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전체 청구항 수 : 총 39 항

(54) 발명의 명칭 **박테리아 균주를 함유한 조성물**

(57) 요 약

본 개시내용은 염증성 및 자가면역성 질환을 치료 또는 예방하기 위한 박테리아 균주를 포함하는 조성물을 제공한다.

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아메드, 수아드
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명 세 서

청구범위

청구항 1

IL-17 또는 Th17 경로에 의해 매개된 질환 또는 병태의 치료 또는 예방하는 방법에 사용하기 위한, 속 *에리시펠라토클로스트리디움*의 박테리아 균주를 포함하는, 조성물.

청구항 2

청구항 1에 있어서, 상기 조성물이 하기로 이루어진 군으로부터 선택된 질환 또는 병태의 치료 또는 예방의 방법에 사용하기 위한 것인, 조성물: 포도막염; 암, 예컨대 유방암, 폐암, 간암, 결장암, 또는 난소암; 다발성 경화증; 관절염, 예컨대 류마티스성 관절염, 골관절염, 건선성 관절염, 또는 유년성 특발성 관절염; 시신경척수염(데빅병); 강직 척추염; 척추관절염; 건선; 전신 홍반성 낭창; 염증성 장 질환, 예컨대 크론병 또는 궤양성 대장염; 소아지방변증; 천식, 예컨대 알러지성 천식 또는 호중구성 천식; 만성 폐쇄성 폐 질환 (COPD); 공막염; 혈관염; 베체트병; 죽상경화증; 아토피 피부염; 폐공기증; 치주염; 알러지성 비염; 및 동종이식편 거부반응.

청구항 3

청구항 2에 있어서, 상기 조성물이 포도막염을 치료 또는 예방하는 방법에 사용하기 위한 것인, 조성물.

청구항 4

청구항 3에 있어서, 상기 조성물이 포도막염에서 망막 손상을 감소 또는 예방하는 방법에 사용하기 위한 것인, 조성물.

청구항 5

청구항 2에 있어서, 상기 조성물이 폐암, 유방암 또는 간암과 같은 암을 치료 또는 예방하는 방법에 사용하기 위한 것인, 조성물.

청구항 6

청구항 5에 있어서, 상기 조성물이 종양 크기를 감소, 종양 성장을 감소, 전이를 예방 또는 혈관신생을 예방하는 방법에 사용하기 위한 것인, 조성물.

청구항 7

청구항 2에 있어서, 상기 조성물이 호중구성 천식 또는 알러지성 천식과 같은 천식을 치료 또는 예방하는 방법에 사용하기 위한 것인, 조성물.

청구항 8

청구항 7에 있어서, 상기 조성물이 천식의 치료에서 호중구증가증 또는 호산구증가증을 감소하는 방법에 사용하기 위한 것인, 조성물.

청구항 9

청구항 2에 있어서, 상기 조성물이 류마티스성 관절염을 치료 또는 예방하는 방법에 사용하기 위한 것인, 조성물.

청구항 10

청구항 9에 있어서, 상기 조성물이 류마티스성 관절염에서 관절 팽윤을 감소시키는 방법에 사용하기 위한 것인, 조성물.

청구항 11

청구항 2에 있어서, 상기 조성물이 다발성 경화증을 치료 또는 예방하는 방법에 사용하기 위한 것인, 조성물.

청구항 12

청구항 11에 있어서, 상기 조성물이 질환 발병률 또는 질환 중증도를 감소시키는 방법에서 사용하기 위한 것인, 조성물.

청구항 13

청구항 1 내지 청구항 12 중 어느 한 항에 있어서, 상기 조성물이 IL-17 또는 Th17 경로에 의해 매개되는 질병 또는 병태의 치료 또는 예방에서 IL-17 생성을 감소시키거나 Th17 세포 분화를 감소시키는 방법에 사용하기 위한 것인, 조성물.

청구항 14

청구항 1 내지 청구항 13 중 어느 한 항에 있어서, 상기 조성물이 증가된 IL-17 수준 또는 Th17 세포를 갖는 환자에서 사용하기 위한 것인, 조성물.

청구항 15

청구항 1 내지 청구항 14 중 어느 한 항에 있어서, 상기 박테리아 균주가 *에리시펠라토클로스트리디움 라모숨*의 것인, 조성물

청구항 16

청구항 1 내지 청구항 14 중 어느 한 항에 있어서, 상기 박테리아 균주가 *에리시펠라토클로스트리디움 라모숨*의 박테리아 균주의 16s rRNA 서열에 적어도 95%, 96%, 97%, 98%, 99%, 99.5% 또는 99.9% 동일한 16s rRNA 서열을 갖는, 조성물.

청구항 17

청구항 1 내지 청구항 14 중 어느 한 항에 있어서, 상기 박테리아 균주가 서열 식별 번호: 1, 2 또는 3에 적어도 95%, 96%, 97%, 98%, 99%, 99.5% 또는 99.9% 동일한 16s rRNA 서열을 갖는, 조성물.

청구항 18

청구항 17에 있어서, 상기 박테리아 균주가 서열 식별 번호: 3에 적어도 95%, 96%, 97%, 98%, 99%, 99.5% 또는 99.9% 동일한 16s rRNA 서열을 갖거나, 상기 박테리아 균주가 서열 식별 번호: 3으로 표시되는 16s rRNA 서열을 갖는, 조성물.

청구항 19

청구항 1에 있어서, 상기 조성물이 류마티스성 관절염의 치료 또는 예방의 방법에 사용하기 위한, 종 *에리시펠라토클로스트리디움 라모숨*의 박테리아 균주를 포함하는, 조성물.

청구항 20

청구항 1에 있어서, 상기 조성물이 천식, 예컨대 호중구성 천식 또는 알러지성 천식의 치료 또는 예방의 방법에 사용하기 위한, 종 *에리시펠라토클로스트리디움 라모숨*의 박테리아 균주를 포함하는, 조성물.

청구항 21

청구항 1에 있어서, 상기 조성물이 다발성 경화증의 치료 또는 예방의 방법에 사용하기 위한, 종 *에리시펠라토클로스트리디움 라모숨*의 박테리아 균주를 포함하는, 조성물.

청구항 22

청구항 1에 있어서, 상기 조성물이 포도막염의 치료 또는 예방의 방법에 사용하기 위한, 종 *에리시펠라토클로스트리디움 라모숨*의 박테리아 균주를 포함하는, 조성물.

청구항 23

청구항 1에 있어서, 상기 조성물이 암의 치료 또는 예방의 방법에 사용하기 위한, 종 *에리시펠라토클로스트리디*

*움 라모숨*의 박테리아 균주를 포함하는, 조성물.

청구항 24

청구항 1 내지 청구항 23 중 어느 한 항에 있어서, 상기 조성물이 경구 투여를 위한 것인, 조성물.

청구항 25

청구항 1 내지 청구항 24 중 어느 한 항에 있어서, 상기 조성물이 하나 이상의 약학적으로 허용가능한 부형제 또는 담체를 포함하는, 조성물.

청구항 26

청구항 1 내지 청구항 25 중 어느 한 항에 있어서, 상기 박테리아 균주가 동결건조되는, 조성물.

청구항 27

청구항 1 내지 청구항 26 중 어느 한 항에 있어서, 상기 박테리아 균주가 생존가능하고 장에서 부분적으로 또는 전적으로 군집할 수 있는, 조성물.

청구항 28

청구항 1 내지 청구항 27 중 어느 한 항에 있어서, 상기 조성물이 속 *에리시펠라토클로스트리디움의 단일 균주를 포함하는, 조성물.*

청구항 29

청구항 1 내지 청구항 28 중 어느 한 항에 있어서, 미생물 컨소시엄의 일부로서 *에리시펠라토클로스트리디움* 박테리아 균주를 포함하는, 조성물.

청구항 30

청구항 1 내지 청구항 29 중 어느 한 항의 용도를 위한, 청구항 1 내지 청구항 29 중 어느 한 항의 조성물을 포함하는 식품.

청구항 31

청구항 1 내지 청구항 30 중 어느 한 항의 용도를 위한, 청구항 1 내지 청구항 30 중 어느 한 항의 조성물을 포함하는 백신 조성물.

청구항 32

속 *에리시펠라토클로스트리디움*의 박테리아 균주를 포함하는 조성물을 필요로 하는 환자에 투여하는 것을 포함하는, IL-17 또는 Th17 경로에 의해 매개된 질환 또는 병태의 치료 또는 예방 방법.

청구항 33

에리시펠라토클로스트리디움 라모숨 NCIMB 42688로서 기탁된 균주 MRX027, 또는 이의 유도체의, 세포.

청구항 34

청구항 33의 세포를 포함하는, 조성물.

청구항 35

청구항 34에 있어서, 약학적으로 허용가능한 캐리어 또는 부형제를 포함하는, 조성물.

청구항 36

에리시펠라토클로스트리디움 라모숨 NCIMB 42688로서 기탁된 균주 MRX027, 또는 이의 유도체의, 생물학적으로 순수한 배양물.

청구항 37

치료법에 사용하기 위한, *에리시펠라토클로스트리디움 라모숨* NCIMB 42688로서 기탁된 균주 MRX027, 또는 이의 유도체의, 세포.

청구항 38

청구항 37에 있어서, 상기 세포가 청구항 1 내지 청구항 14 중 어느 한 항에 있어서 한정된 방법에 사용하기 위한 것인, 세포.

청구항 39

치료법에 사용하기 위한, 임의의 다른 속으로부터 박테리아를 함유하지 않거나 또 다른 속으로부터 박테리아의 최소한 또는 생물학적으로 무관한 양만을 포함하는, 속 에리시펠라토클로스트리디움의 하나 이상의 박테리아 균주를 포함하는, 조성물.

발명의 설명

기 술 분 야

[0001] 본 발명은 포유동물의 소화관으로부터 단리된 박테리아 균주를 포함하는 조성물 분야 및 상기 조성물의 질병 치료에서의 용도에 관한 것이다.

배 경 기 술

[0002] 인간의 장은 *자궁에서* 무균으로 여겨지지만 태어난 직후에는 매우 다양한 모성 및 환경 미생물에 노출된다. 그 후, 미생물 콜로니와 숙계의 역동적인 기간이 발생하며, 이는 수송 방식, 환경, 식이 및 숙주 유전형과 같은 요인에 의해 영향을 받으며, 이들 모두는 특히 초기 생애 동안 소화관 미생물의 조성에 영향을 미친다. 결과적으로, 미생물은 안정화되고 성체와 같이 된다[1]. 인간 장내 미생물은 본질적으로 두 개의 주요 박테리아 분류인 박테리오데테스(Bacteroidetes)와 피르미쿠테스(Firmicutes)에 속하는 500 내지 1000 가지 이상의 다른 계통형(phylotype)을 함유한다[2]. 인간 장내 박테리아 콜로니에서 발생하는 성공적인 공생 관계는 다양한 신진대사, 구조적, 보호 및 기타 유익한 기능을 제공한다. 콜로니화된 장내 신진대사 활동이 강화되면 소화불량 식이 성분이 부산물을 방출하여 숙주에게 중요한 영양 공급원을 제공한다. 유사하게, 장내 미생물의 면역학적 중요성은 잘 알려져 있으며, 공생 박테리아의 도입에 따라 기능적으로 재구성된 면역 체계가 손상된 무균 동물에서 예시된다[3-5].

[0003] 미생물 조성의 급격한 변화는 염증성 장 질환(IBD)과 같은 위장 장애에서 입증되었다. 예를 들어, IBD 환자에서 *클로스트리디움* 클러스터 XIVa 박테리아의 수치가 감소하는 반면 *대장균* 수가 증가하여 장내에서 공생균(symbionts)과 유해균(pathobionts)의 균형이 바뀌었다고 나타났다[6-9]. 흥미롭게도, 이러한 미생물 부조화는 또한 T 효과기 세포 집단내 불균형과 관련된다.

[0004] 특정 박테리아 균주가 동물 장내에 미칠 수 있는 잠재적인 긍정적인 효과를 인식하여 다양한 질병의 치료에 다양한 균주가 제안되었다(예를 들어 [10-13] 참조). 또한 대부분 *락토바실러스(Lactobacillus)* 와 *비티도박테리움(Bifidobacterium)* 균주 를 포함한 특정 균주는 장에 직접 연결되지 않은 다양한 염증성 및 자가면역 질환의 치료에 사용하기 위해 제안되었다(문헌 [14] 및 [15] 참조). 그러나 다른 질병과 다른 박테리아 균주 사이의 관계, 특정 박테리아 균주가 장내와 전신 수준 및 특정 질병 유형에 미치는 정확한 효과에 대해서는 잘 알려져 있지 않다.

[0005] Seres Health, Inc.(참조 [16])은 대변 샘플로부터 수득된 박테리아가 면역계 장애의 치료에 유용할 수 있다고 예상하지만 박테리아가 효과적일 것이라는 지도가 제공되지 않는다.

[0006] Honda 등(참조 [17])은 클로스트리듐 속으로부터 종을 포함하는, 상이한 속의 20 박테리아의 혼합물이 Th17 세포의 증식 및 축적을 유도하는 방법을 기재한다. Honda 등의 조성물은 면역 기능의 개선 및 감염성 질환의 예방 또는 치료에 유용한 것으로 언급된다. 그러나, Honda 등은 개체에서 자가면역 및 염증성 질환을 치료하기 위해, Th17-유도 박테리아가, 예를 들어, 환자에 항생제 투여에 의해 억제 또는 사멸되어야 한다는 것을 교시한다.

[0007] 염증 및 자가면역 질환을 치료하는 새로운 방법에 대한 요구가 있다. 장내 박테리아를 이용한 새로운 치료법을

개발할 수 있도록 장내 박테리아의 잠재적인 효과에 대한 요건도 있다.

발명의 내용

[0008] 본 발명자들은 염증 및 자가면역 질환을 치료하고 예방하기 위한 새로운 치료법을 개발하였다. 특히, 본 발명자들은 IL-17 또는 Th17 경로에 의해 매개되는 질병 및 병태를 치료 및 예방하기 위한 새로운 치료법을 개발하였다. 특히, 본 발명자들은 속 *에리시펠라토클로스트리디움(Erysipelatoclostridium)* 으로부터 박테리아 균주가 IL-17 또는 Th17 경로에 의해 매개된 질환 및 병태의 치료 및 예방에 효과적일 수 있다는 것을 확인하였다. 실시예에서 기재된 대로, *에리시펠라토클로스트리디움 라모숨(Erysipelatoclostridium ramosum)*을 포함하는 조성물의 경구 투여는 포도막염의 마우스 모델에서 Th17 염증 반응을 포함하는 염증 반응의 중증도를 감소시킬 수 있다.

[0009] 따라서, 제1 구현예에서, 본 발명은, IL-17 또는 Th17 경로에 의해 매개된 질환 또는 병태의 치료 또는 예방하는 방법에 사용하기 위한, 속 *에리시펠라토클로스트리디움*의 박테리아 균주를 포함하는 조성물을 제공한다. 본 발명자들은 상기 종으로부터 박테리아 균주로 치료가 IL-17 및 Th17 경로에 의해 매개된 염증성 및 자가면역 질환의 마우스 모델에서 임상 이득을 제공할 수 있고, IL-17을 포함하는, Th17 경로의 일부인 사이토카인의 수준을 감소시킬 수 있고, Th17 염증 반응을 경감시킬 수 있다는 것을 확인하였다.

[0010] 특정한 구현예에서, 본 발명은, 하기로 이루어진 군으로부터 선택된 질환 또는 병태의 치료 또는 예방의 방법에 사용하기 위한, 속 *에리시펠라토클로스트리디움*의 박테리아 균주를 포함하는 조성물을 제공한다:포도막염; 암, 예컨대 유방암, 폐암, 간암, 결장암, 또는 난소암; 다발성 경화증; 관절염, 예컨대 류마티스성 관절염, 골관절염, 건선성 관절염, 또는 유년성 특발성 관절염; 시신경척수염 (데빅병); 강직 척추염; 척추관절염; 건선; 전신 홍반성 낭창; 염증성 장 질환, 예컨대 크론병 또는 궤양성 대장염; 소아지방변증; 천식, 예컨대 알러지성 천식 또는 호중구성 천식; 만성 폐쇄성 폐 질환 (COPD); 공막염; 혈관염; 베체트병; 죽상경화증; 아토피 피부염; 폐공기증; 치주염; 알러지성 비염; 및 동종이식편 거부반응.Th17 염증 반응에서 및 IL-17 및 Th17 경로에 의해 매개된 질환에서 속 *에리시펠라토클로스트리디움* 으로부터 박테리아 균주에 대하여 나타난 효과는 IL-17 및 Th17 경로에 의해 매개된 다른 질환 및 병태에 치료 이점, 예컨대 상기 열거된 것을 제공한다.

[0011] 특히 바람직한 구현예에서, 본 발명은, 포도막염, 예컨대 후측 포도막염의 치료 또는 예방의 방법에 사용하기 위한, 속 *에리시펠라토클로스트리디움*의 박테리아 균주를 포함하는 조성물을 제공한다. 본 발명자들은 *에리시펠라토클로스트리디움* 균주로 치료가 포도막염의 마우스 모델에서 질환 발병률 및 질환 중증도를 감소시킬 수 있고 망막 손상을 예방 또는 감소시킬 수 있다는 것을 확인하였다. 바람직한 구현예에서, 본 발명은, 포도막염의 치료에 사용하기 위한, 종 *에리시펠라토클로스트리디움 라모숨*의 박테리아 균주를 포함하는 조성물을 제공한다. *에리시펠라토클로스트리디움 라모숨* 을 이용하는 조성물은 포도막염 치료에 특히 효과적일 수 있다.

[0012] 추가로 바람직한 구현예에서, 본 발명은, 천식, 예컨대 호중구성 천식 또는 알러지성 천식의 치료 또는 예방의 방법에 사용하기 위한, 속 *에리시펠라토클로스트리디움*의 박테리아 균주를 포함하는 조성물을 제공한다. *에리시펠라토클로스트리디움* 균주로 치료는, 천식의 치료 또는 예방을 도울 수 있는, 폐 속에 호중구 및 호산구의 동원을 감소시킬 수 있다. 특정 구현예에서, 조성물은 호중구성 천식 또는 호산구성 천식을 치료 또는 예방하는 방법에 사용하기 위한 것이다. 본 발명의 조성물은 호중구성 천식 및 호산구성 천식의 치료 또는 예방에 특히 효과적일 수 있다. 실제로, 특정 구현예에서, 조성물은 천식의 치료 또는 예방에서 호중구성 염증 반응을 감소시키는 방법에 사용하기 위한 것이거나, 조성물은 천식의 치료 또는 예방에서 호산구성 염증 반응을 감소시키는 방법에 사용하기 위한 것이다. 바람직한 구현예에서, 본 발명은 천식, 및 특히 호산구성 또는 알러지성 천식의 치료에 사용하기 위한 종 *에리시펠라토클로스트리디움 라모숨*의 박테리아 균주를 포함하는 조성물을 제공한다. 또한, *에리시펠라토클로스트리디움 라모숨* 은 천식 모델의 중성구에서 특히 확연한 효과를 가질 수 있고 *에리시펠라토클로스트리디움 라모숨* 으로 치료는 호중구성 천식 치료에 특히 효과적일 수 있다.

[0013] 추가로 바람직한 구현예에서, 본 발명은, 류마티스성 관절염의 치료 또는 예방의 방법에 사용하기 위한, 속 *에리시펠라토클로스트리디움*의 박테리아 균주를 포함하는 조성물을 제공한다. *에리시펠라토클로스트리디움* 균주로 치료는 류마티스성 관절염의 마우스 모델에서 임상 이득을 제공할 수 있고 관절 팽윤을 감소시킬 수 있다. 바람직한 구현예에서, 본 발명은, 류마티스성 관절염의 치료에 사용하기 위한, 종 *에리시펠라토클로스트리디움 라모숨*의 박테리아 균주를 포함하는 조성물을 제공한다. *에리시펠라토클로스트리디움 라모숨* 을 이용하는 조성물은 류마티스성 관절염 치료에 특히 효과적일 수 있다.

[0014] 추가로 바람직한 구현예에서, 본 발명은, 다발성 경화증의 치료 또는 예방의 방법에 사용하기 위한, 속 *에리시*

*펠라토클로스트리디움*의 박테리아 균주를 포함하는 조성물을 제공한다. *에리시펠라토클로스트리디움* 균주로 치료는 다발성 경화증의 마우스 모델에서 질환 발병률 및 질환 중증도를 감소시킬 수 있다. 바람직한 구현예에서, 본 발명은, 다발성 경화증의 치료에 사용하기 위한, 종 *에리시펠라토클로스트리디움 라모숨*의 박테리아 균주를 포함하는 조성물을 제공한다. *에리시펠라토클로스트리디움 라모숨* 을 이용하는 조성물은 다발성 경화증 치료에 특히 효과적일 수 있다.

[0015] 추가로 바람직한 구현예에서, 본 발명은, 암, 예컨대 유방, 폐 또는 간 암의 치료 또는 예방의 방법에 사용하기 위한, 속 *에리시펠라토클로스트리디움*의 박테리아 균주를 포함하는 조성물을 제공한다. 속 *에리시펠라토클로스트리디움*의 박테리아 균주를 포함하는 조성물은 유방, 폐 및 간 암의 마우스 모델에서 종양 성장을 감소시킬 수 있다. 특정 구현예에서, 조성물은 암 치료에서 종양 크기를 감소시키거나 종양 성장을 예방하는 방법에 사용하기 위한 것이다. 특정 구현예에서, 본 발명은, 암의 치료에 사용하기 위한, 종 *에리시펠라토클로스트리디움 라모숨*의 박테리아 균주를 포함하는 조성물을 제공한다.

[0016] 특정 구현예에서, 본 발명의 조성물은 IL-17 또는 Th17 경로에 의해 매개되는 질병 또는 병태의 치료 또는 예방에서 IL-17 생산을 감소시키거나 Th17 세포 분화를 감소시키는 방법에 사용하기 위한 것이다. 특히, 본 발명의 조성물은 천식, 류마티스성 관절염, 다발성 경화증, 포도막염 또는 암의 치료 또는 예방에서 IL-17 생산 감소 또는 Th17 세포 분화 감소에 사용될 수 있다. 바람직하게는, 본 발명은, 천식, 류마티스성 관절염, 다발성 경화증, 포도막염 또는 암의 치료 또는 예방에서 IL-17 생산 감소 또는 Th17 세포 분화 감소에 사용하기 위한, 속 *에리시펠라토클로스트리디움 라모숨*의 박테리아 균주를 포함하는 조성물을 제공한다.

[0017] 특정 구현예에서, 조성물은 증가된 IL-17 수준 또는 Th17 세포를 갖는 환자에 사용하기 위한 것이다. Th17 염증 반응과 강력하게 관련되는, 포도막염에서 *에리시펠라토클로스트리디움* 균주에 대하여 나타난 효과는 *에리시펠라토클로스트리디움* 균주가 상기 환자에 특히 유익할 수 있다는 것을 의미한다.

[0018] 본 발명의 바람직한 구현예에서, 조성물에서 박테리아 균주는 *에리시펠라토클로스트리디움 라모숨*의 것이다. 밀접하게 관련된 균주, 예컨대 에리시펠라토클로스트리디움 라모숨의 박테리아 균주의 16s rRNA 서열에 적어도 95%, 96%, 97%, 98%, 99%, 99.5% 또는 99.9% 동일한 16s rRNA 서열을 갖는 박테리아 균주가 또한 사용될 수 있다. 바람직하게는, 박테리아 균주는 서열 식별 번호: 1, 2 또는 3에 적어도 95%, 96%, 97%, 98%, 99%, 99.5% 또는 99.9% 동일한 16s rRNA 서열을 갖는다. 바람직하게는, 서열 동일성 서열 식별 번호: 3에 대한 것이다. 바람직하게는, 본 발명에서 사용하기 위한 박테리아 균주는 서열번호: 3으로 표시되는 16s rRNA 서열을 갖는다.

[0019] 특정 구현예에서, 본 발명의 조성물은 경구 투여를 위한 것이다. 본 발명의 균주의 경구 투여는 IL-17 또는 Th17 경로-매개 질병 및 병태의 치료에 효과적일 수 있다. 또한, 경구 투여는 환자 및 종사자에게 편리하며 장내 수송 및/또는 부분적 또는 전체 콜로니화를 허용한다.

[0020] 특정 구현예에서, 본 발명의 조성물은 하나 이상의 약학적으로 허용가능한 부형제 또는 담체를 포함한다.

[0021] 특정 구현예에서, 본 발명의 조성물은 동결 건조된 박테리아 균주를 포함한다. 동결 건조는 박테리아의 수송을 허용하는 안정한 조성물을 제조하기 위한 효과적이고 편리한 기술이다.

[0022] 특정 구현예에서, 본 발명은 상기 기재된 조성물을 포함하는 식품을 제공한다.

[0023] 특정 구현예에서, 본 발명은 전술한 바와 같은 조성물을 포함하는 백신 조성물을 제공한다.

[0024] 추가적으로, 본 발명은, 속 *에리시펠라토클로스트리디움*의 박테리아 균주를 포함하는 조성물의 투여를 포함하는, IL-17 또는 Th17 경로에 의해 매개된 질환 또는 병태의 치료 또는 예방 방법을 제공한다.

[0025] 상기 발명을 개발함에 있어서, 본 발명자들은 치료에 특히 유용한 박테리아 균주를 확인 및 특성화하였다. 본 발명의 *에리시펠라토클로스트리디움 라모숨* 균주는 본원에서 기재된 질환, 예컨대 포도막염의 치료에 효과적인 것으로 나타난다. 따라서, 또 다른 측면에서, 본 발명은 *에리시펠라토클로스트리디움 라모숨* 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027), 또는 이의 유도체의 세포를 제공한다. 본 발명은 또한 이러한 세포를 포함하는 조성물 또는 이러한 세포의 생물학적으로 순수한 배양물을 제공한다. 본 발명은 또한 치료법에서, 특히 본원에서 기재된 질환에 대하여 사용하기 위한, *에리시펠라토클로스트리디움 라모숨* 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027), 또는 이의 유도체의 세포를 제공한다.

도면의 간단한 설명

[0026] **도 1:** 포도막염의 마우스 모델 - 대조군 그룹에서 TEFI 스코어.데이터는 평균± SEM으로 표시된다.

도 2: 포도막염의 마우스 모델 - 28 일째에 TEFI 스코어.데이터는 평균± SEM으로 표시된다.

발명을 실시하기 위한 구체적인 내용

[0027] ***박테리아 균주***

[0028] 본 발명의 조성물은 속 *에리시펠라토클로스트리디움*의 박테리아 균주를 포함한다. 그 예는 상기 속의 박테리아가 포도막염 및 IL-17 또는 Th17 경로에 의해 매개된 질환 및 병태의 치료 또는 예방에 유용하다는 것을 입증한다. 바람직한 박테리아 균주는 종 *에리시펠라토클로스트리디움 라모숨*의 것이다.

[0029] 본 발명은, 치료법에 사용하기 위한, 예를 들어, 염증성 및/또는 자가면역 질환의 치료 또는 예방에 사용하기 위한, *에리시펠라토클로스트리디움, 예를 들어, 에리시펠라토클로스트리디움 라모숨*을 제공한다. 유사하게, 본 발명은, 치료법에 사용하기 위한, 예를 들어, 염증성 및/또는 자가면역 질환의 치료 또는 예방에 사용하기 위한, 속 *에리시펠라토클로스트리디움*, 예를 들어, *에리시펠라토클로스트리디움 라모숨*의 박테리아 균주를 포함하는 조성물을 제공한다. 특정 구현예에서, 본 발명의 조성물은 *에리시펠라토클로스트리디움*, 예를 들어, *에리시펠라토클로스트리디움 라모숨을 포함하고*, 임의의 다른 박테리아 속을 함유하지 않는다. 특정 구현예에서, 본 발명의 조성물은 단일 종의 *에리시펠라토클로스트리디움*, 예를 들어, *에리시펠라토클로스트리디움 라모숨을 포함하고*, 임의의 다른 박테리아 종을 함유하지 않는다. 특정 구현예에서, 본 발명의 조성물은 단일 균주의 *에리시펠라토클로스트리디움*, 예를 들어, *에리시펠라토클로스트리디움 라모숨을 포함하고*, 임의의 다른 박테리아 균주 또는 종을 함유하지 않는다.

[0030] 본 발명에 사용하기 위한 *에리시펠라토클로스트리디움* 종의 예는 하기를 포함한다: *에리시펠라토클로스트리디움 라모숨*, *(클로스트리듐) 코클레아툼*, *(C.) 사카로구미아*, *(C.) 스피로포르메*, 및 *(C.) 인노쿠움* ([18]에서 최근에 재분류됨). *에리시펠라토클로스트리디움*은 그램-양성 염색한, 비-운동성, 절대적 혐기성 선형 또는 나선으로 만곡된 0.3-1.0 μm×2-4 μm의 로드(rod)이다. 포자 형성은 희귀하거나 결여된다. 따라서, 본 발명의 일부 구현예에서, *에리시펠라토클로스트리디움* 박테리아 균주는 포자형성된 형태가 아니거나 임의의 포자가 존재하면 이들은 *최소한* 양으로 존재한다. 게놈 DNA의 G+C 함량은 27-33 mol%이다. 이들은 글루코스, 푸룩토오스 및 수크로오스 [18]를 발효시킨다. *에리시펠라토클로스트리디움 라모숨*의 균주 유형은 ATCC 25582 = DSM 1402이다. *에리시펠라토클로스트리디움 라모숨* 균주 DSM 1402의 16S rRNA 유전자 서열에 대한 유전자은행 수탁 번호는 (서열 식별 번호: 1로서 본원에서 개시된) X73440이다. 예시적인 *에리시펠라토클로스트리디움 라모숨* 균주는 [18]에 기재된다. 본 발명에 사용하기 위한 또 다른 균주는 *에리시펠라토클로스트리디움 라모숨* 균주 JCM 1298이다. *에리시펠라토클로스트리디움 라모숨* 균주 JCM 1298의 16S rRNA 유전자 서열에 대한 유전자은행 수탁 번호는 (서열 식별 번호: 2로서 본원에서 개시된) NR_113243.1이다.

[0031] 실시예에서 시험된 *에리시펠라토클로스트리디움 라모숨* 박테리움은 본원에서 균주 MRX027로서 참조된다. 시험된 MRX027 균주에 대한 16S rRNA 서열은 서열 식별 번호: 3에 제공된다. 균주 MRX027은 국제 수탁기관 NCIMB, Ltd.에 기탁되었고:(Ferguson Building, Aberdeen, AB21 9YA, Scotland) (4D Pharma Research Ltd.에 의해)(Life Sciences Innovation Building, Aberdeen, AB25 2ZS, Scotland) (2016년 11월 15일에) 수탁 번호 NCIMB 42688로 배정되었다. 용어들 "MRX027" 및 "MRx0027"은 본원에서 상호교환적으로 사용된다.

[0032] 실시예에서 시험된 균주와 밀접하게 관련된 박테리아 균주는 포도막염 및 IL-17 또는 Th17 경로에 의해 매개된 질환 및 병태의 치료 또는 예방에 효과적인 것으로 또한 예상된다. 특정 구현예에서, 본 발명에서 사용하기 위한 박테리아 균주는 *에리시펠라토클로스트리디움 라모숨*의 박테리아 균주의 16s rRNA 서열에 적어도 95%, 96%, 97%, 98%, 99%, 99.5% 또는 99.9% 동일한 16s rRNA 서열을 갖는다. 바람직하게는, 본 발명에서 사용하기 위한 박테리아 균주는 서열 식별 번호: 1, 2 또는 3에 적어도 95%, 96%, 97%, 98%, 99%, 99.5% 또는 99.9% 동일한 16s rRNA 서열을 갖는다. 바람직하게는, 서열 동일성 서열 식별 번호: 3에 대한 것이다. 바람직하게는, 본 발명에서 사용하기 위한 박테리아 균주는 서열번호: 3으로 표시되는 16s rRNA 서열을 갖는다.

[0033] 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027), ATCC 25582 및 JCM 1298의 생물형인 박테리아 균주는 포도막염 및 IL-17 또는 Th17 경로에 의해 매개된 질환 및 병태의 치료 또는 예방에 효과적인 것으로 또한 예상된다. 생물형은 동일한 또는 매우 유사한 생리적 및 생화학적 특징을 갖는 밀접하게 관련된 균주이다.

[0034] 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027), ATCC 25582 또는 JCM 1298의 생물형인 그리고 본 발명에서 사용하기에 적합한 균주는 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027), ATCC 25582 또는 JCM 1298용 다른 뉴클레오타이드 서열의 서열분석에 의해 확인될 수 있다. 예를 들어, 실질적으로 전체의 게놈은 서열분석될 수 있고 본 발명에서 사용하기 위한 생물형 균주는 그의 전체의 게놈의 적어도 80%에 걸쳐 (예를 들면 적

어도 85%, 90%, 95% 또는 99%, 또는 그의 전체의 게놈에 걸쳐) 적어도 95%, 96%, 97%, 98%, 99%, 99.5% 또는 99.9% 서열 동일성을 가질 수 있다. 예를 들어, 일부 구현예에서, 생물형 균주는 그의 게놈의 적어도 98%에 걸쳐 적어도 98% 서열 동일성 또는 그의 게놈의 99%에 걸쳐 적어도 99% 서열 동일성을 갖는다. 생물형 균주 확인에서 사용하기 위한 다른 적합한 서열은 hsp60 또는 반복적인 서열 예컨대 BOX, ERIC, $(GTG)_5$, 또는 REP 또는 [19]를 포함할 수 있다. 생물형 균주는 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027), ATCC 25582 또는 JCM 1298의 대응하는 서열에 적어도 95%, 96%, 97%, 98%, 99%, 99.5% 또는 99.9% 서열 동일성을 가진 서열을 가질 수 있다. 일부 구현예에서, 생물형 균주는 NCIMB 42688로서 기탁된 균주 MRX027의 대응하는 서열에 적어도 95%, 96%, 97%, 98%, 99%, 99.5% 또는 99.9% 서열 동일성을 가진 서열을 갖고 서열 식별 번호: 3에 적어도 99% 동일한 (예를 들면 적어도 99.5% 또는 적어도 99.9% 동일한) 16S rRNA 서열을 포함한다. 일부 구현예에서, 생물형 균주는 NCIMB 42688로서 기탁된 균주 MRX027의 대응하는 서열에 적어도 95%, 96%, 97%, 98%, 99%, 99.5% 또는 99.9% 서열 동일성을 가진 서열을 갖고 서열 식별 번호: 3의 16S rRNA 서열을 갖는다.

[0035] 대안적으로, 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027), ATCC 25582 또는 JCM 1298의 생물형인 그리고 본 발명에서 사용하기에 적합한 균주는 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027), ATCC 25582 또는 JCM 1298 및 제한 단편 분석 및/또는 PCR 분석의 이용에 의해, 예를 들어 형광 증폭된 단편 길이 다형성 (FAFLP) 및 반복적인 DNA 요소 (rep)-PCR 지문화, 또는 단백질 프로파일링, 또는 부분적인 16S 또는 23s rDNA 서열분석 이용에 의해 확인될 수 있다. 바람직한 구현예에서, 상기 기술은 다른 *에리시펠라토클로스트리디움 라모숨* 균주를 확인하는 데 사용될 수 있다.

[0036] 특정 구현예에서, 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027), ATCC 25582 또는 JCM 1298의 생물형인 그리고 본 발명에서 사용하기에 적합한 균주는 증폭된 리보솜 DNA 제한 분석 (ARDRA)에 의해 분석된 경우, 예를 들어 Sau3AI 제한 효소를 이용한 경우 (예시적인 방법 및 지도에 대하여 참고, 예를 들어, [20]) 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027), ATCC 25582 또는 JCM 1298과 동일한 패턴을 제공하는 균주이다. 대안적으로, 생물형 균주는 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027), ATCC 25582 또는 JCM 1298과 동일한 탄수화물 발효 패턴을 갖는 균주로서 확인된다.

[0037] 본 발명의 조성물 및 방법에서 유용한 다른 *에리시펠라토클로스트리디움 라모숨* 균주, 예컨대 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027), ATCC 25582 또는 JCM 1298의 생물형은, 실시예에서 기재된 검정을 포함하는, 임의의 적절한 방법 또는 전략을 이용하여 확인될 수 있다. 예를 들면, 본 발명에서 사용하기 위한 균주는 혐기성 YCFA에서 배양 및/또는 2형 콜라겐-유도된 관절염 마우스 모델에 박테리아 투여 및 그 다음 사이토카인 수준 평가에 의해 확인될 수 있다. 특히, 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027), ATCC 25582 또는 JCM 1298과 유사한 성장 패턴, 대사 유형 및/또는 표면 항원을 갖는 박테리아 균주는 본 발명에서 유용할 수 있다. 유용한 균주는 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027), ATCC 25582 또는 JCM 1298과 비교할만한 면역 조절 활성을 가질 것이다. 특히, 생물형 균주는, 실시예에서 기재된 배양 및 투여 프로토콜을 이용함으로써 확인될 수 있는, 실시예에서 나타난 효과에 포도막염 질환 모델에서 비교할만한 효과를 유도할 것이다.

[0038] 본 발명의 특히 바람직한 균주는 균주 MRX027 균주 (특히 NCIMB 42688로서 기탁된 MRX027)이다. 이것은 실시예에서 시험된 예시적인 균주이고 질환 치료에 효과적인 것으로 나타난다. 따라서, 본 발명은 *에리시펠라토클로스트리디움 라모숨* 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027), 또는 이의 유도체의 세포, 예컨대 단리된 세포를 제공한다. 본 발명은 또한 *에리시펠라토클로스트리디움 라모숨* 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027), 또는 이의 유도체의 세포를 포함하는 조성물을 제공한다. 본 발명은 또한 *에리시펠라토클로스트리디움 라모숨* 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027)의 생물학적으로 순수한 배양물을 제공한다. 본 발명은 또한 치료법에서, 특히 본원에서 기재된 질환에 대하여 사용하기 위한, *에리시펠라토클로스트리디움 라모숨* 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027), 또는 이의 유도체의 세포를 제공한다. *에리시펠라토클로스트리디움 라모숨* 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027)의 유도체는 딸 균주 (자손) 또는 최초로부터 배양된 (아클론화된) 균주일 수 있다.

[0039] 본 발명의 균주 유도체는 생물학적 활성을 제거하지 않고 예를 들어 유전자 수준에서 변형될 수 있다. 특히, 본 발명의 유도체 균주는 치료적으로 활성이다. 유도체 균주는 *에리시펠라토클로스트리디움 라모숨* 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027)에 비교할만한 면역 조절 활성을 가질 것이다. 특히, 유도체 균주는, 실시예에서 기재된 배양 및 투여 프로토콜을 이용함으로써 확인될 수 있는, 실시예에서 나타난 효과에 포도막염 질환 모델에서 비교할만한 효과를 유도할 것이다. 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027)의 유도체는 일반적으로 균주 MRX027 (특히 NCIMB 42688로서 기탁된 MRX027)의 생물형일 것이다.

[0040] *에리시펠라토클로스트리디움 라모숨* 균주 MRX027의 세포에 대한 참고문헌은 균주 MRX027과 동일한 안전성 및 치료 효능 특징을 갖는 임의의 세포를 포함하고, 상기 세포는 본 발명에 의해 포함된다. NCIMB 42688로서 기탁된 MRX027에 대한 참고문헌은 기탁된 MRX027 균주만을 지칭한다.

[0041] *에리시펠라토클로스트리디움 라모숨* 균주 DSM 1402의 게놈 서열은 서열 식별 번호: 4로서 본원에서 개시된다. 상기 서열은 전체의 게놈 샷건 서열분석을 이용하여 수득된 게놈 스캐폴드이고 유전자은행 수탁 번호 NZ_DS499659.1을 이용하여 또한 이용가능하다. 특정 구현예에서, 본 발명에 사용하기 위한 박테리아 균주는 서열 식별 번호: 4에 서열 동일성을 가진 염색체를 갖는다. 일부 구현예에서, 본 발명에 사용하기 위한 박테리아 균주는 서열 식별 번호: 4의 적어도 30%에 걸쳐 (예를 들면 적어도 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 95%, 96%, 97%, 98%, 99% 또는 100%에 걸쳐) 서열 식별 번호: 4에 적어도 90% 서열 동일성 (예를 들면 적어도 92%, 94%, 95%, 96%, 97%, 98%, 99% 또는 100% 서열 동일성)을 가진 염색체를 갖는다. 예를 들어, 본 발명에 사용하기 위한 박테리아 균주는 서열 식별 번호: 4의 35%에 걸쳐 서열 식별 번호: 4에 적어도 95% 서열 동일성, 또는 서열 식별 번호: 4의 45%에 걸쳐 서열 식별 번호: 4에 적어도 95% 서열 동일성, 또는 서열 식별 번호: 4의 70%에 걸쳐 서열 식별 번호: 4에 적어도 90% 서열 동일성, 또는 서열 식별 번호: 4의 80%에 걸쳐 서열 식별 번호: 4에 적어도 90% 서열 동일성, 또는 서열 식별 번호: 4의 90%에 걸쳐 서열 식별 번호: 4에 적어도 90% 서열 동일성, 또는 서열 식별 번호: 4의 100%에 걸쳐 서열 식별 번호: 4에 적어도 90% 서열 동일성, 또는 서열 식별 번호: 4의 70%에 걸쳐 서열 식별 번호: 4에 적어도 95% 서열 동일성, 또는 서열 식별 번호: 4의 80%에 걸쳐 서열 식별 번호: 4에 적어도 95% 서열 동일성, 또는 서열 식별 번호: 4의 90%에 걸쳐 서열 식별 번호: 4에 적어도 95% 서열 동일성, 또는 서열 식별 번호: 4의 100%에 걸쳐 서열 식별 번호: 4에 적어도 95% 서열 동일성, 또는 서열 식별 번호: 4의 70%에 걸쳐 서열 식별 번호: 4에 적어도 98% 서열 동일성, 또는 서열 식별 번호: 4의 80%에 걸쳐 서열 식별 번호: 4에 적어도 98% 서열 동일성, 또는 서열 식별 번호: 4의 90%에 걸쳐 서열 식별 번호: 4에 적어도 98% 서열 동일성, 또는 서열 식별 번호: 4의 95%에 걸쳐 적어도 98% 동일성, 또는 서열 식별 번호: 4의 100%에 걸쳐 서열 식별 번호: 4에 적어도 98% 서열 동일성, 또는 서열 식별 번호: 4의 90%에 걸쳐 서열 식별 번호: 4에 적어도 99.5% 서열 동일성, 또는 서열 식별 번호: 4의 95%에 걸쳐 적어도 99.5% 동일성, 또는 서열 식별 번호: 4의 98%에 걸쳐 적어도 99.5% 동일성, 또는 서열 식별 번호: 4의 100%에 걸쳐 서열 식별 번호: 4에 적어도 99.5% 서열 동일성을 가진 염색체를 가질 수 있다.

[0042] 특정 구현예에서, 본 발명에 사용하기 위한 박테리아 균주는 16S rRNA 서열을 측접하는 영역에서 서열 식별 번호: 4에 서열 동일성을 가진 염색체를 갖는다. 일부 구현예에서, 본 발명에 사용하기 위한 박테리아 균주는 서열 식별 번호: 4에서 16S rRNA 서열의 직접 업스트림 및/또는 다운스트림으로 0.5kb 서열에 적어도 95% (예를 들면 적어도 96%, 97%, 98%, 99%, 99.5% 또는 100%) 서열 동일성을 가진 염색체를 갖는다. 일부 구현예에서, 본 발명에 사용하기 위한 박테리아 균주는 서열 식별 번호: 4에서 16S rRNA 서열의 직접 업스트림 및/또는 다운스트림으로 1kb 서열에 적어도 95% (예를 들면 적어도 96%, 97%, 98%, 99%, 99.5% 또는 100%) 서열 동일성을 가진 염색체를 갖는다. 일부 구현예에서, 본 발명에 사용하기 위한 박테리아 균주는 서열 식별 번호: 4에서 16S rRNA 서열의 직접 업스트림 및/또는 다운스트림으로 1.5kb 서열에 적어도 95% (예를 들면 적어도 96%, 97%, 98%, 99%, 99.5% 또는 100%) 서열 동일성을 가진 염색체를 갖는다. 일부 구현예에서, 본 발명에 사용하기 위한 박테리아 균주는 서열 식별 번호: 4에서 16S rRNA 서열의 직접 업스트림 및/또는 다운스트림으로 2kb 서열에 적어도 95% (예를 들면 적어도 96%, 97%, 98%, 99%, 99.5% 또는 100%) 서열 동일성을 가진 염색체를 갖는다.

[0043] 특정 구현예에서, 본 발명에 사용하기 위한 박테리아 균주는, 예를 들어 상기에 기재된 바와 같이, 서열 식별 번호: 4에 서열 동일성을 가진 염색체, 및 예를 들어 상기에 기재된 바와 같이, 임의의 서열 식별 번호: 1, 2 또는 3에 서열 동일성을 가진 16S rRNA 서열, 바람직하게는 하기에 적어도 99% 동일한 16s rRNA 서열을 가진 염색체를 갖는다: 서열 식별 번호: 3, 더 바람직하게는 서열 식별 번호: 3의 16S rRNA 서열을 포함한다.

[0044] 특정 구현예에서, 본 발명에 사용하기 위한 박테리아 균주는, 예를 들어 상기에 기재된 바와 같이, 서열 식별 번호: 4에 서열 동일성을 갖는 염색체를 갖고, IL-17 또는 Th17 경로에 의해 매개된 질환 및 병태의 치료 또는 예방에 효과적이다.

[0045] 특정 구현예에서, 본 발명에 사용하기 위한 박테리아 균주는, 예를 들어 상기에 기재된 바와 같이, 서열 식별 번호: 4에 서열 동일성을 갖는 염색체를 갖고, 하기에 서열 동일성을 가진 16S rRNA 서열을 갖고: 임의의 서열 식별 번호: 1, 2 또는 3, 예를 들어 상기에 기재된 바와 같이, 그리고 IL-17 또는 Th17 경로에 의해 매개된 질환 및 병태의 치료 또는 예방에 효과적이다.

[0046] 특정 구현예에서, 본 발명에 사용하기 위한 박테리아 균주는 하기로 표시되는 16s rRNA 서열에 적어도 99%,

99.5% 또는 99.9% 동일한 16s rRNA 서열을 갖고: 서열 식별 번호: 3 (예를 들어, 서열 식별 번호: 3의 16S rRNA 서열을 포함한다) 및 서열 식별 번호: 4의 적어도 40%에 걸쳐 서열 식별 번호: 4에 적어도 95% 서열 동일성을 가진 염색체, 그리고 IL-17 또는 Th17 경로에 의해 매개된 질환 및 병태의 치료 또는 예방에 효과적이다.

[0047] 특정 구현예에서, 본 발명에 사용하기 위한 박테리아 균주는 하기로 표시되는 16s rRNA 서열에 적어도 99%, 99.5% 또는 99.9% 동일한 16s rRNA 서열을 갖고: 서열 식별 번호: 3 (예를 들어, 서열 식별 번호: 3의 16S rRNA 서열을 포함한다) 및 서열 식별 번호: 4의 적어도 90%에 걸쳐 서열 식별 번호: 4에 적어도 95% 서열 동일성을 가진 염색체, 그리고 IL-17 또는 Th17 경로에 의해 매개된 질환 및 병태의 치료 또는 예방에 효과적이다.

[0048] 특정 구현예에서, 본 발명에 사용하기 위한 박테리아 균주는 *에리시펠라토클로스트리디움 라모숨*이고 하기로 표시되는 16s rRNA 서열에 적어도 99%, 99.5% 또는 99.9% 동일한 16s rRNA 서열을 갖고: 서열 식별 번호: 3 (예를 들어, 서열 식별 번호: 3의 16S rRNA 서열을 포함한다) 및 서열 식별 번호: 4의 적어도 98%에 걸쳐 (예를 들면 적어도 99% 또는 적어도 99.5%에 걸쳐) 서열 식별 번호: 4에 적어도 98% 서열 동일성 (예를 들면 적어도 99% 또는 적어도 99.5% 서열 동일성)을 가진 염색체, 그리고 IL-17 또는 Th17 경로에 의해 매개된 질환 및 병태의 치료 또는 예방에 효과적이다.

[0049] 바람직한 구현예에서, 본 발명의 조성물 중의 박테리아 균주는 생장 가능하고 장을 부분적으로 또는 전체적으로 콜로니화할 수 있다.

[0050] ***치료 용도***

[0051] 실시예에서 입증된 바와 같이, 본 발명의 박테리아 조성물은 Th17 염증 반응을 감소시키는 데 효과적이다. 특히, 본 발명의 조성물로 치료는 IL-17 및 Th17 경로에 의해 매개된 병태의 동물 모델에서 임상 개선을 달성하고 IL-17A 수준 및 다른 Th17 경로 사이토카인에서 감소를 달성할 수 있다. 따라서, 본 발명의 조성물은 염증성 및 자가면역 질환, 특히 IL-17에 의해 매개되는 질병 또는 병태를 치료 또는 예방하는 데 유용할 수 있다. 특히, 본 발명의 조성물은 IL-17 염증 반응의 상승을 감소 또는 방지하는 데 유용할 수 있다.

[0052] Th17 세포는 예를 들어 IL-17A, IL17-F, IL-21 및 IL22를 생성하는 T 헬퍼 세포의 하위 집합이다. Th17 세포 분화 및 IL-17 발현은 IL-23에 의해 유도될 수 있다. 이들 사이토카인 및 다른 것들은 Th17 경로의 중요한 부분을 형성하는데, 이는(예를 들어 [21, 22, 23, 24, 25, 26]에서 기재된 바와 같이) 다수의 염증 및 자가면역 질환에 기여하고 근원이 되는 잘 확립된 염증 신호 수송 경로이다. Th17 경로가 활성화되는 질병은 Th17 경로-매개 질병이다. Th17 경로-매개 질병은 Th17 세포의 분화를 줄이거나 Th17 세포의 활성을 감소시키거나 Th17 경로 사이토카인의 수준을 감소시키는 등 Th17 경로를 억제함으로써 개선 또는 완화될 수 있다. Th17 경로에 의해 매개되는 질병은 IL-17A, IL-17F, IL-21, IL-22, IL-26, IL-9와 같은 Th17 세포에 의해 생성되는 사이토카인의 증가된 수준을 특징으로 할 수 있다([27] 에서 검토). Th17 경로에 의해 매개되는 질병은 Stat3 또는 IL-23R과 같은 Th-17-관련 유전자의 발현 증가를 특징으로 할 수 있다. Th17 경로에 의해 매개되는 질병은 증가된 Th17 세포 수준과 관련이 있을 수 있다.

[0053] IL-17은 염증 및 자가면역 질환 및 병태의 발병 기전에 기여하는 전염증성 사이토카인이다. 본원에 사용된 IL-17은 IL-17A, IL-17B, IL-17C, IL-17D, IL-17E 및 IL-17F를 포함하는 IL-17 계열의 임의의 구성원을 지칭할 수 있다. IL-17-매개 질병 및 조건은 IL-17의 높은 발현 및/또는 질병 또는 병태에 의해 영향을 받는 조직에서의 IL-17-양성 세포의 축적 또는 존재를 특징으로 한다. 유사하게, IL-17-매개 질병 및 병태는 높은 IL-17 수준 또는 IL-17 수준의 증가에 의해 악화되고 낮은 IL-17 수준 또는 IL-17 수준의 감소에 의해 완화되는 질병 및 병태이다. IL-17 염증 반응은 국소 또는 전신성일 수 있다.

[0054] IL-17 또는 Th17 경로에 의해 매개될 수 있는 질환 및 병태의 예는 하기를 포함한다: 포도막염; 암, 예컨대 유방암, 폐암, 간암, 결장암, 또는 난소암; 다발성 경화증; 관절염, 예컨대 류마티스성 관절염, 골관절염, 건선성 관절염, 또는 유년성 특발성 관절염; 시신경척수염 (데빅병); 강직 척추염; 척추관절염; 건선; 전신 홍반성 낭창; 염증성 장 질환, 예컨대 크론병 또는 궤양성 대장염; 소아지방변증; 천식, 예컨대 알러지성 천식 또는 호중구성 천식; 만성 폐쇄성 폐 질환 (COPD); 공막염; 혈관염; 베체트병; 죽상경화증; 아토피 피부염; 폐공기증; 치주염; 알러지성 비염; 및 동종이식편 거부반응. 바람직한 구현예에서, 본 발명의 조성물은 이들 병태 또는 질병 중 하나 이상을 치료 또는 예방하는 데 사용된다. 추가의 바람직한 구현예에서, 이들 병태 또는 질병은 IL-17 또는 Th17 경로에 의해 매개된다.

[0055] 일부 구현예에서, 질환 또는 병태의 발병은 장에 영향을 준다. 일부 구현예에서, 질환 또는 병태의 발병은 장에 영향을 주지 않는다. 일부 구현예에서, 질환 또는 병태의 발병은 장에서 국재화되지 않는다. 일부 구현예에서,

치료 또는 예방은 장이 아닌 부위에서 발생한다. 일부 구현예에서, 치료 또는 예방은 장에서 그리고 또한 장이 아닌 부위에서 발생한다. 특정 구현예에서, 질환 또는 병태는 전신성이다.

[0056] 특정 구현예에서, 본 발명의 조성물은 IL-17 또는 Th17 경로에 의해 매개되는 질병 또는 병태의 치료 또는 예방에서 IL-17 생산을 감소시키거나 Th17 세포 분화를 감소시키는 방법에 사용하기 위한 것이다. 특정 구현예서, 본 발명의 조성물은 염증성 또는 자가면역 질환의 치료 또는 예방에 사용하기 위한 것이며, 상기 치료 또는 예방은 Th17 염증 반응의 상승을 감소 또는 방지함으로써 달성된다. 특정 구현예에서, 본 발명의 조성물은 염증성 또는 자가면역 질환을 갖는 환자를 치료하는 데 사용하기 위한 것으로, 환자는 IL-17 수준의 상승 또는 Th17 세포의 증가 또는 Th17 염증 반응을 나타낸다. 특정 구현예에서, 환자는 만성 염증성 또는 자가면역 질환 또는 병태로 진단되었을 수 있거나, 본 발명의 조성물은 염증성 또는 자가면역 질환 또는 만성 염증성 또는 자가면역 질환 또는 병태로 진행되는 병태를 예방하는 데 사용하기 위한 것일 수 있다. 특정 구현예에서, 질병 또는 병태는 TNF-α 억제제에 의한 치료에 반응하지 않을 수 있다. 본 발명의 이러한 용도는 이전 단락에 열거된 특정 질병 또는 병태 중 어느 하나에 적용될 수 있다.

[0057] IL-17 및 Th17 경로는 종종 만성 염증성 및 자가면역 질환과 관련되기 때문에, 본 발명의 조성물은 상기 열거된 만성 질환 또는 병태를 치료 또는 예방하는 데 특히 유용할 수 있다. 특정 구현예에서, 조성물은 만성 질환을 갖는 환자에게 사용하기 위한 것이다. 특정 구현예에서, 조성물은 만성 질환의 발병을 예방하는 데 사용하기 위한 것이다.

[0058] 본 발명의 조성물은 IL-17 또는 Th17 경로에 의해 매개되는 질병 및 병태를 치료하고 Th17 염증 반응을 다루는 데 유용할 수 있기 때문에, 본 발명의 조성물은 만성 질환의 치료 또는 예방, 다른 치료법에 반응하지 않은 환자의 질병의 치료 또는 예방(예를 들어 TNF-α 억제제에 의한 치료) 및/또는 조직 손상 및 및 IL-17 및 Th17 세포와 관련된 증상의 치료 또는 예방에 특히 유용할 수 있다. 예를 들어, IL-17은 연골 및 뼈 조직에서 기질 파괴를 활성화시키는 것으로 알려져 있으며, IL-17은 연골 세포 및 골아 세포에서의 기질 생성에 억제 효과를 가지기 때문에, 본 발명의 조성물은 골 침식 또는 연골 손상을 치료 또는 예방하는 데 유용할 수 있다.

[0059] 특정 구현예에서, 본 발명의 조성물로 처리하면 IL-17 수준, 특히 IL-17A 수준의 감소를 제공하거나 상승을 방지한다. 특정 구현예에서, 본 발명의 조성물로 치료는 TNFα, IFN-γ 또는 IL-6 수준에서 감소를 제공하거나 상승을 방지한다. 이러한 사이토카인의 증가된 수준의 감소 또는 예방은 염증성 및 자가면역 질환 및 병태, 특히 IL-17 또는 Th17 경로에 의해 매개되는 것들을 치료 또는 예방하는 데 유용할 수 있다.

[0060] *포도막염*

[0061] 바람직한 구현예에서, 본 발명의 조성물은 포도막염의 치료 또는 예방에 사용하기 위한 것이다. 그 예는 본 발명의 조성물이 포도막염의 동물 모델에서 질환 발병률 및 질환 중증도의 감소를 달성하고 그래서 이들이 포도막염의 치료 또는 예방에서 유용할 수 있다는 것을 입증한다. 포도막염은 포도막의 염증으로 망막 조직 파괴를 일으킬 수 있다. 이것은 다른 해부학적 형태(전방, 중간, 후방 또는 확산)로 나타날 수 있으며, 전립선자가면역 장애를 포함하여 다르지만 관련된 원인으로 인해 발생할 수 있다. IL-17 및 Th17 경로는 포도막염에 집중적으로 관여되고, 그래서 포도막염 치료에 대한 본 발명의 조성물의 효능은 본 발명의 조성물이 IL-17 또는 Th17 경로에 의해 매개된 질환 및 병태의 치료 및 예방에 특히 효과적일 수 있다는 것을 나타낸다. 참고문헌 [28, 29, 30, 31, 32, 33, 34, 35]는 하기를 기재한다: 포도막염 환자에서 인터류킨-17A의 상승된 혈청 수준, 범포도막염과 IL17A 유전적 변이체의 특이적인 회합, 실험적 자가면역 포도막염의 발병에서 Th17-관련된 사이토카인의 역할, 단상 실험적 자가면역 포도막염 동안 Th17 세포와 조절 T 세포 사이 불균형, 포도막염 및 활성 아다만티아데스-베체트 및 포크트-고야나기-하라다 (VKH) 질환을 가진 환자에서 IL-17A의 상향조절, 세쿠키누맙 (항-IL-17A 항체)으로 비-감염성 포도막염의 치료, 및 포도막 눈에서의 Th17.

[0062] 특정 구현예에서, 포도막염은 후방 포도막염이다. 후방 포도막염은 망막 및 맥락막의 염증으로 주로 나타나고 그 예는 본 발명의 조성물이 망막 염증 및 손상 감소에 효과적인 것을 입증한다.

[0063] 특정 구현예에서, 본 발명의 조성물로 치료하면 망막 손상이 감소한다. 특정 구현예에서, 본 발명의 조성물은 포도막염의 치료에서 망막 손상을 감소시키거나 예방하는 데 사용하기 위한 것이다. 특정 구현예에서, 조성물은 망막 손상의 위험이 있는 중증 포도막염 환자를 치료하는 데 사용하기 위한 것이다. 특정 구현예에서, 본 발명의 조성물로 치료하면 시신경 유두 염증이 감소된다. 특정 구현예에서, 본 발명의 조성물은 시신경 유두 염증을 감소 또는 예방하는 데 사용하기 위한 것이다. 특정 구현예에서, 본 발명의 조성물로 치료하면 염증 세포에 의한 망막 조직 침윤이 감소된다. 특정 구현예에서, 본 발명의 조성물은 염증 세포에 의한 망막 조직 침윤의 감소

에 사용하기 위한 것이다. 특정 구현예에서, 본 발명의 조성물로 치료하면 시력이 유지되거나 개선된다. 특정 구현예에서, 본 발명의 조성물은 시력 유지 또는 개선에 사용하기 위한 것이다.

[0064] 특정 구현예에서, 조성물은 베체트 병, 크론 병, 푸치 이성변색 홍지모양체염, 다발 혈관염을 동반한 육아종증, HLA-B27 관련 포도막염, 청소년 특발성 관절염, 유육종증, 척추 관절염, 교감 신경 안검, 세뇨관 간질 신염 및 포도막염 증후군 또는 보그-고야나기-하라다 증후군과 같은 비-감염성 또는 자가면역 질환과 관련된 포도막염의 치료 또는 예방에 사용하기 위한 것이다. IL-17A는 예를 들어 베체트 및 보그-고야나기-하라다 질병에 관여하는 것으로 나타났다.

[0065] 포도막염의 치료 또는 예방은 예를 들어 증상의 중증도의 완화 또는 재발 방지를 의미할 수 있다.

[0066] *암*

[0067] 바람직한 구현예에서, 본 발명의 조성물은 암의 치료 또는 예방에 사용하기 위한 것이다. IL-17 및 Th17 경로는 암 발병 및 진행에서 중추적 역할을 갖고, 그래서 본 발명의 조성물은 암 치료 또는 예방에 유용할 수 있다.

[0068] 암에서 IL-17 및 Th17 세포의 역할이 완전히 이해되지 않아도, IL-17 및 Th17 세포의 수많은 전-종양 효과는 공지되어 있다. 예를 들어, Th17 세포 및 IL-17은 혈관신생을 촉진시킬 수 있고, 종양 세포의 증식 및 생존을 증가시킬 수 있고 종양-촉진 전사 인자를 활성화시킬 수 있다 [36, 37, 38].

[0069] 특정 구현예에서, 본 발명의 조성물을 사용한 치료는 종양 크기의 감소 또는 종양 성장의 감소를 초래한다. 특정 구현예에서, 본 발명의 조성물은 종양 크기를 감소시키거나 종양 성장을 감소시키는 데 사용하기 위한 것이다. 본 발명의 조성물은 종양 크기 또는 성장 감소에 효과적일 수 있다. .특정 구현예에서, 본 발명의 조성물은 고형 종양 환자에게 사용하기 위한 것이다. 특정 구현예에서, 본 발명의 조성물은 암 치료에서 혈관신생을 감소 또는 예방하는 데 사용하기 위한 것이다. IL-17 및 Th17 세포는 혈관신생에 중추적 역할을 한다. 특정 구현예에서, 본 발명의 조성물은 전이를 예방하는 데 사용하기 위한 것이다.

[0070] 특정 구현예에서, 본 발명의 조성물은 유방암의 치료 또는 예방에 사용하기 위한 것이다. 본 발명의 조성물은 유방암 치료에 효과적일 수 있고, IL-17 및 Th17 세포는 유방암에서 중요한 역할을 한다[39]. 특정 구현예에서, 본 발명의 조성물은 종양 크기 감소, 종양 성장 감소, 또는 유방암의 치료에서 혈관신생 감소에서 사용하기 위한 것이다. 바람직한 구현예에서, 암은 유방암이다. 바람직한 구현예에서, 암은 IV 기 유방암이다.

[0071] 특정 구현예에서, 본 발명의 조성물은 폐암의 치료 또는 예방에 사용하기 위한 것이다. 본 발명의 조성물은 폐암 치료에 효과적일 수 있고, IL-17 및 Th17 세포는 폐암에서 중요한 역할을 한다[40]. 특정 구현예에서, 본 발명의 조성물은 종양 크기 감소, 종양 성장 감소, 또는 폐암의 치료에서 혈관신생 감소에서 사용하기 위한 것이다. 바람직한 구현예에서, 암은 폐암이다.

[0072] 특정 구현예에서, 본 발명의 조성물은 간암의 치료 또는 예방에 사용하기 위한 것이다. 본 발명의 조성물은 간암 치료에 효과적일 수 있고, IL-17 및 Th17 세포는 간암에서 중요한 역할을 한다[41]. 특정 구현예에서, 본 발명의 조성물은 종양 크기 감소, 종양 성장 감소, 또는 간암의 치료에서 혈관신생 감소에서 사용하기 위한 것이다. 바람직한 구현예에서, 암은 간암(간세포 암종)이다.

[0073] 특정 구현예에서, 본 발명의 조성물은 암종의 치료 또는 예방에 사용하기 위한 것이다. 본 발명의 조성물은 암종 치료에 특히 효과적일 수 있다. 특정 구현예에서, 본 발명의 조성물은 비-면역원성 암을 치료 또는 예방하는 데 사용하기 위한 것이다. 본 발명의 조성물은 비-면역원성 암 치료에 효과적일 수 있다.

[0074] 추가 구현예에서, 본 발명의 조성물은 급성 림프아구성 백혈병(ALL), 급성 골수 백혈병, 부신피질 암종, 기저-세포 암종, 담도암, 방광암, 골 종양, 골육종/악성 섬유질 조직구종, 뇌간 신경아교종, 뇌종양, 소뇌 별아교세포종, 뇌 별아교세포종/악성 신경아교종, 뇌실막세포종, 수모세포종, 천막상 원시 신경외배엽성 종양, 유방암, 기관지 선종/카르시노이드, 버킷 림프종, 유암종, 자궁경부암, 만성 림프구성 백혈병, 만성 골수성 백혈병, 만성 골수증식성 장애, 결장암, 피부 T-세포 림프종, 자궁내막 암, 뇌실막세포종, 식도암, 유잉 육종, 안구내 흑색종, 망막모세포종, 담낭암, 위암, 위장 유암종, 위장 기질 종양(GIST), 생식세포 종양, 신경아교종, 소아기 시각적 경로 및 시상하부, 호지킨 림프종, 흑색종, 소도세포 암종, 카포시 육종, 신장 세포 암, 후두 암, 백혈병, 림프종, 중피종, 신경교세포종, 비-호지킨 림프종, 구강인두 암, 골육종, 난소암, 췌장암, 부갑상선암, 인두 암, 뇌하수체 샘종, 형질 세포 신조직형성, 전립선암, 신장 세포 암종, 망막모세포종, 육종, 고환암, 갑상선암, 또는 자궁암을 치료 또는 예방하는 데 사용하기 위한 것이다.

[0075] 본 발명의 조성물은 추가의 치료제와 조합하여 사용될 때 특히 효과적일 수 있다. 본 발명의 조성물의 면역-조

절 효과는 보다 직접적인 항암제와 조합될 때 효과적일 수 있다. 따라서, 특정 구현예에서, 본 발명은 속 에리시펠라토클로스트리디움의 박테리아 균주 및 항암제를 포함하는 조성물을 제공한다. 바람직한 구현예에서, 항암제는 면역 체크포인트 억제제, 표적 항체 면역요법, CAR-T 세포 요법, 온콜리틱 바이러스 또는 세포증식 억제제이다. 바람직한 구현예에서, 상기 조성물은 하기로 이루어진 군으로부터 선택된 항암제를 포함한다:Yervoy (이필리무맙, BMS); Keytruda (펨브롤리주맙, Merck); Opdivo (니볼루맙, BMS); MEDI4736(AZ/MedImmune); MPDL3280A(Roche/Genentech); 트레멜리무맙(AZ/MedImmune); CT-011(피딜리주맙, CureTech); BMS-986015(리릴루맙, BMS); MEDI0680(AZ/MedImmune); MSB-0010718C(Merck); PF-05082566(Pfizer); MEDI6469(AZ/MedImmune); BMS-986016(BMS); BMS-663513(우렐루맙, BMS); IMP321(Prima Biomed); LAG525(Novartis); ARGX-110(arGEN-X); PF-05082466(Pfizer); CDX-1127(바릴루맙; CellDex Therapeutics); TRX-518(GITR Inc.);MK-4166 (Merck); JTX-2011 (Jounce Therapeutics); ARGX-115 (arGEN-X); NLG-9189 (인독시모드, NewLink Genetics); INCB024360 (Incyte); IPH2201 (Innate Immotherapeutics/AZ); NLG-919 (NewLink Genetics); 항-VISTA (JnJ); Epacadostat (INCB24360, Incyte); F001287 (Flexus/BMS); CP 870893 (University of Pennsylvania); MGA271 (Macrogenix); 에막투주맙 (Roche/Genentech); 갈루니세르팁 (Eli Lilly); 울로쿠플루맙 (BMS); BKT140/BL8040 (Biokine Therapeutics); 바비툭시맙 (Peregrine Pharmaceuticals); CC 90002 (Celgene); 852A (Pfizer); VTX-2337 (VentiRx Pharmaceuticals); IMO-2055 (Hybridon, Idera Pharmaceuticals); LY2157299 (Eli Lilly); EW-7197 (Ewha Women's University, Korea); 베무라페닙 (Plexxikon); 다브라페닙 (Genentech/GSK); BMS-777607 (BMS); BLZ945 (Memorial Sloan-Kettering Cancer Centre); Unituxin (디누툭시맙, United Therapeutics Corporation); Blincyto (블리나투모맙, Amgen); Cyramza (라무시루맙, Eli Lilly); Gazyva (오비누투주맙, Roche/Biogen); Kadcyla (아도-트라스투주맙 엠탄신, Roche/Genentech); Perjeta (페르투주맙, Roche/Genentech); Adcetris (브렌툭시맙 베도틴, Takeda/Millennium); Arzerra (오파투무맙, GSK); Vectibix (파니투무맙, Amgen); Avastin (베바시주맙, Roche/Genentech); Erbitux (세툭시맙, BMS/Merck); Bexxar (토시투모맙-I131, GSK); Zevalin (이브리투모맙 티욱세탄, Biogen); Campath (알렘투주맙, Bayer); Mylotarg (젬투주맙 오조가마이신, Pfizer); Herceptin (트라스투주맙, Roche/Genentech); Rituxan (리툭시맙, Genentech/Biogen); 볼록식시맙 (Abbvie); 에나바투주맙 (Abbvie); ABT-414 (Abbvie); 엘로투주맙 (Abbvie/BMS); ALX-0141 (Ablynx); 오자랄리주맙 (Ablynx); 악티맙-C (Actinium); 악티맙-P (Actinium); 밀라투주맙-독스 (Actinium); Emab-SN-38 (Actinium); 납투몬맙 에스타페나톡스 (Active Biotech); AFM13 (Affimed); AFM11 (Affimed); AGS-16C3F (Agensys); AGS-16M8F (Agensys); AGS-22ME (Agensys); AGS-15ME (Agensys); GS-67E (Agensys); ALXN6000 (samalizumab, Alexion); ALT-836 (Altor Bioscience); ALT-801 (Altor Bioscience); ALT-803 (Altor Bioscience); AMG780 (Amgen); AMG 228 (Amgen); AMG820 (Amgen); AMG172 (Amgen); AMG595 (Amgen); AMG110 (Amgen); AMG232 (아데카투무맙, Amgen); AMG211 (Amgen/MedImmune); BAY20-10112 (Amgen/Bayer); 릴로투무맙 (Amgen); 데노수맙 (Amgen); AMP-514 (Amgen); MEDI575 (AZ/MedImmune); MEDI3617 (AZ/MedImmune); MEDI6383 (AZ/MedImmune); MEDI551 (AZ/MedImmune); 목세투무맙 파수도톡스 (AZ/MedImmune); MEDI565 (AZ/MedImmune); MEDI0639 (AZ/MedImmune); MEDI0680 (AZ/MedImmune); MEDI562 (AZ/MedImmune); AV-380 (AVEO); AV203 (AVEO); AV299 (AVEO); BAY79-4620 (Bayer); 아네투맙 라브탄신 (Bayer); 반틱투맙 (Bayer); BAY94-9343 (Bayer); 시브로투주맙 (Boehringer Ingleheim); BI-836845 (Boehringer Ingleheim); B-701 (BioClin); BIIB015 (Biogen); 오비누투주맙 (Biogen/Genentech); BI-505 (Bioinvent); BI-1206 (Bioinvent); TB-403 (Bioinvent); BT-062 (Biotest) BIL-010t (Biosceptre); MDX-1203 (BMS); MDX-1204 (BMS); 네시투무맙 (BMS); CAN-4 (Cantargia AB); CDX-011 (Celldex); CDX1401 (Celldex); CDX301 (Celldex); U3-1565 (Daiichi Sankyo); 파트리투맙 (Daiichi Sankyo); 티가투주맙 (Daiichi Sankyo); 니모투주맙 (Daiichi Sankyo); DS-8895 (Daiichi Sankyo); DS-8873 (Daiichi Sankyo); DS-5573 (Daiichi Sankyo); MORab-004 (Eisai); MORab-009 (Eisai); MORab-003 (Eisai); MORab-066 (Eisai); LY3012207 (Eli Lilly); LY2875358 (Eli Lilly); LY2812176 (Eli Lilly); LY3012217(Eli Lilly); LY2495655 (Eli Lilly); LY3012212 (Eli Lilly); LY3012211 (Eli Lilly); LY3009806 (Eli Lilly); 식수투무맙 (Eli Lilly); 플란보투맙 (Eli Lilly); IMC-TR1 (Eli Lilly); 라무시루맙 (Eli Lilly); 타발루맙 (Eli Lilly); 자놀리무맙 (Emergent Biosolution); FG-3019 (FibroGen); FPA008 (Five Prime Therapeutics); FP-1039 (Five Prime Therapeutics); FPA144 (Five Prime Therapeutics); 카투막소맙 (Fresenius Biotech); IMAB362 (Ganymed); IMAB027 (Ganymed); HuMax-CD74 (Genmab); HuMax-TFADC (Genmab); GS-5745 (Gilead); GS-6624 (Gilead); OMP-21M18 (demcizumab, GSK); 마파투무맙 (GSK); IMGN289 (ImmunoGen); IMGN901 (ImmunoGen); IMGN853 (ImmunoGen); IMGN529 (ImmunoGen); IMMU-130 (Immunomedics); 밀라투주맙-독스 (Immunomedics); IMMU-115 (Immunomedics); IMMU-132 (Immunomedics); IMMU-106 (Immunomedics); IMMU-102 (Immunomedics); 에프라투주맙 (Immunomedics); 클리바투주맙 (Immunomedics); IPH41 (Innate Immunotherapeutics); 다라투무맙

(Janssen/Genmab); CNTO-95 (인테투무맙, Janssen); CNTO-328 (실툭시맙, Janssen); KB004 (KaloBios); 모가물리주맙 (Kyowa Hakko Kirrin); KW-2871 (에크로멕시맙, Life Sciennce); 소네프시주맙 (Lpath); 마르게툭시맙 (Macrogenics); 에노블리투주맙 (Macrogenics); MGD006 (Macrogenics); MGF007 (Macrogenics); MK-0646 (달로투주맙, Merck); MK-3475 (Merck); Sym004 (Symphogen/Merck Serono); DI17E6 (Merck Serono); MOR208 (Morphosys); MOR202 (Morphosys); Xmab5574 (Morphosys); BPC-1C (엔시툭시맙, Precision Biologics); TAS266 (Novartis); LFA102 (Novartis); BHQ880 (Novartis/Morphosys); QGE031 (Novartis); HCD122 (루카투무맙, Novartis); LJM716 (Novartis); AT355 (Novartis); OMP-21M18 (뎀시주맙, OncoMed); OMP52M51 (Oncomed/GSK); OMP-59R5 (Oncomed/GSK); 반틱투맙 (Oncomed/Bayer); CMC-544 (이노투주맙 오조가마이신, Pfizer); PF-03446962 (Pfizer); PF-04856884 (Pfizer); PSMA-ADC (Progenics); REGN1400 (Regeneron); REGN910 (네스바쿠맙, Regeneron/Sanofi); REGN421 (에노티쿠맙, Regeneron/Sanofi); RG7221, RG7356, RG7155, RG7444, RG7116, RG7458, RG7598, RG7599, RG7600, RG7636, RG7450, RG7593, RG7596, DCDS3410A, RG7414 (파르사투주맙), RG7160 (임가투주맙), RG7159 (오빈투주맙), RG7686, RG3638 (오나투주맙), RG7597 (Roche/Genentech); SAR307746 (Sanofi); SAR566658 (Sanofi); SAR650984 (Sanofi); SAR153192 (Sanofi); SAR3419 (Sanofi); SAR256212 (Sanofi), SGN-LIV1A (린투주맙, Seattle Genetics); SGN-CD33A (Seattle Genetics); SGN-75 (보르세투주맙 마포도틴, Seattle Genetics); SGN-19A (Seattle Genetics) SGN-CD70A (Seattle Genetics); SEA-CD40 (Seattle Genetics); 이브리투모맙 티욱세탄 (Spectrum); MLN0264 (Takeda); 가니투맙 (Takeda/Amgen); CEP-37250 (Teva); TB-403 (Thrombogenic); VB4-845 (Viventia); Xmab2512 (Xencor); Xmab5574 (Xencor); 니모투주맙 (YM Biosciences); Carlumab (Janssen); NY-ESO TCR (Adaptimmune); MAGE-A-10 TCR (Adaptimmune); CTL019 (Novartis); JCAR015 (Juno Therapeutics); KTE-C19 CAR (Kite Pharma); UCART19 (Cellectis); BPX-401 (Bellicum Pharmaceuticals); BPX-601 (Bellicum Pharmaceuticals); ATTCK20 (Unum Therapeutics); CAR-NKG2D (Celyad); Onyx-015 (Onyx Pharmaceuticals); H101 (Shanghai Sunwaybio); DNX-2401 (DNAtrix); VCN-01 (VCN Biosciences); Colo-Ad1 (PsiOxus Therapeutics); ProstAtak (Advantagene); Oncos-102 (Oncos Therapeutics); CG0070 (Cold Genesys); Pexa-vac (JX-594, Jennerex Biotherapeutics); GL-ONC1 (Genelux); T-VEC (Amgen); G207 (Medigene); HF10 (Takara Bio); SEPREHVIR (HSV1716, Virttu Biologics); OrienX010 (OrienGene Biotechnology); Reolysin (Oncolytics Biotech); SVV-001 (Neotropix); Cacatak (CVA21, Viralytics); Alimta (Eli Lilly), 시스플라틴, 옥살리플라틴, 이리노테칸, 폴린산, 메토트렉세이트, 사이클로포스파마이드, 5-플루오로우라실, Zykadia (Novartis), Tafinlar (GSK), Xalkori (Pfizer), Iressa (AZ), Gilotrif (Boehringer Ingelheim), Tarceva (Astellas Pharma), Halaven (Eisai Pharma), Veliparib (Abbvie), AZD9291 (AZ), Alectinib (Chugai), LDK378 (Novartis), Genetespib (Synta Pharma), Tergenpumatucel-L (NewLink Genetics), GV1001 (Kael-GemVax), Tivantinib (ArQule); Cytoxan (BMS); Oncovin (Eli Lilly); Adriamycin (Pfizer); Gemzar (Eli Lilly); Xeloda (Roche); Ixempra (BMS); Abraxane (Celgene); Trelstar (Debiopharm); Taxotere (Sanofi); Nexavar (Bayer); IMMU-132 (Immunomedics); E7449 (Eisai); Thermodox (Celsion); Cometriq (Exellxis); Lonsurf (Taiho Pharmaceuticals); Camptosar (Pfizer); UFT (Taiho Pharmaceuticals); 및 TS-1 (Taiho Pharmaceuticals).

[0076] 일부 구현예에서, 하나 이상의 *에리시펠라토클로스트리디움* 박테리아 균주는 본 발명의 조성물에서 단지 치료적으로 활성제(들)이다. 일부 구현예에서, 조성물에서 박테리아 균주(들)은 본 발명의 조성물에서 단지 치료적으로 활성제(들)이다.

[0077] *천식*

[0078] 바람직한 구현예에서, 본 발명의 조성물은 천식의 치료 또는 예방에 사용하기 위한 것이다. 본 발명의 조성물은 집먼지 진드기 추출물로 감작화 및 공격 이후 기도 내부에 호중구 및/또는 호산구의 동원에서 감소를 달성할 수 있고 그래서 이들은 천식의 치료 또는 예방에서 유용할 수 있다. 천식은 염증과 기도의 제한을 특징으로 하는 만성 질환이다. 천식에서의 염증은 IL-17 및/또는 Th17 세포에 의해 매개될 수 있고, 따라서 본 발명의 조성물은 천식의 예방 또는 치료에 특히 효과적일 수 있다. 천식의 염증은 호산구 및/또는 호중구에 의해 매개될 수 있다.

[0079] 특정 구현예에서, 천식은 호산구성 또는 알레르기성 천식이다. 호산구성 및 알레르기성 천식은 말초 혈액 및 기도 분비의 호산구 수가 증가하고 병리학적으로 기저막 부위가 두꺼워지고 약리학적으로 코르티코스테로이드 반응성과 관련이 있다 [42]. 호산구 모집 또는 활성화를 감소시키거나 억제하는 조성물은 호산구성 및 알레르기성 천식을 치료 또는 예방하는 데 유용할 수 있다.

[0080] 추가의 구현예에서, 본 발명의 조성물은 호중구성 천식(또는 비-호산구성 천식)의 치료 또는 예방에 사용하기

위한 것이다. 호중구 수가 많으면 코티코스테로이드 치료에 민감하지 않은 심각한 천식이 동반된다. 호중구 모집 또는 활성화를 감소시키거나 억제하는 조성물은 호중구성 천식을 치료 또는 예방하는 데 유용할 수 있다.

[0081] 호산구성 및 호중구성 천식은 상호 배타적인 조건이 아니며 호산구와 호중구 반응을 다루는 치료법은 일반적으로 천식 치료에 유용할 수 있다.

[0082] 증가된 IL-17 수준 및 Th17 경로의 활성화는 심한 천식과 관련되기 때문에, 본 발명의 조성물은 중증 천식의 발병을 예방하거나 중증 천식 치료에 유용할 수 있다.

[0083] 특정 구현예에서, 본 발명의 조성물은 천식의 치료 또는 예방에서 호산구성 염증 반응을 감소시키는 방법에 사용하거나, 또는 천식의 치료 또는 예방에서 호중구성 염증 반응을 감소시키는 방법에 사용하기 위한 것이다. 위에서 언급했듯이, 천식의 호산구 수치가 높으면 병리학적으로 기저막 부위가 두꺼워지므로 천식 치료 또는 예방에서 호산구성 염증 반응을 감소시키는 것이 이 질병의 특징을 구체적으로 다룰 수 있다. 또한 상승된 호중구는 호산구 증가와 함께 또는 부재시에 중증 천식 및 만성 기도 협착과 관련이 있다. 따라서 호중구성 염증 반응을 감소시키는 것은 중증 천식을 치료할 때 특히 유용할 수 있다.

[0084] 특정 구현예에서, 조성물은 알레르기성 천식에서의 기관지주위 침윤을 감소시키거나, 알레르기성 천식의 치료에서 기관지주위 침윤을 감소시키는 데 사용하기 위한 것이다. 특정 구현예에서, 조성물은 호중구성 천식에서 기관지주위 및/또는 혈관주위 침윤을 감소시키거나, 알레르기성 호중구성 천식의 치료에서 기관지주위 및/또는 혈관주위 침윤을 감소시키는 데 사용하기 위한 것이다.

[0085] 특정 구현예에서, 본 발명의 조성물로 치료는 TNFα 수준에서 감소를 제공하거나 상승을 방지한다.

[0086] 특정 구현예에서, 본 발명의 조성물은 호산구성 및/또는 호중구성 염증 반응의 감소를 초래하는 천식 치료 방법에 사용하기 위한 것이다. 특정 구현예에서, 치료될 환자는 예를 들어 혈액 샘플링 또는 객담 분석을 통해 확인된 바와 같이, 상승된 호중구 또는 호산구 수치를 갖거나 이전에 확인된 것이다.

[0087] 본 발명의 조성물은 신생아 또는 임산부에게 투여될 때 신생아에서 천식 발병을 예방하는 데 유용할 수 있다. 상기 조성물은 소아 천식의 발병을 예방하는 데 유용할 수 있다. 본 발명의 조성물은 성인-발병 천식을 치료 또는 예방하는 데 유용할 수 있다. 본 발명의 조성물은 천식을 관리하거나 경감시키는 데 유용할 수 있다. 본 발명의 조성물은 집먼지 진드기와 같은 알레르겐에 의해 악화되는 천식과 관련된 증상을 감소시키는 데 특히 유용할 수 있다.

[0088] 천식의 치료 또는 예방은 예를 들어 증상의 중증도의 완화 또는 악화 빈도의 감소 또는 환자에게 문제가 되는 유발인자의 범위를 나타낼 수 있다.

[0089] *관절염*

[0090] 바람직한 구현예에서, 본 발명의 조성물은 류마티스성 관절염(RA)의 치료 또는 예방에 사용하기 위한 것이다. 본 발명의 조성물은 마우스 모델에서 RA의 임상 징후에서의 감소를 달성할 수 있고, 연골 및 골 손상을 감소시킬 수 있고, IL-17 염증 반응을 감소시킬 수 있고, 그래서 이들은 RA의 치료 또는 예방에서 유용할 수 있다. RA는 주로 관절에 영향을 미치는 전신성 염증 질환이다. RA는 관절의 팽윤, 활막의 과형성 및 연골과 뼈의 파괴를 가져오는 염증 반응과 관련이 있다. 예를 들어, IL-17은 연골 세포와 골아 세포에서의 매트릭스 생산을 억제하고 매트릭스 메탈로프로티나아제의 생산과 기능을 활성화시키고 RA 질병 활성은 IL-17 수준 및 Th17 세포수와 상호 관련되기 때문에 IL-17과 Th17 세포는 RA에서 중요한 역할을 할 수 있으며[43, 44], 따라서 본 발명의 조성물은 RA의 예방 또는 치료에 특히 효과적일 수 있다.

[0091] 특정 구현예에서, 본 발명의 조성물은 RA의 치료 또는 예방에서 IL-17 수준을 낮추거나 IL-17 수준의 상승을 방지하는 데 사용하기 위한 것이다. 특정 구현예에서, 본 발명의 조성물로 처리하면 IL-17 수준, 특히 IL-17A 수준의 감소를 제공하거나 상승을 방지한다. 특정 구현예에서, 본 발명의 조성물을 사용한 치료는 IFN-γ 또는 IL-6 수준의 감소를 제공하거나 상승을 방지한다.

[0092] 특정 구현예에서, 본 발명의 조성물로 치료하면 관절의 팽윤이 감소한다. 특정 구현예에서, 본 발명의 조성물은 관절이 부어 오른 환자 또는 관절이 부어질 위험이 있는 환자에게 사용하기 위한 것이다. 특정 구현예에서, 본 발명의 조성물은 RA에서 관절 팽윤을 감소시키는 방법에 사용하기 위한 것이다.

[0093] 특정 구현예에서, 본 발명의 조성물로 치료하면 연골 손상 또는 골 손상이 감소된다. 특정 구현예에서, 본 발명의 조성물은 RA의 치료에서 연골 또는 골 손상을 감소 또는 예방하는 데 사용하기 위한 것이다. 특정 구현예에

서, 조성물은 연골 또는 뼈 손상의 위험이 있는 중증의 RA 환자를 치료하는 데 사용하기 위한 것이다.

[0094] 증가된 IL-17 수준과 Th17 세포수는 RA에서 연골과 뼈 파괴와 관련이 있다[43,44]. IL-17은 연골과 뼈 조직에서 기질 파괴를 활성화시키는 것으로 알려져 있으며 IL-17은 연골 세포와 골아 세포에서 기질 생산에 억제 효과가 있다. 따라서, 특정 구현예에서, 본 발명의 조성물은 RA의 치료에서 골 침식 또는 연골 손상을 예방하는 데 사용하기 위한 것이다. 특정 구현예에서, 조성물은 골 침식 또는 연골 손상을 나타내는 환자 또는 골 침식 또는 연골 손상의 위험이 있는 것으로 확인된 환자를 치료하는 데 사용하기 위한 것이다.

[0095] TNF-α는 또한 RA와 연관되어 있지만 TNF-α는 질병의 후기 단계의 발병 기전에 관여하지 않는다. 대조적으로, IL-17은 만성 질환의 모든 단계에서 역할을 한다[45]. 따라서, 특정 구현예에서, 본 발명의 조성물은 만성 RA 또는 연골의 관절 파괴 및 손실을 포함하는 질병과 같은 말기 RA의 치료에 사용하기 위한 것이다. 특정 구현예에서, 본 발명의 조성물은 이전에 항-TNF-α 치료법을 받은 환자를 치료하기 위한 것이다. 특정 구현예에서, 치료될 환자는 항-TNF-α 치료법에 반응하지 않거나 더 이상 반응하지 않는다.

[0096] 본 발명의 조성물은 환자의 면역계를 조절하는 데 유용할 수 있기 때문에, 특정 구현예에서, 본 발명의 조성물은 RA의 위험이 있다고 밝혀지거나 초기 단계 RA로 진단된 환자에서 RA를 예방하는 데 사용하기 위한 것이다. 본 발명의 조성물은 RA의 발생을 예방하는 데 유용할 수 있다.

[0097] 본 발명의 조성물은 RA를 관리하거나 경감시키는 데 유용할 수 있다. 본 발명의 조성물은 관절 팽윤 또는 골 파괴와 관련된 증상을 감소시키는 데 특히 유용할 수 있다. RA의 치료 또는 예방은 예를 들어 증상의 중증도의 완화 또는 악화 빈도의 감소 또는 환자에게 문제가 되는 유발 요인의 범위를 나타낼 수 있다.

[0098] *다발성 경화증*

[0099] 바람직한 구현예에서, 본 발명의 조성물은 다발성 경화증의 치료 또는 예방에 사용하기 위한 것이다. 본 발명의 조성물은 다발성 경화증의 마우스 모델 (EAE 모델)에서 질환 발병률 및 질환 중증도에서의 감소를 달성할 수 있고, 그래서 이들은 다발성 경화증의 치료 또는 예방에서 유용할 수 있다. 다발성 경화증은 특히 뇌와 척수에서의 신경 세포의 수초 외피에 손상을 일으키는 염증성 질환이다. 다발성 경화증은 만성 질환으로 점차적으로 무력화되고 에피소드로 진화한다. 예를 들어 IL-17 수치가 다발성 경화증 병변과 관련이 있고 IL-17이 혈액 뇌 장벽 내피 세포 결막을 파괴할 수 있고 Th17 세포가 중심 신경계로 이동하여 신경 손실을 일으킬 수 있기 때문에 IL-17 및 Th17 세포는 다발성 경화증에서 핵심적인 역할을 할 수 있다[46, 47]. 따라서, 본 발명의 조성물은 다발성 경화증의 예방 또는 치료에 특히 효과적일 수 있다.

[0100] 특정 구현예에서, 본 발명의 조성물로 치료하면 질병 발병 또는 질병 중증도가 감소한다. 특정 구현예에서, 본 발명의 조성물은 질병 발병 또는 질병 중증도를 감소시키는 데 사용하기 위한 것이다. 특정 구현예에서, 본 발명의 조성물로 치료하면 운동 기능의 저하가 방지되거나 운동 기능이 향상된다. 특정 구현예에서, 본 발명의 조성물은 운동 기능의 저하 또는 운동 기능의 개선에 사용하기 위한 것이다. 특정 구현예에서, 본 발명의 조성물로 치료하면 마비의 발병을 예방할 수 있다. 특정 구현예에서, 본 발명의 조성물은 다발성 경화증의 치료에서 마비를 예방하는 데 사용하기 위한 것이다.

[0101] 본 발명의 조성물은 환자의 면역계를 조절하는 데 유용할 수 있으며, 따라서 특정 구현예에서, 본 발명의 조성물은 다발성 경화증의 위험이 있는 것으로 확인되었거나 초기 단계의 다발성 경화증 또는 "재발-완화형" 다발성 경화증으로 진단된 환자에서 다발성 경화증을 예방하는 데 사용하기 위한 것이다. 본 발명의 조성물은 경화증 발병을 예방하는데 유용할 수 있다.

[0102] 본 발명의 조성물은 다발성 경화증을 치료 또는 경감시키는 데 유용할 수 있다. 본 발명의 조성물은 다발성 경화증과 관련된 증상을 감소시키는 데 특히 유용할 수 있다. 다발성 경화증의 치료 또는 예방은 예를 들어 증상의 중증도의 완화 또는 악화 빈도의 감소 또는 환자에게 문제가 되는 유발 인자의 범위를 나타낼 수 있다.

[0103] ***투여 방식***

[0104] 바람직하게는, 본 발명의 조성물은 본 발명의 박테리아 균주로 장내 수송 및/또는 부분적 또는 전체 콜로니화를 가능하게 하기 위해 위장관에 투여될 수 있다. 일반적으로, 본 발명의 조성물은 경구 투여되지만, 직장, 비내, 또는 협측 또는 설하 경로를 통해 투여될 수 있다.

[0105] 특정 구현예에서, 본 발명의 조성물은 발포체로서, 스프레이 또는 겔로서 투여될 수 있다.

[0106] 특정 구현예에서, 본 발명의 조성물은 예를 들어 테오브로마 오일(코코아 버터), 합성 경질 지방(예를 들어, 붕

해제, 위텝솔), 글리세로-젤라틴, 폴리에틸렌 글리콜, 또는 비누 글리세린 조성물의 형태로 직장 좌약과 같은 좌약으로서 투여될 수 있다.

[0107] 특정 구현예에서, 본 발명의 조성물은 비위관, 위관, 위선, 공막 절개관(J 관), 경피 내시경 위장관(PEG), 또는 포트 예컨대 위장, 공장 및 기타 적합한 액세스 포트에 대한 액세스를 제공하는 흉벽 포트와 같은 관을 통해 위장관으로 투여된다.

[0108] 본 발명의 조성물은 한번 투여될 수 있거나, 치료 요법의 일부로서 순차적으로 투여될 수 있다. 특정 구현예에서, 본 발명의 조성물은 매일 투여될 수 있다.

[0109] 본 발명의 특정 구현예에서, 본 발명에 따른 치료는 환자의 장내 미생물의 평가를 동반한다. 본 발명의 균주로의 수송 및/또는 부분적 또는 전체 콜로니화가 달성되지 않아 유효성이 관찰되지 않는 경우 치료는 반복되거나 또는 수송 및/또는 부분적 또는 전체 콜로니화가 성공적으로 이루어지고 효능이 관찰되는 경우 치료는 중단될 수 있다.

[0110] 특정 구현예에서, 본 발명의 조성물은 *자궁속* 및/또는 태어난 후에 아이에서 발생하는 염증성 또는 자가면역 질환을 예방하기 위해 임신 동물 예를 들어 인간과 같은 포유동물에 투여될 수 있다.

[0111] 본 발명의 조성물은 IL-17 또는 Th17 경로에 의해 매개되는 질병 또는 병태로 진단되거나 IL-17 또는 Th17 경로에 의해 매개되는 질병 또는 병태의 위험이 있는 것으로 확인된 환자에게 투여될 수 있다. 상기 조성물은 또한 건강한 환자에서 IL-17 또는 Th17 경로에 의해 매개되는 질병 또는 증상의 발병을 예방하기 위한 예방적 조치로서 투여될 수 있다.

[0112] 본 발명의 조성물은 비정상적인 내장 미생물을 갖는 것으로 확인된 환자에게 투여될 수 있다. 예를 들어, 환자는 *에리시펠라토클로스트리디움*에 의해 감소된 또는 결여된 군집화를 가질 수 있다.

[0113] 본 발명의 조성물은 영양 보충제와 같은 식품으로 투여될 수 있다.

[0114] 일반적으로, 본 발명의 조성물은 가금류, 돼지, 고양이, 개, 말 또는 토끼와 같은 단포 포유동물을 비롯한 동물을 치료하는 데 사용될 수 있지만, 인간의 치료를 위한 것이다. 본 발명의 조성물은 동물의 성장 및 성능을 향상시키는 데 유용할 수 있다. 동물에게 투여하면, 경구용 위관 영양법을 사용할 수 있다.

[0115] ***조성물***

[0116] 일반적으로, 본 발명의 조성물은 박테리아를 포함한다. 본 발명의 바람직한 구현예에서, 조성물은 동결-건조된 형태로 제형화된다. 예를 들어, 본 발명의 조성물은 본 발명의 박테리아 균주를 포함하는 과립 또는 젤라틴 캡슐 예를 들어 경질 젤라틴 캡슐을 포함할 수 있다.

[0117] 바람직하게는, 본 발명의 조성물은 동결 건조된 박테리아를 포함한다. 박테리아의 동결 건조는 잘 확립된 절차이며 관련 지침은 예를 들어 참고문헌[48, 49, 50]에서 얻을 수 있다.

[0118] 대안적으로, 본 발명의 조성물은 살아있는 활성 박테리아 배양물을 포함할 수 있다.

[0119] 일부 구현예에서, 본 발명의 조성물에서 박테리아 균주는 불활성화되지 않았고, 예를 들어, 열-불활성화되지 않았다. 일부 구현예에서, 본 발명의 조성물에서 박테리아 균주는 사멸되지 않았고, 예를 들어, 열-사멸되지 않았다. 일부 구현예에서, 본 발명의 조성물에서 박테리아 균주는 약화되지 않았고, 예를 들어, 열-약화되지 않았다. 예를 들어, 일부 구현예에서, 본 발명의 조성물에서 박테리아 균주는 사멸, 불활성화 및/또는 약화되지 않았다. 예를 들어, 일부 구현예에서, 본 발명의 조성물에서 박테리아 균주는 살아있다. 예를 들어, 일부 구현예에서, 본 발명의 조성물에서 박테리아 균주는 생존가능하다. 예를 들어, 일부 구현예에서, 본 발명의 조성물에서 박테리아 균주는 장에서 부분적으로 또는 전적으로 군집할 수 있다. 예를 들어, 일부 구현예에서, 본 발명의 조성물에서 박테리아 균주는 생존가능하고 장에서 부분적으로 또는 전적으로 군집할 수 있다.

[0120] 일부 구현예에서, 조성물은 살아있는 박테리아 균주 및 사멸되어 있는 박테리아 균주의 혼합물을 포함한다.

[0121] 바람직한 구현예에서, 본 발명의 조성물은 박테리아 균주를 장내로 수송할 수 있도록 캡슐화된다. 캡슐화는 예를 들어 압력, 효소 활성 또는 pH의 변화에 의해 유발될 수 있는 물리적 붕괴와 같은 화학적 또는 물리적 자극에 의한 파열을 통해 표적 위치로 수송될 때까지 조성물이 분해되지 않도록 보호한다. 임의의 적절한 캡슐화 방법이 사용될 수 있다. 예시적인 캡슐화 기술은 다공성 매트릭스 내의 포착, 고체 담체 표면상의 부착 또는 흡착, 응집 또는 가교 결합제에 의한 자기 응집 및 미세다공성 막 또는 마이크로캡슐 후의 기계적 봉쇄를 포함

한다. 본 발명의 조성물을 제조하는 데 유용한 캡슐화에 대한 지침은 예를 들어 참고문헌 [51] 및 [52]에서 이용가능하다.

[0122] 상기 조성물은 경구 투여될 수 있고, 정제, 캡슐 또는 분말의 형태일 수 있다. 캡슐화된 생성물이 바람직한 것은 *에리시펠라토클로스트리디움 라모숨* 이 산소성생물이기 때문이다. 기타 성분(예컨대, 비타민 C, 예를 들어)은 *생체 내에서* 수송 및/또는 부분적 또는 전체 콜로니화 및 생존을 개선하기 위해 산소 제거제 및 프리바이오틱 기질로서 포함될 수 있다. 대안적으로, 본 발명의 프로바이오틱 조성물은 우유 또는 유청 기반의 발효 낙농 제품과 같은 식품 또는 영양 제품 또는 의약품으로서 경구 투여될 수 있다.

[0123] 상기 조성물은 프로바이오틱으로 제형화될 수 있다.

[0124] 본 발명의 조성물은 치료 유효량의 본 발명의 박테리아 균주를 포함한다. 치료 유효량의 박테리아 균주는 환자에게 유익한 효과를 발휘하기에 충분하다. 박테리아 균주의 치료학적 유효량은 환자의 장내 수송 및/또는 부분적 또는 전체 콜로니화를 초래하기에 충분할 수 있다.

[0125] 예를 들어, 성인 인간에 대한 박테리아의 적합한 일일 투여량은 약 1×10^{3} 내지 약 1×10^{11} 콜로니 형성 단위(CFU)일 수 있고; 예를 들어, 약 1×10^{7} 내지 약 1×10^{10} CFU; 다른 예에서는 약 1×10^{6} 내지 약 1×10^{10} CFU이다.

[0126] 특정 구현예에서, 조성물은 조성물의 중량에 대하여 약 1×10^{6} 내지 약 1×10^{11} CFU/g의 양으로 박테리아 균주를 함유한다; 예를 들어, 약 1×10^{8} 내지 약 1×10^{10} CFU/g이다. 투여량은 예를 들어 1g, 3g, 5g 및 10g일 수 있다.

[0127] 전형적으로, 본 발명의 조성물과 같은 프로바이오틱은 임의로 적어도 하나의 적합한 프리바이오틱 화합물과 배합된다. 프리바이오틱 화합물은 일반적으로 올리고- 또는 폴리사카라이드 또는 설탕 알코올과 같은 비-소화성 탄수화물이며, 이는 상부 소화관에서 분해되거나 흡수되지 않는다. 공지의 프리바이오틱은 이눌린 및 트랜스갈락토-올리고사카라이드와 같은 시판 중인 제품을 포함한다.

[0128] 특정 구현예에서, 본 발명의 프로바이오틱 조성물은 총 중량 조성물에 대해 약 1 내지 약 30 중량%(예를 들어, 5 내지 20 중량%)의 양으로 프리바이오틱 화합물을 포함한다. 탄수화물은 하기로 이루어진 군으로부터 선택될 수 있다:프룩토-올리고사카라이드(또는 FOS), 단쇄 프룩토-올리고사카라이드, 이눌린, 이소말토-올리고사카라이드, 펙틴, 자일로-올리고사카라이드(또는 XOS), 키토산-올리고사카라이드(또는 COS), 베타-글루칸, 경질 검 개질 및 저항성 전분, 폴리덱스트로스, D-타가토스, 아카시아 섬유, 캐롭, 귀리 및 감귤류 섬유.하나의 측면에서, 프리바이오틱은 단쇄 프룩토오스-올리고사카라이드(이하, 간단히 FOSs-c.c로 나타냄)이다; 상기 FOSs-c.c는 일반적으로 사탕무 설탕의 전환에 의해 얻어지고 3개의 글루코오스 분자가 결합된 사카로스 분자를 포함하는 소화가 가능한 탄수화물은 아니다.

[0129] 본 발명의 조성물은 약학적으로 허용가능한 부형제 또는 담체를 포함할 수 있다. 적합한 부형제의 예는 참고문헌 [53]에서 확인할 수 있다. 치료적 사용을 위한 허용가능한 담체 또는 희석제는 약학 분야에 잘 알려져 있으며, 예를 들어 문헌 [54]에 기재되어 있다. 적합한 담체의 예로는 락토오스, 전분, 글루코오스, 메틸 셀룰로오스, 마그네슘 스테아레이트, 만니톨, 솔비톨 등이 포함된다. 적합한 희석제의 예는 에탄올, 글리세롤 및 물을 포함한다. 약학적 담체, 부형제 또는 희석제의 선택은 의도된 투여 경로 및 표준 약제 실습과 관련하여 선택될 수 있다. 약학적 조성물은 담체, 부형제 또는 희석제로서 또는 이들 외에 임의의 적합한 결합제, 윤활제, 현탁화제, 코팅제, 가용화제를 포함할 수 있다. 적합한 결합제의 예는 전분, 젤라틴, 천연 당류 예컨대 글루코오스, 무수 락토오스, 자유-유동 락토오스, 베타-락토오스, 옥수수 감미료, 천연 및 합성 검 예컨대 아카시아, 트라가칸트 또는 나트륨 알기네이트, 카복시메틸 셀룰로오스 및 폴리에틸렌 글리콜을 포함한다. 적합한 윤활제의 예로는 올레산 나트륨, 스테아린산 나트륨, 스테아린산 마그네슘, 안식향산 나트륨, 아세트산 나트륨, 염화나트륨 등이 포함된다. 보존제, 안정화제, 염료 및 향미제조차도 약학 조성물 중에 제공될 수 있다. 보존제의 예는 나트륨 벤조에이트, 소르브산 및 p-하이드록시벤조산의 에스테르를 포함한다. 항산화제 및 현탁화제가 또한 사용될 수 있다.

[0130] 본 발명의 조성물은 식품으로서 제형화될 수 있다. 예를 들어, 식품은 영양 보충제와 같이 본 발명의 치료 효과 이외에 영양적인 이득을 제공할 수 있다. 유사하게, 식품 조성물은 본 발명의 조성물의 맛을 증강시키거나 또는 약학 조성물보다는 일반적인 식품 품목에 보다 유사함으로써 조성물을 소비하기에 더 매력적이도록 제형화될 수 있다. 특정 구현예에서, 본 발명의 조성물은 우유-기재 제품으로 제형화된다. "우유-기재 제품"이란 용어는 다

양한 지방 함량을 갖는 액체 또는 반고체 우유 또는 유청 기반 제품을 의미한다. 우유-기재 제품은 예를 들어 암소 우유, 염소 우유, 양 우유, 탈지유, 전유, 분유로부터 재조합된 우유 및 임의의 비-가공 우유 또는 가공된 제품 예를 들어 요구르트, 응유, 커드(curd), 산유, 산전유, 버터 밀크 및 다른 산유 제품일 수 있다. 또 다른 중요한 그룹에는 우유 음료, 예를 들어 유장 음료, 발효 우유, 응축 우유, 유아 또는 아기용 우유와; 맛을 낸 우유, 아이스크림; 과자와 같은 우유-함유 식품이 포함된다.

[0131] 일부 구현예에서, 본 발명의 조성물은 속 *에리시펠라토클로스트리디움*의 하나 이상의 박테리아 균주를 포함하고 임의의 다른 속으로부터 박테리아를 함유하지 않거나, 또 다른 속으로부터 박테리아의 겨우 *최소한* 또는 생물학적으로 무관한 양을 포함한다. 따라서, 일부 구현예에서, 본 발명은, 치료법에서, 임의의 다른 속으로부터 박테리아를 함유하지 않거나 또 다른 속으로부터 박테리아의 겨우 최소한 또는 생물학적으로 무관한 양을 포함하는, 속 에리시펠라토클로스트리디움의 하나 이상의 박테리아 균주를 포함하는 조성물을 제공한다.

[0132] 특정 구현예에서, 본 발명의 조성물은 단일 박테리아 균주 또는 종을 함유하고 임의의 다른 박테리아 균주 또는 종을 함유하지 않는다. 이러한 조성물은 다른 박테리아 균주 또는 종의 *최소한* 또는 생물학적으로 무관한 양만을 포함할 수 있다. 이러한 조성물은 다른 유기체 종이 실질적으로 없는 배양물일 수 있다. 따라서, 일부 구현예에서, 본 발명은 치료법에서 사용하기 위해 임의의 다른 속으로부터 박테리아를 함유하지 않거나 또 다른 속으로부터 박테리아의 겨우 최소한 또는 생물학적으로 무관한 양을 포함하는, 속 에리시펠라토클로스트리디움의 단일 박테리아 균주 또는 종을 포함하는 조성물을 제공한다.

[0133] 일부 구현예에서, 본 발명의 조성물은 1 초과 박테리아 균주 또는 종을 포함한다. 예를 들어, 일부 구현예에서, 본 발명의 조성물은 동일한 종 내로부터 1 초과 균주 (예를 들면 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40 또는 45 초과 균주) 를 포함하고, 선택적으로, 임의의 다른 종으로부터 박테리아를 함유하지 않는다. 일부 구현예에서, 본 발명의 조성물은 동일한 종 내로부터 50 미만 균주 (예를 들면 45, 40, 35, 30, 25, 20, 15, 12, 10, 9, 8, 7, 6, 5, 4 또는 3 미만 균주)를 포함하고, 선택적으로, 임의의 다른 종으로부터 박테리아를 함유하지 않는다. 일부 구현예에서, 본 발명의 조성물은 동일한 종 내로부터 1-40, 1-30, 1-20, 1-19, 1-18, 1-15, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 2-50, 2-40, 2-30, 2-20, 2-15, 2-10, 2-5, 6-30, 6-15, 16-25, 또는 31-50 균주를 포함하고, 선택적으로, 임의의 다른 종으로부터 박테리아를 함유하지 않는다. 일부 구현예에서, 본 발명의 조성물은 동일한 속 내로부터 1 초과 종 (예를 들면 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 15, 17, 20, 23, 25, 30, 35 또는 40 초과 종)을 포함하고, 선택적으로, 임의의 다른 속으로부터 박테리아를 함유하지 않는다. 일부 구현예에서, 본 발명의 조성물은 동일한 속 내로부터 50 미만 종 (예를 들면 50, 45, 40, 35, 30, 25, 20, 15, 12, 10, 8, 7, 6, 5, 4 또는 3 미만 종)을 포함하고, 선택적으로, 임의의 다른 속으로부터 박테리아를 함유하지 않는다. 일부 구현예에서, 본 발명의 조성물은 동일한 속 내로부터 1-50, 1-40, 1-30, 1-20, 1-15, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 2-50, 2-40, 2-30, 2-20, 2-15, 2-10, 2-5, 6-30, 6-15, 16-25, 또는 31-50 종을 포함하고, 선택적으로, 임의의 다른 속으로부터 박테리아를 함유하지 않는다. 본 발명은 전술한 것의 임의의 조합을 포함한다.

[0134] 일부 구현예에서, 조성물은 미생물 컨소시엄을 포함한다. 예를 들어, 일부 구현예에서, 조성물은 미생물 컨소시엄의 일부로서 *에리시펠라토클로스트리디움* 박테리아 균주를 포함한다. 예를 들어, 일부 구현예에서, *에리시펠라토클로스트리디움* 박테리아 균주는 장에서 *생체내* 공생적으로 살 수 있는 다른 속으로부터 하나 이상의 (예를 들면 적어도 2, 3, 4, 5, 10, 15 또는 20) 다른 박테리아 균주와 조합으로 존재한다. 예를 들어, 일부 구현예에서, 조성물은 상이한 속으로부터 박테리아 균주와 조합으로 *에리시펠라토클로스트리디움 라모숨*의 박테리아 균주를 포함한다. 일부 구현예에서, 미생물 컨소시엄은 단일 유기체, 예를 들면 인간의 대변 샘플로부터 수득된 2개 이상의 박테리아 균주를 포함한다. 일부 구현예에서, 미생물 컨소시엄은 사실상 함께 발견되지 않는다. 예를 들어, 일부 구현예에서, 미생물 컨소시엄은 적어도 2개의 상이한 유기체의 대변 샘플로부터 수득된 박테리아 균주를 포함한다. 일부 구현예에서, 2개의 상이한 유기체는 동일한 종, 예를 들면 2명의 상이한 인간이다. 일부 구현예에서, 2개의 상이한 유기체는 영아 인간 및 성인 인간이다. 일부 구현예에서, 2개의 상이한 유기체는 인간 및 비-인간 포유동물이다.

[0135] 일부 구현예에서, 본 발명의 조성물은 NCIMB 42688로서 기탁된 균주 MRX027과 동일한 안전성 및 치료 효능 특징을 갖지만, NCIMB 42688로서 기탁된 MRX027이 아니거나, *에리시펠라토클로스트리디움 라모숨* 이 아니거나 *에리시펠라토클로스트리디움*이 아닌 박테리아 균주를 추가적으로 포함한다.

[0136] 본 발명의 조성물이 1 초과 박테리아 균주, 종 또는 속을 포함하는 일부 구현예에서, 개별적인 박테리아 균주, 종 또는 속은 개별, 동시 또는 순차적인 투여를 위한 것일 수 있다. 예를 들어, 조성물은 1 초과 박테리아

균주, 종 또는 속의 모두를 포함할 수 있거나, 박테리아 균주, 종 또는 속은 개별적으로 저장될 수 있고 개별적으로, 동시에 또는 순차적으로 투여될 수 있다. 일부 구현예에서, 1 초과 박테리아 균주, 종 또는 속은 개별적으로 저장되지만 사용에 앞서 함께 혼합된다.

[0137] 일부 구현예에서, 본 발명에서 사용하기 위한 박테리아 균주는 인간 성인 대변으로부터 수득된다. 본 발명의 조성물이 1 초과 박테리아 균주를 포함하는 일부 구현예에서, 모든 박테리아 균주는 인간 성인 대변으로부터 수득되거나 다른 박테리아 균주가 존재하면 이들은 *최소한* 양으로만 존재한다. 박테리아는 인간 성인 대변으로부터 수득된 및 본 발명의 조성물에서 사용된 다음 배양되어질 수 있다.

[0138] 상기에서 언급된 바와 같이, 일부 구현예에서, 하나 이상의 *에리시펠라토클로스트리디움* 박테리아 균주는 본 발명의 조성물에서 단지 치료적으로 활성제(들)이다. 일부 구현예에서, 조성물에서 박테리아 균주(들)은 본 발명의 조성물에서 단지 치료적으로 활성제(들)이다.

[0139] 본 발명에 따라 사용하기 위한 조성물은 시판 승인을 필요로 할 수도 있고 필요로 하지 않을 수도 있다.

[0140] 특정 구현예에서, 본 발명은 상기 박테리아 균주가 동결건조되는 약학적 조성물을 제공한다. 특정 구현예에서, 본 발명은 상기 박테리아 균주가 분무 건조되는 상기 약제학적 조성물을 제공한다. 특정 구현예에서, 본 발명은 상기 박테리아 균주가 동결건조되거나 분무 건조되고 살아있는 상기 약제학적 조성물을 제공한다. 특정 구현예에서, 본 발명은 상기 박테리아 균주가 동결건조되거나 분무 건조되고 생존가능한 상기 약제학적 조성물을 제공한다. 특정 구현예에서, 본 발명은 상기 박테리아 균주가 동결건조되거나 분무 건조되고 장에서 부분적으로 또는 전적으로 군집할 수 있는 상기 약제학적 조성물을 제공한다. 특정 구현예에서, 본 발명은 상기 박테리아 균주가 동결건조되거나 분무 건조되고 생존가능하고 장에서 부분적으로 또는 전적으로 군집할 수 있는 상기 약제학적 조성물을 제공한다.

[0141] 일부 경우에, 동결건조된 또는 분무 건조된 박테리아 균주는 투여에 앞서 재구성된다. 일부의 경우, 재구성은 본원에 기재된 희석제의 사용에 의한다.

[0142] 본 발명의 조성물은 약학적으로 허용가능한 부형제, 희석제 또는 담체를 포함할 수 있다.

[0143] 특정 구현예에서, 본 발명은 하기를 포함하는 약학적 조성물을 제공한다:본 발명에서 사용된 바와 같이 박테리아 균주; 및 약학적으로 허용가능한 부형제, 캐리어 또는 희석제; 여기서 상기 박테리아 균주는 필요로 하는 대상체에 투여된 경우 장애를 치료하는 데 충분한 양이고; 여기서 상기 장애는 하기로 이루어진 군으로부터 선택된다: 포도막염; 암, 예컨대 유방암, 폐암, 간암, 결장암, 또는 난소암; 다발성 경화증; 관절염, 예컨대 류마티스성 관절염, 골관절염, 건선성 관절염, 또는 유년성 특발성 관절염; 시신경척수염 (데빅병); 강직 척추염; 척추관절염; 건선; 전신 홍반성 낭창; 염증성 장 질환, 예컨대 크론병 또는 궤양성 대장염; 소아지방변증; 천식, 예컨대 알러지성 천식 또는 호중구성 천식; 만성 폐쇄성 폐 질환 (COPD); 공막염; 혈관염; 베체트병; 죽상경화증; 아토피 피부염; 폐공기증; 치주염; 알러지성 비염; 및 동종이식편 거부반응.

[0144] 특정 구현예에서, 본 발명은 하기를 포함하는 약학적 조성물을 제공한다:본 발명에서 사용된 바와 같이 박테리아 균주; 및 약학적으로 허용가능한 부형제, 캐리어 또는 희석제; 여기서 상기 박테리아 균주는 IL-17 또는 Th17 경로에 의해 매개된 질환 또는 병태를 치료 또는 예방하는 데 충분한 양이다. 바람직한 구현예에서, 상기 질환 또는 병태는 하기로 이루어진 군으로부터 선택된다: 포도막염; 암, 예컨대 유방암, 폐암, 간암, 결장암, 또는 난소암; 다발성 경화증; 관절염, 예컨대 류마티스성 관절염, 골관절염, 건선성 관절염, 또는 유년성 특발성 관절염; 시신경척수염 (데빅병); 강직 척추염; 척추관절염; 건선; 전신 홍반성 낭창; 염증성 장 질환, 예컨대 크론병 또는 궤양성 대장염; 소아지방변증; 천식, 예컨대 알러지성 천식 또는 호중구성 천식; 만성 폐쇄성 폐 질환 (COPD); 공막염; 혈관염; 베체트병; 죽상경화증; 아토피 피부염; 폐공기증; 치주염; 알러지성 비염; 및 동종이식편 거부반응.

[0145] 특정 구현예에서, 본 발명은 박테리아 균주의 양이 조성물의 중량에 대하여 약 1×10^3 내지 약 1×10^{11} 콜로니 형성 단위/g인 상기 약학적 조성물을 제공한다.

[0146] 특정 구현예에서, 본 발명은 조성물이 1 g, 3 g, 5 g 또는 10 g의 투여량으로 투여되는 상기 약학적 조성물을 제공한다.

[0147] 특정 구현예에서, 본 발명은 경구, 직장, 피하, 비강, 협측 및 설하로 이루어진 군으로부터 선택된 방법에 의해 조성물이 투여되는 상기 약학적 조성물을 제공한다.

[0148] 특정 구현예에서, 본 발명은 락토오스, 전분, 글루코오스, 메틸 셀룰로오스, 마그네슘 스테아레이트, 만니톨 및 솔비톨로 이루어진 군으로부터 선택된 담체를 포함하는 상기 약학적 조성물을 제공한다.

[0149] 특정 구현예에서, 본 발명은 에탄올, 글리세롤 및 물로 이루어진 군으로부터 선택된 희석제를 포함하는 상기 약학적 조성물을 제공한다.

[0150] 특정 구현예에서, 본 발명은 전분, 젤라틴, 글루코오스, 무수 락토오스, 자유-유동 락토오스, 베타-락토오스, 옥수수 감미료, 아카시아, 트라가칸트, 알긴산 나트륨, 카복시메틸 셀룰로오스, 폴리에틸렌 글리콜, 올레산 나트륨, 스테아르 산 나트륨, 스테아르산 마그네슘, 안식향산 나트륨, 아세트산 나트륨 및 염화나트륨으로 이루어진 군으로부터 선택되는 부형제를 포함하는 상기 약학적 조성물을 제공한다.

[0151] 특정 구현예에서, 본 발명은 보존제, 항산화제 및 안정화제 중 적어도 하나를 추가로 포함하는 상기 약학적 조성물을 제공한다.

[0152] 특정 구현예에서, 본 발명은 나트륨 벤조에이트, 소르브산 및 p-하이드록시벤조산의 에스테르로 이루어진 군으로부터 선택된 보존제를 포함하는 상기 약학적 조성물을 제공한다.

[0153] 특정 구현예에서, 본 발명은 조성물을 약 4℃ 또는 약 25℃에서 밀봉된 용기에 저장하고 상기 용기를 50% 상대 습도를 갖는 대기에 두었을 때, 콜로니 형성 단위로 측정한 박테리아 균주의 적어도 80%가 적어도 약 하기의 기간 이후 남아있는 상기 약학적 조성물을 제공한다:1 개월, 3 개월, 6 개월, 1 년, 1.5 년, 2 년, 2.5 년 또는 3 년.

[0154] 일부 구현예에서, 본 발명의 조성물은 본원에서 기재된 바와 같이 조성물을 포함하는 밀봉된 용기로 제공된다. 일부 구현예에서, 밀봉된 용기는 샤세트 또는 병이다. 일부 구현예에서, 본 발명의 조성물은 본원에서 기재된 바와 같이 조성물을 포함하는 주사기로 제공된다.

[0155] 본 발명의 조성물은, 일부 구현예에서, 약제학적 제형으로서 제공될 수 있다. 예를 들어, 조성물은 정제 또는 캡슐로서 제공될 수 있다. 일부 구현예에서, 캡슐은 젤라틴 캡슐 (“겔-캡”)이다.

[0156] 일부 구현예에서, 본 발명의 조성물은 경구로 투여된다. 경구 투여는 화합물이 위장관에 들어가도록 연하 및/또는 화합물이 입으로부터 직접적으로 혈류에 들어가는 구강, 혀, 또는 설하 투여를 포함할 수 있다.

[0157] 경구 투여에 적합한 약제학적 제형은 하기를 포함한다: 고형 플러그, 고형 미세미립자, 반-고체 및 액체 (다중상 또는 분산된 시스템 포함) 예컨대 정제; 다중- 또는 나노-미립자, 액체 (예를 들면 수용액), 에멀젼 또는 분말을 함유하는 연질 또는 경질 캡슐; 로젠지 (액체-충전된 것 포함); 츄스; 겔; 빠른 분산 복용 형태; 필름; 질좌약; 스프레이; 및 구강/점막접착성 패치.

[0158] 일부 구현예에서 약제학적 제형은 경구 투여로 장에 본 발명의 조성물의 전달에 적합한 장용성 제형, 즉 위-저항성 (예를 들어, 위 pH에 저항성) 제형이다. 장용성 제형은 조성물의 박테리아 또는 또 다른 성분이 산-감수성인, 예를 들면 위 병태하에 분해하기 쉬운 경우 특히 유용할 수 있다.

[0159] 일부 구현예에서, 장용성 제형은 장용 코팅물을 포함한다. 일부 구현예에서, 제형은 장용 코팅된 복용 형태이다. 예를 들어, 제형은 장용 코팅된 정제 또는 장용 코팅된 캡슐, 등등일 수 있다. 장용 코팅물은 경구 전달을 위한 종래의 장용 코팅물, 예를 들어, 정제, 캡슐, 등등용 종래의 코팅물일 수 있다. 제형은 필름 코팅물, 예를 들어, 장용성 폴리머, 예를 들면 산-불용성 폴리머의 박막 층을 포함할 수 있다.

[0160] 일부 구현예에서, 장용성 제형은 장용 코팅물에 대한 필요 없이 본질적으로 장용성, 예를 들어, 위-저항성이다. 따라서, 일부 구현예에서, 제형은 장용 코팅물을 포함하지 않는 장용성 제형이다. 일부 구현예에서, 제형은 열겔화 물질로부터 제조된 캡슐이다. 일부 구현예에서, 열겔화 물질은 셀룰로오스 물질, 예컨대 메틸셀룰로오스, 하이드록시메틸셀룰로오스 또는 하이드록시프로필메틸셀룰로오스 (HPMC)이다. 일부 구현예에서, 캡슐은 임의의 막 형성 폴리머를 함유하지 않는 외피를 포함한다. 일부 구현예에서, 캡슐은 외피를 포함하고 외피는 하이드록시프로필메틸셀룰로오스를 포함하고 임의의 막 형성 폴리머를 포함하지 않는다 (예를 들면 참고 [55]). 일부 구현예에서, 제형은 본질적으로 장용성 캡슐이다 (예를 들어, Capsugel제 Vcaps®).

[0161] 일부 구현예에서, 제형은 연질 캡슐이다. 연질 캡슐은, 캡슐 외피에서 존재하는, 연화제, 예컨대, 예를 들어, 글리세롤, 소르비톨, 말티톨 및 폴리에틸렌 글리콜의 첨가 때문에, 특정 탄력성 및 유연도를 가질 수 있는 캡슐이다. 연질 캡슐은, 예를 들어, 젤라틴 또는 전분에 기초하여 생산될 수 있다. 젤라틴-기재 연질 캡슐은 다양한 공급자로부터 상업적으로 입수가능하다. 투여의 방법에 의존하여, 예컨대, 예를 들어, 경구로 또는 직장으로,

연질 캡슐은 다양한 형상을 가질 수 있고, 이들은, 예를 들어, 원통형, 타원형, 직사각형 또는 어뢰형일 수 있다. 연질 캡슐은 종래의 방법으로, 예컨대, 예를 들어, 쉬어러(Scherer) 방법, 악코겔(Accogel) 방법 또는 액적 또는 취입 방법으로 생산될 수 있다.

[0162] ***배양 방법***

[0163] 본 발명에 사용하기 위한 박테리아 균주는 예를 들어 참고 참고문헌 [56]-[58]에 기재된 표준 미생물 기술을 사용하여 배양될 수 있다.

[0164] 배양에 사용되는 고체 또는 액체 배지는 YCFA 한천 또는 YCFA 배지일 수 있다. YCFA 배지는 하기를 포함할 수 있다(100ml 당, 근사값): 카시톤 (1.0 g), 효모 추출물 (0.25 g), $NaHCO_3$ (0.4 g), 시스테인 (0.1 g), K_2HPO_4 (0.045 g), KH_2PO_4 (0.045 g), NaCl (0.09 g), $(NH_4)_2SO_4$ (0.09 g), $MgSO_4$, · $7H_2O$ (0.009 g), $CaCl_2$ (0.009 g), 레사주린 (0.1 mg), 헤민 (1 mg), 바이오틴 (1 μg), 코발라민 (1 μg), *p*-아미노벤조산 (3 μg), 엽산 (5 μg), 및 피리독사민 (15 μg).

[0165] ***백신 조성물에 사용하기 위한 박테리아 균주***

[0166] 본 발명자들은 본 발명의 박테리아 균주가 IL-17 또는 Th17 경로에 의해 매개되는 질병 또는 병태의 치료 또는 예방에 유용하다는 것을 확인하였다. 이는 본 발명의 박테리아 균주가 숙주 면역계에 미치는 효과의 결과일 가능성이있다. 따라서, 본 발명의 조성물은 또한 백신 조성물로서 투여될 때 IL-17 또는 Th17 경로에 의해 매개되는 질병 또는 증상을 예방하는데 유용할 수 있다. 특정 상기 구현예에서, 본 발명의 박테리아 균주는 생존가능하다. 특정 상기 구현예에서, 본 발명의 박테리아 균주는 장에서 부분적으로 또는 전적으로 군집할 수 있다. 특정 상기 구현예에서, 본 발명의 박테리아 균주는 생존가능하고 장에서 부분적으로 또는 전적으로 군집할 수 있다. 다른 특정 상기 구현예에서, 본 발명의 박테리아 균주는 사멸, 불활성화 또는 약화될 수 있다. 이러한 특정 구현예에서, 조성물은 백신 보조제를 포함할 수 있다. 특정 구현예에서, 조성물은 피하 주사와 같은 주사를 통한 투여를 위한 것이다.

[0167] ***일반***

[0168] 본 발명의 실시는, 달리 명시하지 않는 한, 당해 분야의 숙련 범위 내에서 화학, 생화학, 분자생물학, 면역학 및 약리학의 통상적인 방법을 사용할 것이다. 이러한 기술은 문헌에 충분히 설명되어 있다. 참고, *예를 들면*, 참고문헌 [59] 및 [60-66]*등*.

[0169] 용어 "포함하는"은 "포함하는"뿐만 아니라 "이루어지는"을 포함하고, *예를 들면*, X를 "포함하는" 조성물은 X만으로 이루어질 수 있거나, 예를 들어, 부가적인 것 *예를 들어 하기를 포함할 수 있다:* X + Y.

[0170] 수치 *x*와 관련하여 "약"이라는 용어는 선택 사항이며 예를 들어 *x* 플마기호 10%를 의미한다.

[0171] "실질적으로"라는 용어는 "완전히" 제외하지 않고, *예를 들어* Y가 "실질적으로 없는" 조성물은 Y를 전혀 함유하지 않을 수 있다. 필요한 경우, "실질적으로"라는 용어는 본 발명의 정의로부터 생략될 수 있다.

[0172] 2개의 뉴클레오타이드 서열 사이의 백분율 서열 동일성에 대한 언급은, 정렬시, 뉴클레오타이드의 백분율이 2개의 서열을 비교할 때 동일하다는 것을 의미한다. 이러한 정렬 및 퍼센트 상동성 또는 서열 동일성은 당해 기술분야에 공지된 소프트웨어 프로그램 예를 들어 하기의 참고문헌 [67]의 섹션 7.7.18에 기재된 소프트웨어 프로그램을 사용하여 결정할 수 있다. 바람직한 정렬은 12의 갭 오픈 패널티 및 2의 갭 연장 패널티, 62의 BLOSUM 매트릭스를 수반한 아핀 갭 조사를 이용하는 스미쓰-워터맨(Smith-Waterman) 상동성 검색 알고리즘에 의해 결정된다. 스미쓰-워터맨 상동 검색 알고리즘은 참고문헌 [68]에 기술되어 있다.

[0173] 특별히 언급하지 않는 한, 다수의 단계를 포함하는 공정 또는 방법은 상기 방법의 시작 또는 끝에서 추가적인 단계를 포함하거나, 또는 추가적인 개재 단계를 포함할 수 있다. 또한, 적절한 경우, 단계들은 결합되거나 생략되거나 대체 순서로 수행될 수 있다.

[0174] 본 발명의 다양한 구현예가 본원에 기술된다. 각 구현예에서 특정된 특징은 추가의 구현예를 제공하기 위해 다른 특정 특징과 결합될 수 있음을 이해할 것이다. 특히, 본원에서 적합한, 전형적 또는 바람직한 것으로 강조되는 구현예는 (상호 배타적일 때를 제외하고) 서로 조합될 수 있다.

[0175] **실시예**

[0176] ***실시예 1 - 포도막염의 마우스 모델에서 박테리아 접종물의 효능***

[0177] *요약*

[0178] 본 연구는 포도막염에 관한 박테리아 투여의 효과를 시험하기 위해 인터포토리셉터 레티노이드-결합 단백질 (IRBP)-유도된 포도막염의 마우스 모델을 사용하였다. 포도막염은 안구내 염증 및 망막 조직 파괴에서 비롯한 시각을 위협하는 병태이다. 상기 질환은 실험적 자가면역 포도막망막염 (EAU)의 모델로 설치류에서 연구될 수 있다 [69]. EAU는 Th1/Th17 세포가 망막 항원을 향해 유도되고 조직 파괴를 초래하는 상주하는 및 침투하는 단핵 세포를 활성화하는 사이토카인을 생산하는 장기-특이적인 장애이다. EAU는 인터포토리셉터 레티노이드 결합 단백질 펩타이드 (IRBPp)를 포함하는 망막 항원으로 공격함으로써 마우스에서 유도될 수 있다. 질환 개시는 정상적으로 8-9 일째부터 발생하고 14-15 일째 이후 피크이다. 임상 질환의 징후는 국소 내시경 안저 이미지형성 (TEFI)을 이용하여 모니터링될 수 있다.

[0179] *균주*

[0180] MRX027:*에리시펠라토클로스트리디움 라모숨*.

[0181] 이 실시예에서 사용된 균주는 NCIMB 42688로서 기탁되어 있다.

[0182] 생물학적 치료는 글리세롤 스톡으로 제공되었다. 미생물학적 성장 배지 (YCFA)는 제제의 배양에 사용되었다.

[0183] *마우스*

[0184] 마우스는 균주 C57BL/6이었고 연구의 초기에 6 주령 이상이었다. 72 마우스는 사용되었다 (+ 36 위성 동물). 병약한 동물은 연구로부터 제외되었다. 동물은 자동온도조절장치로 모니터링된 대기실 (22 ± 4 ℃)에서 특이적인 병원체 없는 (spf) 병태로 하우징되었다. 동물은 사용에 앞서 최소의 1 주 동안 표준 동물 하우스 병태하에 순응하게 되었다. 동물의 건강 상황은 상기 기간 내내 모니터링되었고 실험적 용도로 각각의 동물의 적합성은 연구 시작에 앞서 평가되었다. 마우스는 연구의 지속기간 동안 케이지당 최대 10 동물의 그룹으로 하우징되었다. 조사된 펠렛 다이어트 (Lab 다이어트, EU 설치류 다이어트 22%, 5LF5) 및 물은 순응 및 연구 기간 내내 선택적으로 이용가능하였다. 다이어트 또는 물의 임의의 구성요소가 연구를 방해하지 않았을 것 같다.

[0185] *실험적 개요*

[0186] 성체 암컷 C57BL/6 마우스는 실험적 그룹으로 무작위로 위치되었고 1 주 동안 순응하게 되었다. 치료는 아래 계획에 따라 투여되었다. 0 일째, 동물은 피하 주사에 의해 2.5 mg/ml *마이코박테리움 투베르쿨로시스* H37 Ra로 보충된 완전한 프로인트 아쥬반트 (CFA)내 200 μg의 인터포토리셉터 레티노이드 결합 단백질 펩타이드 1-20 (IRBP p1-20)을 함유하는 에멀젼으로 투여되었다. 또한 0 일째, 동물은 복막내 주사에 의해 1.5 μg *보데텔라 페르투시스* 독소로 투여되었다. -14 일째부터, 동물은 주당 3회 계량된다. -1 일째부터 42 일째 실험의 끝까지, 동물은 국소 내시경 안저 이미지형성 (TEFI)을 이용하여 포도막염의 임상 징후에 대하여 매주 2회 모니터링된다.

[0187] *투여 계획*

[0188] 모든 그룹은 n=12이다

[0189] 경구 투여용 비히클은 YCFA 배지이다.

[0190] 매일 2회 경구 투여용 투여 용적은 5 ml/kg이다.

[0191]

그룹	*치료*	*용량*	*경로*	*주파수*	*질병 유도*
1	*비히클*	*5 ml/kg*	*PO*	*BID - 14일-끝*	*0일:IRBP/CFA, SC 0일:PTx, IP*
2	*MRX027*	*5 ml/kg*			

PO: 경구 투여, BID: 매일 2 회, SC: 피하 주사, IP: 복막내 주사, IRBP: 인터포토리셉터 결합 단백질, CFA: 완전한 프로인트 아쥬반트, PTx: 백일해 독소

[0192] 양성 대조군 그룹은 약물 사이클로스포린 A로 치료를 이용하여 또한 시험되었다.

[0193] *관독*

[0194] **체중**.-14 일째부터, 동물은 1 주 3회 계량된다. 2 연속 사례로 그의 초기 (0 일째) 체중보다 15% 이상의 체중 감소를 가진 동물은 도태된다.

[0195] **비-특이적 임상 관찰.**-14 일째부터 실험의 끝까지, 동물은 비정상 자세 (굽은), 비정상 모질 상태 (털세움) 및 비정상 활성 수준 (감소된 또는 증가된 활성)을 포함하는 비-특이적 임상 징후에 대하여 매일 체크된다.

[0196] **임상 점수:국소 내시경 안저 이미지형성 (TEFI)에 의한 망막 이미지형성.**-1 일째부터 실험의 끝까지, 동물은 포도막염의 임상 징후에 대하여 매주 2회 채점된다. 망막 이미지는 트로피카마이드 1% 그 다음 페닐에프린 하이드로클로라이드 2.5%를 이용한 동공 팽창 이후 비-마취된 그러나 구속된 동물에서 TEFI를 이용하여 포착된다. 망막 이미지는 하기 시스템을 이용한 스코어이다. 최대 누적 스코어는 20이다.

스코어	시신경 유두 염증	망막 혈관	망막 조직 침윤	구조적 손상
1	최소	1-4 온화한 커핑	1-4 작은 병변 또는 1 선형 병변	망막 영역의 ¼ to ¾ 연루한 망막 병변 또는 위축증
2	경증	>4 온화한 커핑 또는 1-3 중간 정도의 커핑	5-10 작은 병변 또는 2-3 선형 병변	다중 작은 병변 (흉터) 또는 ≤3 선형 병변 (흉터)를 수반한 범망막 위축증
3	보통	>3 중간 정도의 커핑	>10 작은 병변 또는 >3 선형 병변	>3 선형 병변 또는 융합성 병변 (흉터)를 수반한 범망막 위축증
4	중증	>1 중증 커핑	선형 병변 융합성	폴딩을 수반한 망막 탈착
5	보이지 않음 (화이트-아웃 또는 중증 탈착)			

[0197]

[0198] *결과*

[0199] 연구 결과는 도 1 및 2에 나타낸다.

[0200] **임상 점수:국소 내시경 안저 이미지형성 (TEFI)에 의한 망막 이미지형성.**0 일째부터 28 일째까지 대조군 그룹에서 측정된 TEFI 스코어 데이터는 비-매개변수 데이터에 대한 크루스칼-왈리스 시험 그 다음 실험적 일자 사이 다중 비교를 위한 던의 사후-시험에 의해 분석되었다.

[0201] IRBP 투여는 대조군 그룹에서 0 일째에 비교된 경우 14 일 ($p < 0.01$)째부터 및28 일 ($p < 0.0001$)째에 측정된 TEFI 스코어에서 유의미한 증가를 유도하였다 (도 1).

[0202] 28 일째에 실험적 그룹에서 측정된 TEFI 스코어는 단방향 ANOVA를 이용하여 분석되었다. 예상대로, 스코어에서 상당한 감소는 양성 대조군 사이클로스포린 A 그룹에서 관측되었다. 음성 대조군에 비하여, MRX027-치료된 그룹 ($p<0.05$)에 대한 스코어에서 통계적으로 상당한 감소가 또한 있었다 (도 73).

[0203] **결론.** TEFI에 의해 결정된 임상 점수는, IRBP-유도된 포도막염의 상기 모델에서 예상대로, 14 일째부터 증가하였다. 28 일째까지, 질환 발병률 및 질환 중증도에서 놀랄만한 및 통계적으로 상당한 감소는 MRX027-치료된 그룹에서 관측되었고, 이는 양성 대조군 그룹에 대하여 보여진 것과 비교할만한 하였다. 특히, 이들 데이터는 균주 MRX027로 치료가 염증성 세포에 의한 망막 손상, 시신경 유두 염증 및/또는 망막 조직 침윤을 감소시켰다는 것을 나타낸다 (참조 상기 TEFI 망막 이미지 평점 체계). 이들 데이터는 균주 MRX027이 포도막염의 치료 또는 예방에 유용할 수 있다는 것을 나타낸다.

[0204] ***실시예 2 - 안정성 시험***

[0205] 본원에 기재된 적어도 하나의 박테리아 균주를 함유하는 본원에 기재된 조성물은 25℃ 또는 4℃에서 밀봉된 용기에 저장되고, 상기 용기는 30%, 40%, 50%, 60%, 70%, 75%, 80%, 90% 또는 95%의 상대 습도를 갖는 대기 중에 배치된다. 1 개월, 2 개월, 3 개월, 6 개월, 1 년, 1.5 년, 2 년, 2.5 년 또는 3 년 후, 박테리아 균주의 적어

도 50%, 60%, 70%, 80% 또는 90%는 표준 프로토콜에 의해 결정된 콜로니 형성 단위로 측정시 그대로 유지되어야 한다.

[0206] **서열**

[0207] 서열 식별 번호: 1 (*에리시펠라토클로스트리디움 (클로스트리듐) 라모숨* 16S rRNA 유전자, 균주 DSM 1402 - X73440)

```
   1 nnnnnnngag agtttgatcc tggctcagga tgaacgctgg cggcgtgcct aatacatgca
  61 agtcgaacgc gagcacttgt gctcgagtgg cgaacgggtg agtaatacat aagtaacctg
 121 ccctagacag ggggataact attggaaacg gatagctaag accgcatagg tacggacact
 181 gcatggtgac cgtattaaaa gtgcctcaaa gcactggtag aggatggact tatggcgcat
 241 tagctggttg gcggggtaac ggcccaccaa ggcgacgatg cgtagccgac ctgagagggt
 301 gaccggccac actgggactg agacacggcc cagactccta cgggaggcag cagtagggaa
 361 ttttcggcaa tgggggaaac cctgaccgag caacgccgcg tgaaggaaga aggttttcgg
 421 attgtaaact tctgttataa agaagaacgg cggctacagg aaatggtagc cgagtgacgg
 481 tactttattt tagaaagcca cggctaacta cgtgccagca gccgcggtaa tacgtaggtg
 541 gcaagcgtta tccggaatta ttgggcgtaa agagggagca ggcggcagca agggtctgtg
 601 gtgaaagcct gaagcttaac ttcagtaagc catagaaacc aggcagctag agtgcaggag
 661 aggatcgtgg aattccatgt gtagcggtga aatgcgtaga tatatggagg aacaccagtg
 721 gcgaaggcga cgatctggcc tgcaactgac gctcagtccc gaaagcgtgg ggagcaaata
 781 ggattagata ccctagtagt ccacgccgta aacgatgagt actaagtgtt ggatgtcaaa
 841 gttcagtgct gcagttaacg caataagtac tccgcctgag tagtacgttc gcaagaatga
 901 aactcaaagg aattgacggg ggccgcacaa gcggtggagc atgtggttta attcgaagca
 961 acgcgaagaa ccttaccagg tcttgacata ctcataaagg ctccagagat ggagagatag
1021 ctatatgaga tacaggtggt gcatggttgt cgtcagctcg tgtcgtgaga tgttgggtta
1081 agtcccgcaa cgagcgcaac ccttatcgtt agttaccatc attaagttgg ggactctagc
1141 gagactgcca gtgacaagct ggaggaaggc ggggatgacg tcaaatcatc atgcccctta
1201 tgacctgggc tacacacgtg ctacaatgga tggtgcagag ggaagcgaac cgcgaggtga
1261 agcaaaaccc ataaaaacca ttctcagttc ggattgtagt ctgcaactcg actacatgaa
1321 gttggaatcg ctagtaatcg cgaatcagca tgtcgcggtg aatacgttct cgggccttgt
1381 acacaccgcc cgtcacacca cgagagttga taacacccga agccggtggc ctaaccgcaa
1441 ggaaggagct gtctaaggtg ggattgatga ttggggtgaa gtcgtaacaa ggtatcccta
1501 cgggaacgtg cggctggatc acctcc
```

[0208]

[0209] 서열 식별 번호: 2 (*에리시펠라토클로스트리디움 라모숨* 균주 JCM 1298 16S 리보솜

[0210] RNA 유전자, 부분 서열 - NR_113243.1)

```
   1 agagtttgat cctggctcag gatgaacgct ggcggcgtgc ctaatacatg caagtcgaac
  61 gcgagcactt gtgctcgagt ggcgaacggg tgagtaatac ataagtaacc tgccctagac
 121 agggggataa ctattggaaa cgatagctaa gaccgcatag gtacggacac tgcatggtga
 181 ccgtattaaa agtgcctcaa agcactggta gaggatggac ttatggcgca ttagctggtt
 241 ggcggggtaa cggcccacca aggcgacgat gcgtagccga cctgagaggg tgaccggcca
 301 cactgggact gagacacggc ccagactcct acgggaggca gcagtaggga attttcggca
 361 atgggggaaa ccctgaccga gcaacgccgc gtgaaggaag aaggttttcg gattgtaaac
 421 ttctgttata aaggaagaac ggcggctaca ggaaatggta gccgagtgac ggtactttat
 481 tagaaagcca cggctaacta cgtgccagca gccgcggtaa tacgtaggtg gcaagcgtta
 541 tccggaatta ttgggcgtaa agagggagca ggcggcagca agggtctgtg gtgaaagcct
 601 gaagcttaac ttcagtaagc catagaaacc aggcagctag agtgcaggag aggatcgtgg
 661 aattccatgt gtagcggtga aatgcgtaga tatatggagg aacaccagtg gcgaaggcga
 721 cgatctggcc tgcaactgac gctcagtccc gaaagcgtgg ggagcaaata ggattagata
 781 ccctagtagt ccacgccgta aacgatgagt actaagtgtt ggatgtcaaa gttcagtgct
 841 gcagttaacg caataagtac tccgcctgag tagtacgttc gcaagaatga aactcaaagg
 901 aattgacggg ggcccgcaca agcggtggag catgtggttt aattcgaagc aacgcgaaga
 961 accttaccag gtcttgacat actcataaag gctccagaga tggagagata gctatatgag
1021 atacaggtgg tgcatggttg tcgtcagctc gtgtcgtgag atgttgggtt aagtcccgca
1081 acgagcgcaa cccttatcgt tagttaccat cattaagttg gggactctag cgagactgcc
1141 agtgacaagc tggaggaagg cggggatgac gtcaaatcat catgcccctt atgacctggg
1201 ctacacacgt gctacaatgg atggtgcaga gggaagcgaa gccgcgaggt gaagcaaaac
1261 ccataaaacc attctcagtt cggattgtag tctgcaactc gactacatga agttggaatc
1321 gctagtaatc gcgaatcagc atgtcgcggt gaatacgttc tcgggccttg tacacaccgc
1381 ccgtcacacc acgagagttg ataacacccg aagccggtgg cctaaccgca aggaaggagc
1441 tgtctaaggt gggattgatg attggggtga agtcgtaaca aggtaacc
```

[0211]

[0212] 서열 식별 번호: 3 (*에리시펠라토클로스트리디움 라모숨* 균주 MRX027에 대한 공통 16S rRNA 서열)

```
TGCGGTTAGGCCACCGGCTTCGGGTGTTATCAACTCTCGTGGTGTGACGGGCGGTGTGTACAAGGCCCGAGAACGTA
TTCACCGCGACATGCTGATTCGCGATTACTAGCGATTCCAACTTCATGTAGTCGAGTTGCAGACTACAATCCGAACT
GAGAATGGTTTTATGGGTTTTGCTTCACCTCGCGGCTTCGCTTCCCTCTGCACCATCCATTGTAGCACGTGTGTAGC
CCAGGTCATAAGGGGCATGATGATTTGACGTCATCCCCGCCTTCCTCCAGCTTGTCACTGGCAGTCTCGCTAGAGTC
CCCAACTTAATGATGGTAACTAACGATAAGGGTTGCGCTCGTTGCGGGACTTAACCCAACATCTCACGACACGAGCT
GACGACAACCATGCACCACCTGTATCTCATATAGCTATCTCTCCATCTCTGGAGCCTTTATGAGTATGTCAAGACCT
GGTAAGGTTCTTCGCGTTGCTTCGAATTAAACCACATGCTCCACCGCTTGTGCGGGCCCCCGTCAATTCCTTTGAGT
TTCATTCTTGCGAACGTACTACTCAGGCGGAGTACTTATTGCGTTAACTGCAGCACTGAACTTTGACATCCAACACT
TAGTACTCATCGTTTACGGCGTGGACTACTAGGGTATCTAATCCTATTTGCTCCCCACGCTTTCGGGACTGAGCGTC
AGTTGCAGGCCAGATCGTCGCCTTCGCCACTGGTGTTCCTCCATATATCTACGCATTTCACCGCTACACATGGAATT
CCACGATCCTCTCCTGCACTCTAGCTGCCTGGTTTCTATGGCTTACTGAAGTTAAGCTTCAGGCTTTCACCACAGAC
CCTTGCTGCCGCCTGCTCCCTCTTTACGCCCAATAATTCCGGATAACGCTTGCCACCTACGTATTACCGCGGCTGCT
GGCACGTAGTTAGCCGTGGCTTTCTAATAAAGTACCGTCACTCGGCTACCATTTCCTGTAGCCGCCGTTCTTCCTTT
ATAACAGAAGTTTACAATCCGAAAACCTTCTTCCTTCACGCGGCGTTGCTCGGTCAGGGTTTCCCCCATTGCCGAAA
ATTCCCTACTGCTGCCTCCCGTAGGAGTCTGGGCCGTGTCTCAGTCCCAGTGTGGCCGGTCACCCTCTCAGGTCGGC
TACGCATCGTCGCCTTGGTGGGCCGTTACCCCGCCAACCAGCTAATGCGCCATAAGTCCATCCTCTACCAGTGCTTT
```

[0213]

[0214] 서열 식별 번호: 4 (*에리시펠라토클로스트리디움 라모숨* 균주 DSM 140의 게놈 서열) - 참고 전자 서열 목록.

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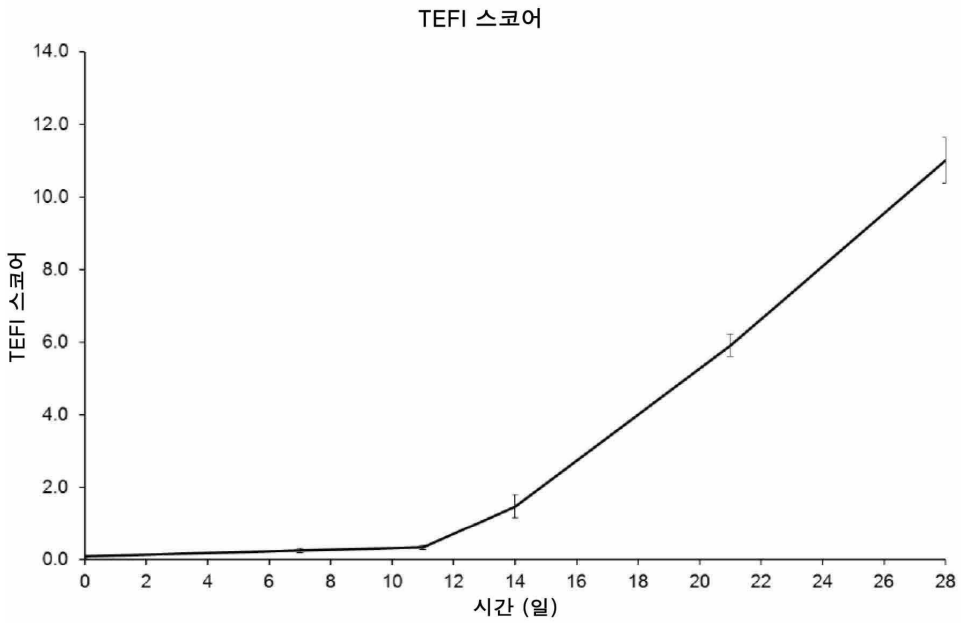

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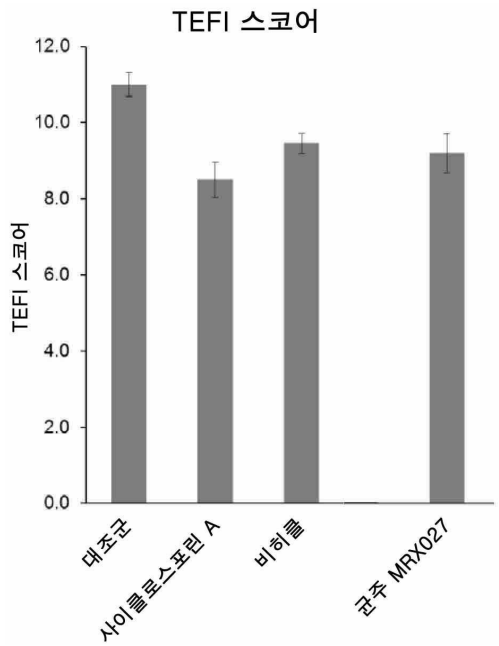

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