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(54) **TREATING AND PREVENTING MICROBIAL INFECTIONS**

(71) Applicant: **SNIPR Biome ApS**, Copenhagen Ø (DK)

(72) Inventors: **Morten Sommer**, Copenhagen Ø (DK); **Virginia Martinez**, Copenhagen Ø (DK); **Eric Van Der Helm**, Copenhagen Ø (DK); **Jakob Krause Haaber**, Copenhagen Ø (DK); **Ana De Santiago Torio**, Copenhagen Ø (DK); **Christian Grøndahl**, Copenhagen Ø (DK); **Jasper Clube**, London (GB)

(73) Assignee: **SNIPR BIOME APS**, Copenhagen Ø (DK)

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(51) **Int. Cl.**

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CPC ***C12N 15/11*** (2013.01); ***A61K 38/465*** (2013.01); ***A61K 39/3955*** (2013.01); ***A61K 39/39558*** (2013.01); ***A61P 31/04*** (2018.01); ***C07K 16/2818*** (2013.01); ***C07K 16/2827*** (2013.01); *C12N 2310/20* (2017.05); *C12N 2320/30* (2013.01); *C12N 2320/31* (2013.01); *Y02A 50/30* (2018.01)

(58) **Field of Classification Search**
None
See application file for complete search history.

(56) **References Cited**

To view the complete listing of prior art documents cited during the proceeding for Reexamination Control Number 90/014,681, please refer to the USPTO's public Patent Application Information Retrieval (PAIR) system under the Display References tab.

Primary Examiner — Sharon Turner

(57) **ABSTRACT**

The invention provides methods for treating or preventing microbial (eg, bacterial) infections and means for performing these methods. In particular, treatment of infections requiring rapid and durable therapy is made possible, such as for treating acute conditions such as septicemia, sepsis, SIRS or septic shock. The invention is particularly useful, for example, for treatment of microbes such as for environmental, food and beverage use. The invention relates inter alia to methods of controlling microbiologically influenced corrosion (MIC) or biofouling of a substrate or fluid in an industrial or domestic system. The invention also useful for the treatment of pathogenic bacterial infections in subjects receiving a treatment for a disease or condition, such as a transplant or a treatment for cancer, a viral infection or an autoimmune disease.

EX PARTE REEXAMINATION CERTIFICATE

THE PATENT IS HEREBY AMENDED AS INDICATED BELOW.

Matter enclosed in heavy brackets [ ] appeared in the patent, but has been deleted and is no longer a part of the patent; matter printed in italics indicates additions made to the patent.

AS A RESULT OF REEXAMINATION, IT HAS BEEN DETERMINED THAT:

The patentability of claims **20-22** is confirmed.

Claim **1** is cancelled.

Claims **2-3**, **6**, **9**, **15-16**, **18-19** and **23-26** are determined to be patentable as amended.

Claims 4-**5**, **7-8**, **10-14**, **17** and **27-28**, dependent on an amended claim, are determined to be patentable.

New claims **29-42** are added and determined to be patentable.

2. The method of claim **[1]** *9*, wherein the infection is a urinary tract infection, a lung infection, or a kidney infection.

3. The method of claim **[1]** *9*, wherein the infection is a urinary tract infection.

6. The method of claim **[1]** *9*, wherein the infection is a lung infection.

9. The method of claim **[1]***20*, wherein **[**and**]** the subject has a compromised immune system.

15. The method of claim **[1]** *9*, wherein the first bacteria are comprised by a gut, kidney or lung microbiota of the subject.

16. The method of claim **[1]** *9*, wherein the subject is a human.

18. The method of claim **[1]** *9*, wherein the Cas nuclease is a Cas3.

19. The method of claim **[1]** *9*, wherein the Cas nuclease is a Cas9.

23. The method of claim **[1]** *20*, wherein the infection is reduced by at least 90% for 1 hour or more.

24. The method of claim **[1]** *20*, wherein the infection is durably treated.

25. The method of claim **[1]** *9*, wherein the method comprises administering the Cas nuclease and/or the guide RNA to the subject at a first time (T1) and at a second time (T2), wherein T2 is at least 1 hour after T1.

26. The method of claim **[1]** *9*, wherein the method comprises administering to the subject a nucleic acid vector comprising the guide RNA or a DNA encoding the guide RNA.

29. The method of claim 21, wherein the subject has a compromised immune system.

30. The method of claim 22, wherein the subject has a compromised immune system.

31. The method of claim 23, wherein the subject has a compromised immune system.

32. The method of claim 24, wherein the subject has a compromised immune system.

33. The method of claim 29, wherein the first bacteria are enterohemorrhagic E. coli (EHEC).

34. The method of claim 20, wherein the subject is a liver, kidney or lung transplant patient.

35. The method of claim 21, wherein the subject is a liver, kidney or lung transplant patient.

36. The method of claim 34, wherein the reduction of the infection persists for at least 30 minutes immediately after the first 30 minutes of the treatment.

37. The method of claim 20, wherein the subject is a cancer patient, a transplant patient, or a patient suffering from a viral infection.

38. The method of claim 21, wherein the subject is a cancer patient, a transplant patient, or a patient suffering from a viral infection.

39. The method of claim 37, wherein the reduction of the infection persists for at least 30 minutes immediately after the first 30 minutes of the treatment.

40. The method of claim 20, wherein the infection is a urinary tract infection.

41. The method of claim 20, wherein the infection is a lung infection.

42. The method of claim 20, wherein the first bacteria are comprised by a gut, kidney or lung microbiota of the subject.

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