, title and interest in and to the Trade Marks and the goodwill attached thereto.

2. COUNTERPARTS

This Deed may be executed in any number of counterparts, which shall together constitute one Deed.

3. LAW & JURISDICTION

This Deed shall be governed by and construed in accordance with English law and any disputes arising out of this Deed shall be settled by arbitration in accordance with section 42 of the MSBA.

IN WITNESS WHEREOF the parties have executed this assignment the day and year first above written.

EXECUTED as a DEED by Assignor	**EXECUTED as a DEED by Assignee**
Acting by: Stefan HORN Position: Senior Lawyer Signature:	Acting by: ☐ Position: ☐ Signature:
Name of witness: ☐ Address of witness: ☐ Occupation of witness: ☐ Signature of witness:	Name of witness: ☐ Address of witness: ☐ Occupation of witness: ☐ Signature of witness:

SCHEDULE

TITLE	APPL.	REG.	COUNTRY	OWNER	STATUS
bactimedia	88240	88240	Tunisia	Degussa Ferments D'Aromatisation France S.A.S.	Registered
bactimedia	272388	128417	Ireland	Cargill France S.A.S.	Registered
bactimedia	272488	128418	Ireland	Cargill France S.A.S.	Registered
bactimedia	272588	128419	Ireland	Cargill France S.A.S.	Registered
bactimedia	*527829*	***527829***	***International Bureau (WIPO)***	*Cargill France S.A.S.*	*Registered*
bactimedia	*527829*	***527829***	*Algeria*	*Cargill France S.A.S.*	*Registered*
bactimedia	*527829*	***527829***	*Austria*	*Cargill France S.A.S.*	*Registered*
bactimedia	*527829*	***527829***	*Benelux*	*Cargill France S.A.S.*	*Registered*
bactimedia	*527829*	***527829***	*Hungary*	*Cargill France S.A.S.*	*Registered*
bactimedia	*527829*	***527829***	*Italy*	*Cargill France S.A.S.*	*Registered*
bactimedia	*527829*	***527829***	*Liechtenstein*	*Cargill France S.A.S.*	*Registered*
bactimedia	*527829*	***527829***	*Monaco*	*Cargill France S.A.S.*	*Registered*
bactimedia	*527829*	***527829***	*Morocco*	*Cargill France S.A.S.*	*Registered*
bactimedia	*527829*	***527829***	*Portugal*	*Cargill France S.A.S.*	*Registered*
bactimedia	*527829*	***527829***	*Russian Federation*	*Cargill France S.A.S.*	*Registered*
bactimedia	*527829*	***527829***	*Switzerland*	*Cargill France S.A.S.*	*Registered*
bactimedia	*527829*	***527829***	*Germany*	*Cargill France S.A.S.*	*Registered*
bactimedia	*527829*	***527829***	*Spain*	*Cargill France S.A.S.*	*Registered*
bactimedia	897746	1449089	France	Cargill France S.A.S.	Registered
bactimedia	1350126	1350126B	United Kingdom	Cargill France S.A.S.	Registered
bactimedia	1350127	1350127B	United Kingdom	Cargill France S.A.S.	Registered
bactimedia	1350128	1350128A	United Kingdom	Cargill France S.A.S.	Registered
bactimedia	1520683		Canada	Cargill France S.A.S.	Pending
bactistart	5471992	125174	Finland	Degussa Ferments D'Aromatisation France S.A.S.	Registered
bactistart	920991	257357	Sweden	Degussa Ferments D'Aromatisation France S.A.S.	Registered
bactistart	920137	920137	Tunisia	Cargill France S.A.S.	Registered
bactistart	7771992	30041993	Denmark	Degussa Ferments D'Aromatisation France S.A.S.	Registered
bactisystem	*596158*	***596158***	***International Bureau (WIPO)***	*Cargill France S.A.S.*	*Registered*
bactisystem	*596158*	***596158***	*Algeria*	*Cargill France S.A.S.*	*Registered*
bactisystem	*596158*	***596158***	*Austria*	*Cargill France S.A.S.*	*Registered*
bactisystem	*596158*	***596158***	*Benelux*	*Cargill France S.A.S.*	*Registered*
bactisystem	*596158*	***596158***	*Italy*	*Cargill France S.A.S.*	*Registered*
bactisystem	*596158*	***596158***	*Morocco*	*Cargill France S.A.S.*	*Registered*

bactisystem	*596158*	***596158***	*Portugal*	*Cargill France S.A.S.*	*Registered*
bactisystem	*596158*	***596158***	*Switzerland*	*Cargill France S.A.S.*	*Registered*
bactisystem	*596158*	***596158***	*Germany*	*Cargill France S.A.S.*	*Registered*
bactisystem	*596158*	***596158***	*Spain*	*Cargill France S.A.S.*	*Registered*
bactisystem	930040	930040	Tunisia	Cargill France S.A.S.	Registered
bactisystem	20293	20581993	Denmark	Cargill France S.A.S.	Registered
bactitest	54982	125175	Finland	Degussa Ferments D'Aromatisation France S.A.S.	Registered
bactitest	920481	167973	Norway	Degussa Ferments D'Aromatisation France S.A.S.	Registered
bactitest	920992	249800	Sweden	Degussa Ferments D'Aromatisation France S.A.S.	Registered
bactitest	9201366	920136	Tunisia	Cargill France S.A.S.	Registered
ecostart	3036542	3036542	France	Cargill France S.A.S.	Registered

DEED OF ASSIGNMENT

THIS DEED OF ASSIGNMENT is made the 6th day of December 2012 **BETWEEN**

CARGILL, INCORPORATED, a private limited liability company incorporated under the laws of Delaware, United States, with its offices at 15407 McGinty Road West, Wayzata, Minnesota 55391, United States (the **Assignor**); and

DSM IP ASSETS B.V. whose registered office is at Het Overloon 1, 6411 TE, Heerlen, the Netherlands (the **Assignee**).

WHEREAS the Assignor is proprietor of or applicant for the patents and patent applications detailed in the Schedule to this Deed (the **Patents**).

WHEREAS pursuant to the Master Sale of Business Agreement relating to the sale of the Cargill cultures, culture media and enzymes business between CARGILL, INCORPORATED, CARGILL FRANCE SAS and DSM FOOD SPECIALTIES CULTURES USA, INC., DSM FOOD SPECIALTIES CULTURES SAS, DSM IP ASSETS B.V., DSM FOOD SPECIALTIES B.V. dated 25 October 2012 (the **MSPA**) the Assignor has agreed to assign, and the Assignee has agreed to accept the assignment of, the Patents on the terms of this Deed.

NOW THEREFORE, the parties hereby agree as follows:

1. ASSIGNMENT OF PATENTS

Against consideration of €1 (one Euro) which has been paid by Assignee and received by Assignor, the Assignor hereby assigns to the Assignee and the Assignee hereby accepts the assignment of the legal title in and to the Patents.

2. COUNTERPARTS

This Deed may be executed in any number of counterparts, which shall together constitute one Deed.

3. LAW & JURISDICTION

This Deed shall be governed by and construed in accordance with English law and any disputes arising out of this Deed shall be settled by arbitration in accordance with section 42 of the MSBA.

IN WITNESS WHEREOF the parties have executed this assignment the day and year first above written.

EXECUTED as a DEED by Assignor	**EXECUTED as a DEED by Assignee**
Acting by: Stefan Horn Position: Senior Lawyer Signature: Name of witness: Address of witness: Occupation of witness: Signature of witness:	Acting by: Position: Attorney in Law Signature: Name of witness: Address of witness: Occupation of witness: Signature of witness:

SCHEDULE

SCHEDULE

PATENTS

Title	Matter type	Country	Status	Patent/ Application number
STRAINS OF SPONTANEOUS MUTANTS OF BREVIBACTERIUM LINENS	Utility	France	Issued	2,731,012 9502139
NUCLEIC ACID SEQUENCE AND PLASMIDS COMPRISING AT LEAST ONE PHAGE RESISTANCE MECHANISM, BACTERIA CONTAINING THEM AND THEIR USE	Utility	U.S.A.	Issued	5,712,150 08/689,916
NUCLEIC ACID SEQUENCE AND PLASMIDS COMPRISING AT LEAST ONE PHAGE RESISTANCE MECHANISM, BACTERIA IN WHICH THEY ARE PRESENT, AND THEIR USE	Utility	U.S.A.	Issued	5,658,770 08/286,325

US005658770A

United States Patent [19]

Prevots et al.

[11] Patent Number: 5,658,770

[45] Date of Patent: Aug. 19, 1997

[54] **NUCLEIC ACID SEQUENCE AND PLASMIDS COMPRISING AT LEAST ONE PHAGE RESISTANCE MECHANISM, BACTERIA IN WHICH THEY ARE PRESENT, AND THEIR USE**

[75] Inventors: **Fabien Prevots**; **Elisabeth Remy**, both of Toulouse; **Paul Ritzenthaler**, Castanet, all of France

[73] Assignees: **Sanofi**, Paris; **Elf Aquitaine**, Courbevoie, both of France

[21] Appl. No.: **286,325**

[22] Filed: **Aug. 4, 1994**

[30] **Foreign Application Priority Data**

Aug. 9, 1993 [FR] France 93 09777

[51] **Int. Cl.**[6] **C07H 21/04**; C12P 21/00; C12N 15/00

[52] **U.S. Cl.** **435/172.2**; 435/69.1; 435/172.3; 435/320.1; 536/23.7

[58] **Field of Search** 435/172.3, 69.1, 435/172.1; 536/23.7

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,883,756 11/1989 Klaenhammer et al. 435/252.3

FOREIGN PATENT DOCUMENTS

A-0 208 468	1/1987	European Pat. Off. .
0208468A2	1/1987	European Pat. Off. .
A-0 246 909	11/1987	European Pat. Off. .
0355036	2/1990	European Pat. Off. .
0452224A1	10/1991	European Pat. Off. .
WOA9205260	4/1992	WIPO .

OTHER PUBLICATIONS

Van Belkum et al., Applied & Environmental Microbiology, 55(5): 1187–1191 (May 1989).

Sing et al., Applied & Environmental Microbiology, 51(6): 1264–1271 (Jun. 1986).

Sanders et al., *Applied and Environmental Microbiology*, vol. 46, No. 5, 1983, 1125–1133.

Steenson et al., *Applied and Environmental Microbiology*, vol. 50, No. 4, Oct. 1985, 851–858.

Jarvis et al., *Applied and Environmental Microbiology*, vol. 55, No. 6, Jun. 1989, 1537–1543.

Hill et al., *Applied and Environmental Microbiology*, vol. 55, No. 7, Jul. 1989, 1684–1689.

Hill et al., *Applied and Environmental Microbiology*, vol. 56, No. 7, Jul. 1990, 2255–2258.

Prevots et al., *Applied and Environmental Microbiology*, vol. 56, No. 7, Jul. 1990, 2180–2185.

Klaenhammer, *Journal of Dairy Science*, vol. 72, No. 12, 1989, 3429–3443.

Vlegels et al., *Netherlands Milk and Dairy Journal*, vol. 43, 1989, 245–259.

Jarvis, *Applied and Environmental Microbiology*, Mar. 1988, 777–783.

Lerayer et al., *Revista De Microbiologia*, vol. 20, No. 2, Apr.–Jun. 1989, 197–209.

Sanders et al., *Applied and Environmental Microbiology*, vol. 47, No. 5, May 1984, 979–985.

van Belkum et al., *Applied and Environmental Microbiology*, vol. 55, No. 5, May 1989, 1187–1191.

Sanders, *Biochemie*, vol. 70, 1988, 411–421.

Coffey et al., *Netherlands Milk and Dairy Journal*, vol. 43, 1989, 229–244.

Froseth et al., *Journal of Dairy Science*, vol. 71, 1988, 275–284.

Laible et al., *Journal of Dairy Science*, vol. 70, 1987, 2211–2219.

Steele et al., *Plasmid*, vol. 22, No. 1, 1989, 32–43.

Josephson et al., *Plasmid*, vol. 23, No. 1, Jan. 1990, 71–75.

Klaenhammer et al., *Journal of General Microbiology*, vol. 131, Jun. 1985, 1531–1541.

Gautier et al., *Applied and Environmental Microbiology*, vol. 53, No. 5, May 1987, 923–927.

Primary Examiner—James Ketter
Assistant Examiner—John S. Brusca
Attorney, Agent, or Firm—Foley & Lardner

[57] **ABSTRACT**

The invention relates to a DNA sequence of about 1.9 kb comprising at least one phage resistance mechanism, said sequence being obtained from the HindIII—HindIII DNA sequence of 3.3 kb contained in the strain *Lactococcus lactis* ssp *lactis*, deposited in the CNCM under no. I-945, by the PCR method.

5 Claims, 2 Drawing Sheets

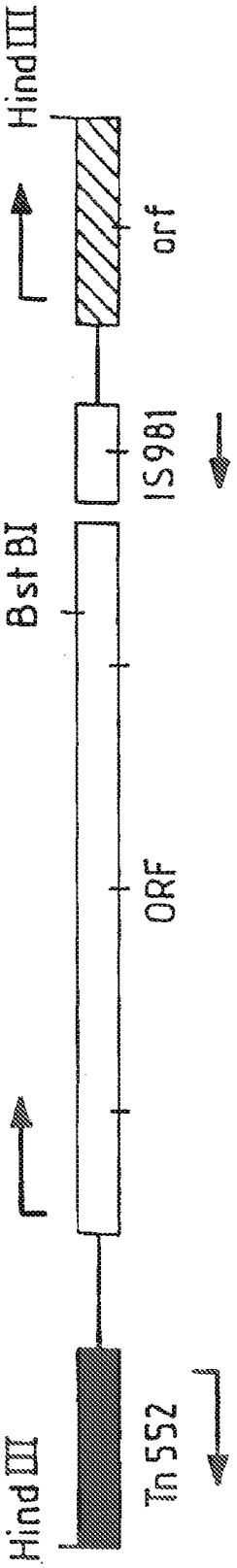

FIG. 1

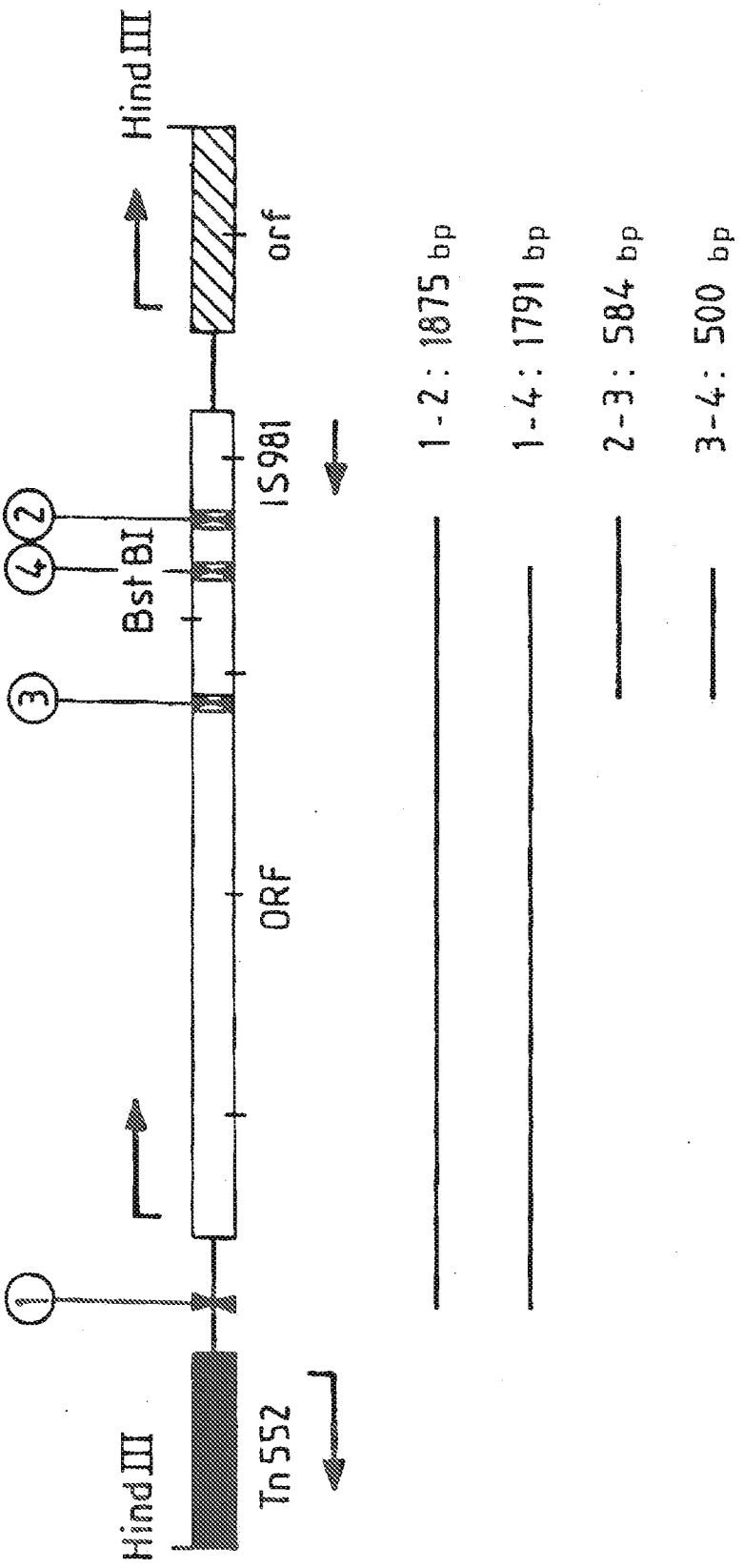
Hind III
orf
IS981
1-2: 1875 bp
1-4: 1791 bp
2-3: 584 bp
3-4: 500 bp
2
4
Bst BI
3
ORF
1
Hind III
Tn552

FIG. 2

NUCLEIC ACID SEQUENCE AND PLASMIDS COMPRISING AT LEAST ONE PHAGE RESISTANCE MECHANISM, BACTERIA IN WHICH THEY ARE PRESENT, AND THEIR USE

The present invention relates to a novel nucleic acid sequence and plasmids capable of hybridizing therewith which carry at least one phage resistance mechanism, to the lactic acid bacteria in which this sequence or these plasmids are present, in particular the lactococci belonging to the species *Lactococcus lactis*, to the use of certain strains of these lactococci for the transfer, especially by conjugation, of a phage resistance mechanism to strains of industrial interest, in particular in the dairy industry, and to the use of certain strains of *Lactococcus lactis* for the preparation of these plasmids.

Lactic acid bacteria are involved in the production and storage of a large number of food products such as cheese, butter, yogurt, sausage or pickled cabbage. Dairy products are of particular importance among these foods. The industrial processing of milk is carried out in ever larger fermentation vats, in which the appearance of phages of lactic acid bacteria can have serious or even catastrophic consequences, namely a variation in the characteristics, especially organoleptic characteristics, of the final product, the loss of the product present in the vat, and the need to decontaminate the latter as well as the surrounding installations. The dairy industry therefore has a pressing need for new means and new methods by which lactic acid bacteria can be rendered more resistant to phages.

The phages of lactic acid bacteria belong to three major homology groups, (I), (II) and (III), defined by DNA/DNA hybridization studies according to RELANO P. et al., (1987), J. Gen. Microbiol. 133, 3053–3063. Groups (I) and (III) comprise only virulent phages. Group (II) comprises virulent phages and temperate phages. The homologies are strong within one and the same group and very weak between groups. Group (I) phages have an oblong nucleocapsid, whereas group (I) and (III) phages have an isometric nucleocapsid.

Several phage resistance mechanisms are known to exist, the three main ones being:

- the inhibition of phage adsorption; in this mechanism, the adsorption of the phage by the bacterium is inhibited or delayed.
- the restriction/modification system; this system involves a restriction enzyme which degrades the phage DNA as soon as it enters the bacterium.
- abortive infection; according to this third mechanism, the phages are adsorbed normally but do not multiply.

These mechanisms are described in detail by SANDERS M. in Biochimie 70, (1988), 411–421.

Numerous studies have already been carried out with the aim of developing phage-resistant lactic acid bacteria.

In this connection, reference may be made in particular to the following articles:

- VLEGELS et al., Neth. Milk and Dairy J. 43, (1989), 245–259;
- SANDERS and KLAENHAMMER, Applied and Environ. Microbiol. (1983), vol. 46, 1125–1133, relating to plasmids which inhibit phage adsorption;
- Audrey W. JARVIS, Applied and Environ. Microbiol. March 1988, p.777–783;
- EP-A3-0 208 468;
- COFFEY et al., Neth. Milk and Dairy J. 43, (1989), 229–244;

- KLAENHAMMER and SANOZKY, Journal of General Microbiology (1985), 131, 1531–1541, describing plasmids which confer phage resistance by the abortive infection mechanism;
- JOSEPHSEN and KLAENHAMMER, Plasmid 23, 71–75, (1990);
- U.S. Pat. No. 4,883,756;
- GAUTIER and CHOPIN, Applied and Environ. Microbiology (1987), 53, p. 923–927,

the two latter articles especially describing plasmids which confer phage resistance by the restriction/modification mechanism.

The Applicants have also worked in this field and described in EP-A1-452 224 as well as in U.S. patent application Ser. No.08/144,611 filed on Nov. 1st, 1993 as a continuation of U.S. Pat. No. 07/778,097 of Dec. 13, 1991, both incorporated herein by way of reference, a DNA molecule comprising at least one phage resistance mechanism, said molecule containing a functional part of the HindIII—HindIII fragment of about 3.3 kb of plasmid pPF144-1 present in the strain of *Escherichia coli* deposited in the National Collection of Cultures of Microorganisms (CNCM) of the Pasteur Institute, Paris under no. I-1070 on 9th Apr. 1991.

This HindIII—HindIII fragment of about 3.3 kb was isolated from plasmid pPF144 contained in the strain *Lactococcus lactis* ssp *lactis*, deposited in the CNCM under no. I-945, which is a transconjugant derived from the crossing of the donor strain *Lactococcus lactis* ssp *lactis* S91, deposited in the CNCM under no. I-940 on 12th Apr. 1990, with the recipient strain *Lactococcus lactis* ssp *lactis* S45, derived from the strain *Lactococcus lactis* ssp *lactis* C2-L. L. McKay et al., 1977, J. Bacteriol. 257–265. This fragment carries one or more phage resistance mechanisms.

Continuing their work, the Applicants isolated, from this HindIII—HindIII DNA sequence of 3.3 kb, a DNA sequence of 1.9 kb which on its own confers phage resistance.

The present invention therefore relates to a novel nucleic acid sequence comprising at least one phage resistance mechanism, said sequence having about 1.9 kb and consisting of:

a) the DNA sequence having the nucleic acid series of SEQ ID no. 1;

b) the DNA sequences hybridizing with the above sequence or a fragment thereof; and

c) the corresponding mRNA and cDNA sequences.

The sequence [SEQ ID no. 2] is the amino acid sequence deduced from sequence SEQ ID no. 1.

The DNA sequence [SEQ ID no. 1] can be obtained from the HindIII—HindIII DNA sequence of 3.3 kb contained in the strain *Lactococcus lactis* ssp *lactis*, deposited in the CNCM under no. I-945, by the PCR method using the following two oligonucleotides:

Oligonucleotide no. 1 [SEQ ID no. 3]:
5' GGGAATTCGAACATAGAATAGATTACGG 3'
EcoRI
Oligonucleotide no. 2 [SEQ ID no. 4]:
5' GGGGATCCAAACTGTTCTGTTGCGAGTG 3'
BamHI

The invention further relates to the DNA sequences which have a high degree of homology with the above DNA sequence [SEQ ID no. 1]. Here a high degree of homology means a homology (ratio of the identical nucleotides to the total number of nucleotides) of at least 70%, preferably at

least 80%, of the nucleotide sequences when they are aligned according to maximum homology, using the optimal sequence alignment method of Needleman and Wunsch, 1970, J. Mol. Biol. 48, 443–453. This method is used especially in the UWGCG software of the University of Wisconsin: Devereux et al., 1984, Nucl. Ac. Res. 12, 8711–8721-option GAP.

The present invention particularly relates to the DNA sequences which hybridize with the DNA sequence [SEQ ID no. 1] or a fragment thereof. In the present specification the term "hybridization" designated the conventional hybridization conditions and more particularly the stringent hybridization conditions.

The invention further relates to the plasmids transformed with one of the nucleic acid sequences according to the invention. These plasmids can be for example plasmid pPF144-12 into which the DNA sequence according to the invention has been cloned by the usual techniques well known to those skilled in the art.

The invention further relates to the phage-resistant lactic acid bacteria, preferably belonging to the species *Lactococcus lactis*, which contain at least one nucleic acid sequence or one plasmid as defined above.

This nucleic acid sequence or this plasmid may have been introduced into the lactic acid bacteria by conjugation, transformation, protoplast fusion or another gene transfer method.

Examples of the lactic acid bacteria which can advantageously be transformed with the nucleic acid sequence according to the invention or a plasmid containing said sequence are the strains *Lactococcus lactis* ssp *cremoris*, *Lactococcus lactis* ssp *lactis* and *Lactococcus lactis* ssp *lactis var. diacetylous*.

These strains, transformed in this way, can be used for the transfer, by conjugation, transformation, transduction, protoplast fusion or another gene transfer method, of a phage resistance mechanism to a strain of industrial interest. This mechanism can be carried by a plasmid or by another part of the genome of the bacterium. If said mechanism is carried by a plasmid, it is advantageously transferred by conjugation.

The invention further relates to the resulting phage-resistant strains of industrial interest.

The invention will be understood more clearly with the aid of the following Examples, which include experimental results and a discussion thereof. Some of these Examples relate to experiments performed in order to carry out the invention; other Examples of how to carry out the invention are of course given purely by way of illustration.

A large part of all the techniques described in these Examples, which are well known to those skilled in the art, is described in detail in the work by Sambrook, Fritsch and Maniatis: "Molecular cloning; a Laboratory Manual" published in 1989 by Cold Spring Harbor Press in New York (2nd edition).

The following description will be understood more clearly with the aid of FIGS. 1 and 2 below, in which:

FIG. 1 shows the restriction map of the 3.3 kb fragment of pPF144-1. Tn552 is a region having a high degree of Homology with part of transposon Tn552. The term "ORF" signifies an open reading frame of 1620 bp. IS981 is a region having a high degree of homology with part of insertion sequence IS981. The term "orf" signifies the beginning of an open reading frame.

FIG. 2 shows the amplification by the PCR method of internal fragments of the 3.3 kb fragment of pPF144-1.

Fragment 1-2 confers phage resistance.

Fragments 1-4, 2-3 and 3-4 do not confer phage resistance.

EXAMPLE 1

Sequence of the HindIII—HindIII fragment of 3.3 kb

The strain *Lactococcus lactis* S45-91-1, deposited in the CNCM under no. I-945 on 12th Apr. 1990, contains a plasmid with a size of 144 kb, called pPF144, which confers phage resistance. This strain is totally resistant to phage Ø59 (group III). On the other hand, it has a partial resistance to phage Ø53 of group I, which develops but forms abnormally small lysis plates of the size of a pinhead. The HindIII—HindIII restriction fragment of 3.3 kb, conferring phage resistance, was cloned from plasmid pPF144 in vector pVA838 disclosed by MACRINA F. L. et al (1982), Gène, 19, 345–353, according to the procedure disclosed in Example 7 of EP-A1-452 224 and of U.S. Ser. No.08/144, 611, incorporated herein by way of reference. This recombinant plasmid, pPF144-2, confers on the strain *Lactococcus lactis* ssp *lactis* S56 the same level of phage resistance as plasmid pPF144 in its entirety.

The nucleic acid sequence of this 3.3 kb fragment, determined by the method of Sanger et al. (PNAS-USA, 14, 5463, 1977), is the sequence [SEQ ID no. 7] below.

Enzymic restriction analyses of this 3.3 kb fragment showed the presence in this fragment of a single site for recognition of the enzyme BstBI. Subcloning of the two HindIII-BstBI restriction fragments and their introduction into the strain *L. lactis* S56 made it possible to show that neither of them confers phage resistance. From this it was deduced that the BstBI site is within the assumed resistance gene. This hypothesis was strengthened by determination of the nucleotide sequence of the two fragments, showing that the BstBI site is within an open reading frame (ORF) of 1.62 kb, which would correspond to the resistance gene. FIG. 1 shows the restriction map of the HindIII—HindIII fragment of 3.3 kb.

Other analyses also showed that the HindIII—HindIII fragment of 3.3 kb possesses:

- a region Tn552 having a high degree of homology with part of transposon Tn552 (ref.: Tn552, a novel transposable element from *Staphylococcus aureus* (1990), S. J. ROWLAND, K. G. H. DYKE, Molecular Microbiology 4, 961–975);
- an ORF of 1620 bp which would correspond to the resistant gene;
- a region IS981 having a high degree of homology with part of insertion sequence IS981. (ref.: Identification, DNA sequence and distribution of IS98, a new high-copy-number insertion sequence in Lactococci (1991), K. M. POLZIN, L. L. McKAY, Applied and Environ. Microbiol. 57, 734–743;
- the beginning of an open reading frame (orf).

EXAMPLE 2

Amplification by the PCR method of internal fragments of the HindIII—HindIII fragment of 3.3 kb

The "PCR" (Polymerase Chain Reaction) technique, described for example in the work by Maniatis cited above, makes it possible to amplify a DNA fragment located between two oligonucleotides. This amplified DNA can easily be cloned if restriction sites are provided by the oligonucleotides. In fact, the sequences of these oligonucleotides can contain, at their 5' end, a heterologous part of the DNA to be amplified, consisting for example of 8 base pairs, 6 of which constitute a restriction site.

This technique was applied in order to determine whether the ORF revealed in the nucleotide sequence of the 3.3 kb

fragment did indeed correspond to the phage resistance gene, but also in order to form a specific probe for this ORF.

4 oligonucleotides of 28 bases (6 of which constitute a restriction site) were synthesized.

These 4 oligonucleotides have the following sequences:

Oligonucleotide no. 1 [SEQ no. 3]:		
5'	GGGAATTCGAACATAGAATAGATTACGG	3'
	EcoRI	
Oligonucleotide no. 2 [SEQ no. 4]:		
5'	GCGGATCCAAACTGTTCTGTTGCGAGTG	3'
	BamHI	
Oligonucleotide no. 3 [SEQ no. 5]:		
5'	GCGAATTCAACGAGTAACTTTTAGTCTT	3'
	EcoRI	
Oligonucleotide no. 4 [SEQ no. 6]:		
5'	GCGAATTCTAAAAATTGAACGATTTCCA	3'
	EcoRI	

Their locations on the 3.3 kb fragment are indicated in FIG. 2.

Oligonucleotides no. 1 and 2 made it possible to amplify a DNA fragment of 1875 bp containing the entire ORF plus 201 bp directly upstream of the latter, a region capable of containing gene expression signals. This DNA was amplified in the form of an EcoRI-BamHI fragment by virtue of the restriction sites provided by the oligonucleotides, allowing a directional cloning in shuttle vector pVA838.

In the same way, oligonucleotides no. 3 and 4 made it possible to amplify a region of 500 bp, overlapping the BstBI site, in the form of an EcoRi-EcoRi fragment. This region was chosen for forming a specific probe since it was shown that the two HindIII-BstBI subfragments of the 3.3 kb fragment did not on their own confer phage resistance, and hence that the region of the BstBI site was essential for the activity of the gene.

Two other fragments within the ORF could be amplified by the "PCR" method by virtue of the oligonucleotide pairs no. 1 and 4 and no. 2 and 3.

Starting from plasmid pPF144-2 purified on CsCl, the 4 DNA fragments were amplified by the "PCR" method with Vent polymerase (Biolabs), which possesses an exonuclease activity increasing its fidelity by a factor of 15 compared with the conventional Taq polymerase. The PCR products were purified by extraction with phenol/chloroform, precipitated with ethanol, digested with EcoRI or BamHI and EcoRI, depending on the fragment, and cloned in vector pVA838.

Cloning of the fragments in vector pVA838 made it possible to introduce them into a strain of *L. lactis*, after amplification of the recombinant plasmids in the strain *E. coli* TG1, and to determine whether they confer phage resistance.

A synopsis of the results relating to the cloning of the different amplified DNA fragments is presented in Table I below:

TABLE I

Oligonucléotide pair	Fragment size	Added sites	Cloned in pVA838
1-2	1875 pb	EcoRI-BamHI	pPF144-12
1-4	1791 pb	EcoRI-EcoRI	pPF144-14
2-3	584 pb	BamHI-EcoRI	pPF144-23
4-3	500 pb	EcoRI-EcoRI	pPF144-43

EXAMPLE 3

Phage resistance conferred by plasmid pPF144-12

Plasmids pPF144-12, pPF144-14, pPF144-23 and pPF144-43 were introduced into the strain *L. lactis* S56. The phage resistance of the clones obtained was tested by performing a titration (PFU/ml) with phages Ø53 and Ø59.

The results are given below:

	phage Ø53 (I)		phage Ø59 (III)	
Strain	Titer (PFU/ml)	Plate size (mm)	Titer (PFU/ml)	Plate size (mm)
S56	10^{10}	3	3.10^{9}	2
S56(pPF144-1)	2.10^{7}	<0,25	0	0
S56(pPF144-12)	4.10^{7}	<0,25	0	0
S56(pPF144-14)	8.10^{9}	3	6.10^{9}	2
S56(pPF144-23)	6.10^{9}	3	6.10^{9}	2
S56(pPF144-43)	10^{10}	3	2.10^{9}	2

PFU/ml = plate forming units per ml

Plasmid pPF144-12, containing the 1875 bp fragment amplified by the PCR method, confers the same phage resistance as plasmid pPF144-1. The other plasmids, namely pPF144-14, pPF144-23 and pPF144-43, comprising only part of the ORF of 1.62 kb, do not confer phage resistance.

EXAMPLE 4

Test on the replication of phage DNA in the presence of plasmid pPF144-12

Phages Ø53 and Ø59 belong to genetic groups I and III respectively. A genetic map of these phages was constructed and it was demonstrated in particular that the genome of these phages, consisting of double-stranded DNA, possesses sticky ends. This result implies that the replication of the DNA of these phages takes place according to a model identical to that of *E. coli* phage lambda: formation of concatemers during the lytic cycle and cleavage of these concatemers with a specific enzyme at the moment of encapsidation in the nucleocapsid of the phage.

The method of Hill et al. (Hill, C., Massey, I. J., Klaenhammer, T. R. (1991), Rapid method to characterize lactococcal bacteriophage genomes, Appl. Environ. Microbiol. 57, 283–288) was used to follow the fate of the phage DNA after injection into the bacterium. The strain *L. lactis* S56, containing the vector pVA838 or the plasmid pPF144-12, was infected with Ø53 and Ø59 with a multiplicity of infection of 2. Aliquots of the infected cultures are taken at regular intervals of time. The total DNA, i.e. cell and phage DNA, of each aliquot is extracted and digested with a restriction enzyme and the fragments obtained are separated electrophoretically by migration on agarose gel. The DNA is then transferred to a nylon membrane and hybridized with the DNA of the phage used as the probe (ECL kit, Amersham).

This method makes it possible to follow the appearance of, and change in, the phage DNA within the infected cell as a function of time.

The results obtained with the enzymes EcoRI, HindIII and EcoRV showed that the phage DNA replicates in the S56 strains with the vector pVA838 or the plasmid pPF144-12. An accumulation of the phage DNA in the form of concatemers is observed with the plasmid pPF144-12, whereas in the strain containing the vector pVA838, these concatemers start to disappear twenty minutes after infection.

EXAMPLE 5

Test on the production of phage proteins in the presence of plasmid pPF144-12

Phage Ø53 and Ø59 preparations purified on cesium chloride were used to prepare polyclonal antibodies in rabbits. The 56 strain, containing the vector pVA838 (control) or the plasmid pPF144-12, was infected with one of these phages with a multiplicity of 1. Every five minutes after infection, a fraction of the cells is taken and heated for three minutes at 100° C. in the presence of 2.3% of SDS and 5% of β-mercaptoethanol and the proteins are fractionated on a 12.5% SDS-polyacrylamide gel [Laemmli, U. K. 1970, Cleavage of structural proteins during the assembly of the head of bacteriophage T4, NATURE (London) 227, 680–685] and then transferred to nitrocellulose filters.

Immunological detection of the phage proteins on the nitrocellulose was effected with anti-Ø53 or anti-Ø59 rabbit antibodies and the immune complex was then localized with anti-rabbit mouse antibodies (ECL kit, Amersham) using streptavidin/alkaline phosphatase.

These results show that the proteins of phage Ø53 or Ø59 are found with and without the plasmid pPF144-12, but that, in the presence of this plasmid, the amount of proteins produced is small and the rate of appearance of these proteins is slowed down compared with a strain containing the vector pVA838. This phenomenon is more pronounced for Ø59 than for Ø53.

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i i i) NUMBER OF SEQUENCES: 7

(2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1875 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i i) MOLECULE TYPE: DNA (genomic)

(i i i) HYPOTHETICAL: NO

(i i i) ANTI-SENSE: NO

(v i) ORIGINAL SOURCE:
(A) ORGANISM: Lactococcus lactis

(i x) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 202..1821

(x i) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

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TAAGAAAAGA AGAGTGTCCA GAAAATGACC ATTTTCTGAA CGCCATATTA AAAATTTTTT  120

GATAATTCCC AATATATTAT AATATAGCTT CAATGTTAAA ATTTATATGA TATAATATAA  180

GAAAATTTTT AAAAAAATAG A ATG GAT ATA ATA ATG GAC TTT AAA ACT ATG      231
                       Met Asp Ile Ile Met Asp Phe Lys Thr Met
                         1               5                  10

TTA AGC TAT CTT GTA AGT CAA GAT GAT GAA ATT TCT TTA AGA AAT GAT      279
Leu Ser Tyr Leu Val Ser Gln Asp Asp Glu Ile Ser Leu Arg Asn Asp
                    15                  20                  25

ATT AAA CAT GAA GAA GTA TAT AAA ATT TTA GAG AAT AAG TTT GCT TCT      327
Ile Lys His Glu Glu Val Tyr Lys Ile Leu Glu Asn Lys Phe Ala Ser
                30                  35                  40

ATA ATG CCG AAG TTT AAA ACA AAA GGT TAT AAG TTT AAA GAT ACT ACT      375
Ile Met Pro Lys Phe Lys Thr Lys Gly Tyr Lys Phe Lys Asp Thr Thr
            45                  50                  55

GAA GTT TTG ACA TTC GCT AAA TTT GTA TTT TTG CTA CAA GAG TGG GGG      423
Glu Val Leu Thr Phe Ala Lys Phe Val Phe Leu Leu Gln Glu Trp Gly
        60                  65                  70

TTG AAG GAT ATA CAG TTT TAT AAG AAC ACT AAT AGT TTC TTA TTT GGA      471
Leu Lys Asp Ile Gln Phe Tyr Lys Asn Thr Asn Ser Phe Leu Phe Gly
 75                  80                  85                  90

TAT ATT ATA CCG CAA ATT AAT AAA GAA TTT GAT TTA TTG AGA TTT GGG      519
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Tyr Ile Ile Pro Gln Ile Asn Lys Glu Phe Asp Leu Leu Arg Phe Gly
                95                  100                 105

GAA AAT TAC AAT ATT AGT ATA GAA CTC AAA AGT AAA ACA ACA GTA GAA      567
Glu Asn Tyr Asn Ile Ser Ile Glu Leu Lys Ser Lys Thr Thr Val Glu
            110                 115                 120

GCA CAA AAG CAA CAA CTT TGT AAG AAC TAT TTT TAC CTA AAT TTT TTA      615
Ala Gln Lys Gln Gln Leu Cys Lys Asn Tyr Phe Tyr Leu Asn Phe Leu
        125                 130                 135

TCA ACT AAA ACT AGG TAT ATT AGT ATA TCC CCA GAT ATA TCT AGT TAC      663
Ser Thr Lys Thr Arg Tyr Ile Ser Ile Ser Pro Asp Ile Ser Ser Tyr
    140                 145                 150

ATA GAA TAT ATT CCA AGT GAA AAT AAG TAT ATC AAT TTA AGT GGA ACT      711
Ile Glu Tyr Ile Pro Ser Glu Asn Lys Tyr Ile Asn Leu Ser Gly Thr
155                 160                 165                 170

GAA ATT TGT GAT ATT ATT ATT AAA CAA GAG TTT TTA GAG TAT AAT ACA      759
Glu Ile Cys Asp Ile Ile Ile Lys Gln Glu Phe Leu Glu Tyr Asn Thr
                175                 180                 185

AAA GAG GTT GAT AGT TTT TTT GAT ATA AAA AAT TAT TTA GTT TCT CCT      807
Lys Glu Val Asp Ser Phe Phe Asp Ile Lys Asn Tyr Leu Val Ser Pro
            190                 195                 200

TTC AAT GAT GTT GAA AAA TTT CTT GAT GAT AAA TAT TTT TTA ACA CCT      855
Phe Asn Asp Val Glu Lys Phe Leu Asp Asp Lys Tyr Phe Leu Thr Pro
        205                 210                 215

CAC CAA GAC CAG ATT GTT AAA GAA ATT ACT GAA CCA AGT GAC AAA AAA      903
His Gln Asp Gln Ile Val Lys Glu Ile Thr Glu Pro Ser Asp Lys Lys
    220                 225                 230

ACT TTT GGT ATA AAA GGA AAT CCA GGA ACA GGA AAA TCT TTG CTA GTT      951
Thr Phe Gly Ile Lys Gly Asn Pro Gly Thr Gly Lys Ser Leu Leu Val
235                 240                 245                 250

TAC CAT ATA TGT AAA AAA TTA ATG GAG AAA AAT AAA AGA GTT GCT ATA      999
Tyr His Ile Cys Lys Lys Leu Met Glu Lys Asn Lys Arg Val Ala Ile
                255                 260                 265

GTT CAT GGA GCA AAT CTA AAT AAT GGT CAA CAA AGA TTA GCT CTG CGT     1047
Val His Gly Ala Asn Leu Asn Asn Gly Gln Gln Arg Leu Ala Leu Arg
            270                 275                 280

GGT TTC ACA ATT TTT CCT GTT AAA TCG ATC ATA GAG GTA TTA GAT AAT     1095
Gly Phe Thr Ile Phe Pro Val Lys Ser Ile Ile Glu Val Leu Asp Asn
        285                 290                 295

GCA GAC AAA TAC GAT TAC ATT GTT GTT GAC GAA GCT CAA CGT CTA AGA     1143
Ala Asp Lys Tyr Asp Tyr Ile Val Val Asp Glu Ala Gln Arg Leu Arg
    300                 305                 310

CAA GAC TTA GGA GAA CAA TAT ACT AAA TTG GTT GAT ACT ATT GAA AAT     1191
Gln Asp Leu Gly Glu Gln Tyr Thr Lys Leu Val Asp Thr Ile Glu Asn
315                 320                 325                 330

TCT CAA ACA AAA TTT ATT ATC TCA CTA GAT GGA AGA CAA ACT TTG AAT     1239
Ser Gln Thr Lys Phe Ile Ile Ser Leu Asp Gly Arg Gln Thr Leu Asn
                335                 340                 345

AAA TAT GAA ATA GAA GAA AAT TCC ATA AAA TTA TTT AAA TAT ATA AAA     1287
Lys Tyr Glu Ile Glu Glu Asn Ser Ile Lys Leu Phe Lys Tyr Ile Lys
            350                 355                 360

AAT AAA GGA GTA ACT TTT AGT CTT AAA GAT AAG TTT AGA ACT AAC CCA     1335
Asn Lys Gly Val Thr Phe Ser Leu Lys Asp Lys Phe Arg Thr Asn Pro
        365                 370                 375

GAA ATG AGC AAA TTT ATC CAA CTT CTA TTC AAA ATA CCC ATG TAT AAA     1383
Glu Met Ser Lys Phe Ile Gln Leu Leu Phe Lys Ile Pro Met Tyr Lys
    380                 385                 390

AAA ATA GAT TTA ATT TCA AAC ATA GAT CAT AAT ATT ATA ATT ATT AAA     1431
Lys Ile Asp Leu Ile Ser Asn Ile Asp His Asn Ile Ile Ile Lys Tyr
395                 400                 405                 410

TTT GAT AAC AGA GAA TCG GGA AAT GAA TAT ATT TCC GAT ATG GAT TCA     1479
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Phe Asp Asn Arg Glu Ser Gly Asn Glu Tyr Ile Ser Asp Met Asp Ser
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AAC TCA GAT TGG GAA GTA CTT AAT TAC ACG AAG GAT AGA TTT AGG AAA      1527
Asn Ser Asp Trp Glu Val Leu Asn Tyr Thr Lys Asp Arg Phe Arg Lys
            430                 435                 440

ACA GGA ATT GGT AAA ATG TGT GGT AAT GGT TTA ACA TCA CAT AGT ATT      1575
Thr Gly Ile Gly Lys Met Cys Gly Asn Gly Leu Thr Ser His Ser Ile
        445                 450                 455

ATC GGT CAA GAA TTT GAT AAA GTT ATT ATA CCT TTG GAT TCG AAT TTT      1623
Ile Gly Gln Glu Phe Asp Lys Val Ile Ile Pro Leu Asp Ser Asn Phe
    460                 465                 470

TTT TAT AAA GAA CAA AAA ATA ATT GAT AGT AAA ACG GGT GAA AGT AAA      1671
Phe Tyr Lys Glu Gln Lys Ile Ile Asp Ser Lys Thr Gly Glu Ser Lys
475                 480                 485                 490

GTT TTT AAA TTA TTG GAA ACG ACT GAT AAT TTT TAC CCA CTT GAA AAA      1719
Val Phe Lys Leu Leu Glu Thr Thr Asp Asn Phe Tyr Pro Leu Glu Lys
                495                 500                 505

ATG TTA TAT CAA AAT CTT ACT CGC ACA AGG GGA AAA ATA GAA TTT GTA      1767
Met Leu Tyr Gln Asn Leu Thr Arg Thr Arg Gly Lys Ile Glu Phe Val
            510                 515                 520

ATT ATT GGA AAT CGT TCA ATT TTT AAT GAA ATA TGT GGA TTG CTA GAT      1815
Ile Ile Gly Asn Arg Ser Ile Phe Asn Glu Ile Cys Gly Leu Leu Asp
        525                 530                 535

AGT TTA TAAAGTTCTG TCTCAAAGTT AAAAAAAGTG AAATCACTCG CAACAGAACA      1871
Ser Leu
    540

GTTT                                                                1875
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(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 540 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(i i) MOLECULE TYPE: protein

(x i) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

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Met Asp Ile Ile Met Asp Phe Lys Thr Met Leu Ser Tyr Leu Val Ser
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            20                  25                  30

Tyr Lys Ile Leu Glu Asn Lys Phe Ala Ser Ile Met Pro Lys Phe Lys
        35                  40                  45

Thr Lys Gly Tyr Lys Phe Lys Asp Thr Thr Glu Val Leu Thr Phe Ala
    50                  55                  60

Lys Phe Val Phe Leu Leu Gln Glu Trp Gly Leu Lys Asp Ile Gln Phe
65                  70                  75                  80

Tyr Lys Asn Thr Asn Ser Phe Leu Phe Gly Tyr Ile Ile Pro Gln Ile
                85                  90                  95

Asn Lys Glu Phe Asp Leu Leu Arg Phe Gly Glu Asn Tyr Asn Ile Ser
            100                 105                 110

Ile Glu Leu Lys Ser Lys Thr Thr Val Glu Ala Gln Lys Gln Gln Leu
        115                 120                 125

Cys Lys Asn Tyr Phe Tyr Leu Asn Phe Leu Ser Thr Lys Thr Arg Tyr
    130                 135                 140

Ile Ser Ile Ser Pro Asp Ile Ser Ser Tyr Ile Glu Tyr Ile Pro Ser
145                 150                 155                 160

Glu Asn Lys Tyr Ile Asn Leu Ser Gly Thr Glu Ile Cys Asp Ile Ile
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                    165                 170                 175

Ile Lys Gln Glu Phe Leu Glu Tyr Asn Thr Lys Glu Val Asp Ser Phe
            180                 185                 190

Phe Asp Ile Lys Asn Tyr Leu Val Ser Pro Phe Asn Asp Val Glu Lys
        195                 200                 205

Phe Leu Asp Asp Lys Tyr Phe Leu Thr Pro His Gln Asp Gln Ile Val
    210                 215                 220

Lys Glu Ile Thr Glu Pro Ser Asp Lys Lys Thr Phe Gly Ile Lys Gly
225                 230                 235                 240

Asn Pro Gly Thr Gly Lys Ser Leu Leu Val Tyr His Ile Cys Lys Lys
                245                 250                 255

Leu Met Glu Lys Asn Lys Arg Val Ala Ile Val His Gly Ala Asn Leu
            260                 265                 270

Asn Asn Gly Gln Glu Arg Leu Ala Leu Arg Gly Phe Thr Ile Phe Pro
        275                 280                 285

Val Lys Ser Ile Ile Glu Val Leu Asp Asn Ala Asp Lys Tyr Asp Tyr
    290                 295                 300

Ile Val Val Asp Glu Ala Gln Arg Leu Arg Gln Asp Leu Gly Glu Gln
305                 310                 315                 320

Tyr Thr Lys Leu Val Asp Thr Ile Glu Asn Ser Gln Thr Lys Phe Ile
                325                 330                 335

Ile Ser Leu Asp Gly Arg Gln Thr Leu Asn Lys Tyr Glu Ile Glu Glu
            340                 345                 350

Asn Ser Ile Lys Leu Phe Lys Tyr Ile Lys Asn Lys Gly Val Thr Phe
        355                 360                 365

Ser Leu Lys Asp Lys Phe Arg Thr Asn Pro Glu Met Ser Lys Phe Ile
    370                 375                 380

Gln Leu Leu Phe Lys Ile Pro Met Tyr Lys Lys Ile Asp Leu Ile Ser
385                 390                 395                 400

Asn Ile Asp His Asn Ile Ile Ile Lys Tyr Phe Asp Asn Arg Glu Ser
                405                 410                 415

Gly Asn Glu Tyr Ile Ser Asp Met Asp Ser Asn Ser Asp Trp Glu Val
            420                 425                 430

Leu Asn Tyr Thr Lys Asp Arg Phe Arg Lys Thr Gly Ile Gly Lys Met
        435                 440                 445

Cys Gly Asn Gly Leu Thr Ser His Ser Ile Ile Gly Gln Glu Phe Asp
    450                 455                 460

Lys Val Ile Ile Pro Leu Asp Ser Asn Phe Phe Tyr Lys Glu Gln Lys
465                 470                 475                 480

Ile Ile Asp Ser Lys Thr Gly Glu Ser Lys Val Phe Lys Leu Leu Glu
                485                 490                 495

Thr Thr Asp Asn Phe Tyr Pro Leu Glu Lys Met Leu Tyr Gln Asn Leu
            500                 505                 510

Thr Arg Thr Arg Gly Lys Ile Glu Phe Val Ile Ile Gly Asn Arg Ser
        515                 520                 525

Ile Phe Asn Glu Ile Cys Gly Leu Leu Asp Ser Leu
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(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

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(i i) MOLECULE TYPE: DNA (genomic)

(i i i) HYPOTHETICAL: NO

(i i i) ANTI-SENSE: NO

(i x) FEATURE:
(A) NAME/KEY: misc_signal
(B) LOCATION: 3..8
(D) OTHER INFORMATION: /function="EcoRI restriction site"

(i x) FEATURE:
(A) NAME/KEY: misc_structure
(B) LOCATION: 9..28
(D) OTHER INFORMATION: /function="seq. homologous to nucleotides 1-20 of SEQ ID NO:1"

(x i) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

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(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i i) MOLECULE TYPE: DNA (genomic)

(i i i) HYPOTHETICAL: NO

(i i i) ANTI-SENSE: NO

(i x) FEATURE:
(A) NAME/KEY: misc_signal
(B) LOCATION: 3..8
(D) OTHER INFORMATION: /function="BamHI restriction site"

(i x) FEATURE:
(A) NAME/KEY: misc_structure
(B) LOCATION: 9..28
(D) OTHER INFORMATION: /function="seq. homolog. to cDNA corresp. to nucleot. 1856-1875 of seq ID No.1"

(x i) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

GGGGATCCAA ACTGTTCTGT TGCGAGTG 28

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i i) MOLECULE TYPE: DNA (genomic)

(i i i) HYPOTHETICAL: NO

(i i i) ANTI-SENSE: NO

(i x) FEATURE:
(A) NAME/KEY: misc_signal
(B) LOCATION: 3..8
(D) OTHER INFORMATION: /function="EcoRI restriction site"

(i x) FEATURE:
(A) NAME/KEY: misc_structure
(B) LOCATION: 9..28
(D) OTHER INFORMATION: /function="seq. homologous to nucleotides 1292-1311 of SEQ ID NO:1"

(x i) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

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(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i i) MOLECULE TYPE: DNA (genomic)

(i i i) HYPOTHETICAL: NO

(i i i) ANTI-SENSE: NO

(i x) FEATURE:
(A) NAME/KEY: misc_signal
(B) LOCATION: 3..8
(D) OTHER INFORMATION: /function="EcoRI restriction site"

(i x) FEATURE:
(A) NAME/KEY: misc_structure
(B) LOCATION: 9..28
(D) OTHER INFORMATION: /function="seq. homol. to cDNA corresp. to nucleot. 1773-1792 of seq. ID No.1"

(x i) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

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(2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3234 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i i) MOLECULE TYPE: DNA (genomic)

(i i i) HYPOTHETICAL: NO

(i i i) ANTI-SENSE: NO

(v i) ORIGINAL SOURCE:
(A) ORGANISM: Lactococcus lactis

(x i) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

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TTCTTGCAAG CTATGGAAAC TTACTCCTTT ATCATTAAGT GAATTAACTA TGCTAATTAA 240

GTCCTCCATA TTTCTTCCTA ATCTATCTAA CCGCCAAACA ACAATTGTAT CTCCAGAACG 300

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AGTAAATATT TTTTCACAGT TATATTTTTT GAGACTATCT TTTTGTAAAT CCAAATTTTG 420

AAGTCCAGTT GAAACTCGTG CGTATCCTAT ATTCATTTTT TTCTCCTTCA TTTTAATTTA 480

TTGTATCATA ACTTAAAAAT ATATGTATAA ATGAACATAG AATAGATTAC GGGTTAATGG 540

ACAATAAATG CAAACGATTT TGAGAAATTT AATAAGAAAA GAAGAGTGTC CAGAAAATGA 600

CCATTTTCTG AACGCCATAT TAAAAATTTT TTGATAATTC CCAATATATT ATAATATAGC 660

TTCAATGTTA AAATTTATAT GATATAATAT AAGAAAATTT TTAAAAAAAT AGAATGGATA 720

TAATAATGGA CTTTAAAACT ATGTTAAGCT ATCTTGTAAG TCAAGATGAT GAAATTTCTT 780

TAAGAAATGA TATTAAACAT GAAGAAGTAT ATAAAATTTT AGAGAATAAG TTTGCTTCTA 840

TAATGCCGAA GTTTAAAACA AAAGGTTATA AGTTTAAAGA TACTACTGAA GTTTTGACAT 900

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TCGCTAAATT TGTATTTTTG CTACAAGAGT GGGGGTTGAA GGATATACAG TTTTATAAGA  960
ACACTAATAG TTTCTTATTT GGATATATTA TACCGCAAAT TAATAAAGAA TTTGATTTAT 1020
TGAGATTTGG GGAAAATTAC AATATTAGTA TAGAACTCAA AAGTAAAACA ACAGTAGAAG 1080
CACAAAAGCA ACAACTTTGT AAGAACTATT TTTACCTAAA TTTTTTATCA ACTAAAACTA 1140
GGTATATTAG TATATCCCCA GATATATCTA GTTACATAGA ATATATTCCA AGTGAAAATA 1200
AGTATATCAA TTTAAGTGGA ACTGAAATTT GTGATATTAT TATTAAACAA GAGTTTTTAG 1260
AGTATAATAC AAAAGAGGTT GATAGTTTTT TTGATATAAA AAATTATTTA GTTTCTCCTT 1320
TCAATGATGT TGAAAAATTT CTTGATGATA AATATTTTTT AACACCTCAC CAAGACCAGA 1380
TTGTTAAAGA AATTACTGAA CCAAGTGACA AAAAAACTTT TGGTATAAAA GGAAATCCAG 1440
GAACAGGAAA ATCTTTGCTA GTTTACCATA TATGTAAAAA ATTAATGGAG AAAAATAAAA 1500
GAGTTGCTAT AGTTCATGGA GCAAATCTAA ATAATGGTCA ACAAAGATTA GCTCTGCGTG 1560
GTTTCACAAT TTTTCCTGTT AAATCGATCA TAGAGGTATT AGATAATGCA GACAAATACG 1620
ATTACATTGT TGTTGACGAA GCTCAACGTC TAAGACAAGA CTTAGGAGAA CAATATACTA 1680
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TTATCCAACT TCTATTCAAA ATACCCATGT ATAAAAAAAT AGATTTAATT TCAAACATAG 1920
ATCATAATAT TATAATTAAA TATTTTGATA ACAGAGAATC GGGAAATGAA TATATTTCCG 1980
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GCTCACTCCA GAAATGCTAA GTTTCGGAAA AAATTTGAAT TTTTCGTAAA GATATTATTT 2580
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GAGATGATAA CATATCTTAT GATGAATGGT AGAGAACAAT TTCTTCGCAA AGTTGATTAT 3120
CTAAAATATA ATAATAAGTC ATACTATAAA TACTATAAAA AATTATCTTG TAGAAATATT 3180
TTATTGAGTC AGTCAATGAT TTTAACTTAT GATAAAGAAA AACTTAAAAA GCTT       3234
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What is claimed is:

1. A polynucleotide conferring at least one phage resistance mechanism, wherein said polynucleotide encodes a polypeptide according to SEQ ID NO:2.

2. A plasmid encoding at least one phage resistance mechanism, said plasmid containing a polynucleotide encoding a polypeptide according to SEQ ID NO:2.

3. A method of conferring phage resistance to a bacterium, comprising the step of contacting said bacterium with a polynucleotide encoding a polypeptide according to SEQ ID NO:2.

4. A method according to claim 3, wherein said contacting occurs through conjugation or fusion.

5. A method according to claim 3, wherein said contacting occurs through transformation.

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UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 5,658,770
DATED : August 19, 1997
INVENTOR(S) : PREVOTS et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Title page,

item [73] Assignees: Please delete "SANOFI, Paris, France", and insert

--SYSTEMS BIO-INDUSTRIES, Boulogne-

Billancourt Cedex, France--.

Signed and Sealed this

Sixteenth Day of December, 1997

Bruce Lehman

Attest:

BRUCE LEHMAN

Attesting Officer

Commissioner of Patents and Trademarks