inflammatory responses. Inflammatory responses triggered by infection are known to be central components of disease pathogenesis. An ability to increase host resistance to infection, while controlling inflammation, would be very beneficial in the ongoing battle against infection, including infection caused by resistant organisms.

IDRs and the Innate Immune System

Innate Defense Regulators (IDRs) interact with intracellular signaling events and modulate the innate defense response. Whereas much of the initial work with the IDRs focused on their role in fighting infection while controlling inflammation, recent results in animal models of chemotherapy- or radiation-induced mucositis and wound healing suggest that IDRs can be beneficial during the responses to a broader range of damage-inducing agents beyond pathogens. IDRs treat and prevent infections by selectively modifying the body's innate defense responses when they are activated by PAMPs or DAMPs, without triggering associated inflammation responses (Matzinger 2002). The same mechanisms underlie positive effects seen in mucositis and wound healing models, where signaling downstream of the recognition of DAMPs is affected. RIVPA (SEQ ID NO. 5) has demonstrated safety in humans and efficacy in animal models of fractionated radiation-induced and chemotherapy-induced oral mucositis, in models of chemotherapy induced damage to the gastro-intestinal tract and in models of local and systemic Gram-positive and Gram-negative infection in immunocompetent and immunocompromised hosts.

Summary

In one aspect, there is provided a use of:

a) a peptide comprising an amino acid sequence of up to 7 amino acids, said peptide comprising the amino acid sequence of $X_1X_2X_3P$ (SEQ ID NO: 56), wherein:

X1 is R;

X2 is I or V, wherein X2 can be N-methylated;

X3 is I or V, wherein X3 can be N-methylated;

P is proline or a proline analogue;

wherein SEQ ID NO: 56 if the first four amino acids at the N-terminus of the peptide, or a pharmaceutical salt, ester or amide thereof and a pharmaceutically-acceptable carrier, diluent, or excipient; or

b) a peptide comprising the amino acid sequence of any of SEQ ID NOs: 5, 7, 10, 14, 17, 18, 22, 23, 24, 27, 28, 31, 34, 35, 63, 64, 66-69, 72, 76, 77, 90 and 92 or a pharmaceutical salt, ester or amide thereof and a pharmaceutically-acceptable carrier, diluent or excipient in the manufacture of a medicament for treating oral mucositis in a subject who has been exposed to a damaging amount of radiation or chemotherapeutic agents.

In another aspect, there is provided an isolated peptide comprising the amino acid SEQ ID NO. 91 or SEQ ID NO. 92 or a pharmaceutical salt, ester or amide thereof.

In another aspect, there is provided an isolated peptide consisting of the amino acid sequence of

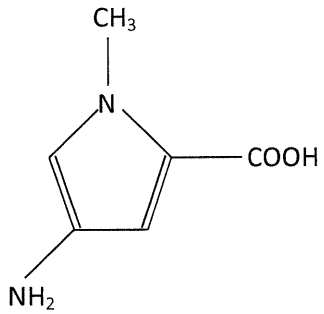
R(tBg)V1KR(tBg)V2,

wherein tBg = tert-butyl glycine

futher wherein R(tBg)V2 is linked via an amide bond between V2 and the lysine amino group in the side chain (SEQ ID NO. 91).

In another aspect, there is provided an isolated peptide consisting of the amino acid sequence RIV(mp2)A-NH2,

wherein mp2 = 4-Amino-1-methyl-1H-pyrrole-2-carboxylic acid



(SEQ ID NO. 92).

In another aspect, there is provided use of a peptide consisting of an amino acid sequence of Table 1 in the manufacture of a medicament for treating an individual suffering from a disease selected from the group consisting of bacterial infection, mucositis and colitis or exposure to acute radiation.

In another aspect, there is provided use of : a) a peptide comprising an amino acid sequence of up to 7 amino acids, said peptide comprising the amino acid sequence of $X_1X_2X_3P$ (SEQ ID NO: 56), wherein:

X1 is R;

X2 is I or V, wherein X2 can be N-methylated;

X3 is I or V, wherein X3 can be N-methylated;

P is proline or a proline analogue;

wherein SEQ ID NO: 56 if the first four amino acids at the N-terminus of the peptide, or a pharmaceutical salt, ester or amide thereof and a pharmaceutically-acceptable carrier, diluent, or excipient; or b) a peptide comprising the amino acid sequence of any of SEQ ID NOs: 5, 7, 10, 14, 17, 18, 22, 23, 24, 27, 28, 31, 34, 35, 63, 64, 66-69, 72, 76, 77, 90 and 92 or a pharmaceutical salt, ester or amide thereof and a pharmaceutically-acceptable carrier, diluent or excipient in the manufacture of a medicament for preventing an infection in a subject.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1. RIVPA (SEQ ID NO. 5) reduces the duration of severe oral mucositis in a fractionated radiation model.

Figure 2. RIVPA (SEQ ID NO. 5) reduces the duration of severe oral mucositis in a fractionated radiation model using an optimized dosing regimen.

Figure 3. RIVPA (SEQ ID NO. 5) reduces the severity of DSS-induced colitis as measured by endoscopy on days 7, 14, and 21 (A) and histopathology on day 21 (B,C,D).

What is claim is:

1. Use of ~~A method of treating oral mucositis in a subject who has been exposed to a damaging amount of radiation or chemotherapeutic agents, comprising administering to the patient an effective amount of~~:

a) a peptide comprising an amino acid sequence of up to 7 amino acids, said peptide comprising the amino acid sequence of $X_1X_2X_3P$ (SEQ ID NO: 56), wherein:

X1 is R;

X2 is I or V, wherein X2 can be N-methylated;

X3 is I or V, wherein X3 can be N-methylated;

P is proline or a proline analogue;

wherein SEQ ID NO: 56 if the first four amino acids at the N-terminus of the peptide, or a pharmaceutical salt, ester or amide thereof and a pharmaceutically-acceptable carrier, diluent, or excipient; or

b) a peptide comprising the amino acid sequence of any of SEQ ID NOs: 5, 7, 10, 14, 17, 18, 22, 23, 24, 27, 28, 31, 34, 35, 63, 64, 66-69, 72, 76, 77, 90 and 92 or a pharmaceutical salt, ester or amide thereof and a pharmaceutically-acceptable carrier, diluent or excipient in the manufacture of a medicament for treating oral mucositis in a subject who has been exposed to a damaging amount of radiation or chemotherapeutic agents.

2. The ~~method~~ use of claim 1, wherein the peptide is SEQ ID NO: 5 or a pharmaceutical salt, ester, or amide thereof and a pharmaceutically-acceptable carrier, diluent, or excipient.

3. The ~~method~~ use of claim 1, wherein the ~~peptide~~ medicament is to be administered orally, subcutaneously, intramuscularly, intravenously, transdermally, intranasally, by pulmonary administration, or by osmotic pump.

4. The ~~method~~ use of claim 1, wherein the effective amount of ~~peptide~~ medicament is at least 1.5 mg/kg.

5. The ~~method~~ use of claim 1, wherein the medicament~~peptide~~ is to be administered to the patient every third day during radiation or chemotherapeutic agent administration.

6. The ~~method~~ use of claim 1, wherein the ~~peptide~~ medicament is to be administered in combination with an oral dosage form of a topically active corticosteroid or a metabolite thereof to a patient, wherein the oral dosage form is effective for topical or local treatment of the gastrointestinal tract and oral cavity of the patient and further wherein the patient exhibits symptoms of inflammation due to tissue damage arising from radiation or chemotherapy treatment.

7. The ~~method~~ use of claim 6, wherein the topical active corticosteroid is beclomethasone dipropionate.

8. The ~~method~~ use of claim 6, wherein the metabolite is 17-beclomethasone monopropionate.

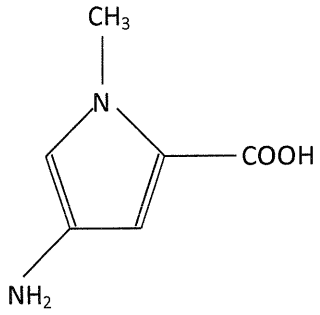
9. The ~~method~~ use of claim 6, wherein the effective amount of the topically active corticosteroid is 8 mg/day.

10. The ~~method~~ use of claim 1, wherein the ~~peptide~~ medicament is to be administered in combination with an effective amount of antibiotic.

11. An isolated peptide comprising the amino acid SEQ ID NO. 91 or SEQ ID NO. 92 or a pharmaceutical salt, ester or amide thereof.

12. An isolated peptide consisting of the amino acid sequence of
R(tBg)V1KR(tBg)V2,
wherein tBg = tert-butyl glycine
futher wherein R(tBg)V2 is linked via an amide bond between V2 and the lysine amino group in the side chain (SEQ ID NO. 91).

13. An isolated peptide consisting of the amino acid sequence
RIV(mp2)A-NH2,
wherein mp2 = 4-Amino-1-methyl-1H-pyrrole-2-carboxylic acid



(SEQ ID NO. 92).

14. ~~A~~Use of a peptide consisting of an amino acid sequence of Table 1 in the manufacture of a medicament for ~~method of~~ treating an individual suffering from a disease selected from the group consisting of bacterial infection, mucositis and colitis or exposure to acute radiation ~~comprising administering to the individual a peptide consisting of an amino acid sequence of Table 1~~.

15. The ~~method~~ use of claim 14, wherein the amino acid sequence is selected from the group consisting of SEQ ID NO. 5, SEQ ID NO. 91 and SEQ ID NO. 92.

16. The ~~method~~ use of claim 15, wherein the disease is a bacterial infection.

17. The ~~method~~ use of claim 15, wherein the amino acid sequence is SEQ ID NO. 91 or SEQ ID NO. 92 and further wherein the ~~peptide~~ medicament is to be administered in combination with an effective amount of antibiotic.

18. Use of ~~A method of preventing an infection in a subject, comprising administering to the patient an effective amount of~~:

a) a peptide comprising an amino acid sequence of up to 7 amino acids, said peptide comprising the amino acid sequence of $X_1X_2X_3P$ (SEQ ID NO: 56), wherein:

X1 is R;

X2 is I or V, wherein X2 can be N-methylated;

X3 is I or V, wherein X3 can be N-methylated;

P is proline or a proline analogue;

wherein SEQ ID NO: 56 if the first four amino acids at the N-terminus of the peptide, or a pharmaceutical salt, ester or amide thereof and a pharmaceutically-acceptable carrier, diluent, or excipient; or

b) a peptide comprising the amino acid sequence of any of SEQ ID NOs: 5, 7, 10, 14, 17, 18, 22, 23, 24, 27, 28, 31, 34, 35, 63, 64, 66-69, 72, 76, 77, 90 and 92 or a pharmaceutical salt, ester or amide thereof and a pharmaceutically-acceptable carrier, diluent or excipient in the manufacture of a medicament for preventing an infection in a subject.

19. The ~~method~~ use of claim 15, wherein the peptide comprises the amino acid sequence of SEQ ID NO. 91 or SEQ ID NO. 92.

20. The ~~method~~ use of claim 19, wherein the ~~peptide~~ medicament is to be administered in combination with an effective amount of antibiotic.