AQP1 GENE THERAPY TO PREVENT RADIATION INDUCED SALIVARY HYPOFUNCTION

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This patent application claims the benefit of U.S. Provisional Patent Application No. 63/229,279, filed August 4, 2021, which is incorporated by reference. This patent application also claims the benefit of U.S. Provisional Patent Application No. 63/297,342, filed January 7, 2022, which is incorporated by reference.

INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ELECTRONICALLY

[0002] Incorporated by reference in its entirety herein is a computer-readable nucleotide/amino acid sequence listing submitted concurrently herewith and identified as follows: One 6,274 byte file named "763111.xml," dated August 4, 2022.

BACKGROUND OF THE INVENTION

[0003] Common treatment for head and neck cancer patients involves ionizing radiation (IR). However, administration of IR to these patients damages salivary glands, which suffer irreversible damage, negatively impacting patients' quality of life.

[0004] No conventional therapy exists for this condition. However, it has been found that administration of a vector encoding aquaporin-1 (AQP1) after radiation therapy can affect the repair and reengineering of salivary glands. While effective in some respects, this process can result in considerable pain and suffering to the patient, as well as significant oral health problems. Accordingly, there remains a need for an improved method for treatment of patients undergoing IR treatment, such as head and neck cancer patients, to combat the negative impact of IR therapy on salivary glands.

BRIEF SUMMARY

[0005] In accordance with the present disclosure, it has been surprisingly discovered that, by administering a vector encoding AQPI before irradiation, the detrimental effects of IR therapy can be reduced or prevented. Administration of AQP1 complementary

deoxyribonucleic acid (cDNA) to a salivary gland prior to treatment with IR prevents the subsequent IR-induced loss in function. The administration of AQP1 (e.g., human AQP1; hAQP1) prior to IR treatment (e.g., in patients with head and neck cancer) can reduce or prevent IR-induced salivary hypofunction, resulting in an elevated salivary output.

[0006] In one aspect, the present disclosure provides a use of a vector encoding an aquaporin (AQP) protein in the manufacture of a medicament for preventing or reducing radiation-induced salivary dysfunction in a subject, wherein the use comprises: (a) that the medicament is to be administered to the subject, and (b) that ionizing radiation is to be administered to the subject following (a), thereby preventing or reducing radiation-induced salivary dysfunction in the subject. Accordingly, in accordance with an example, the disclosure provides a vector (e.g., AAV vector) and a virion comprising such a vector (e.g., AAV virion) that encodes an AQP1 protein for the prevention or reduction of radiation-induced salivary dysfunction (e.g., hypofunction) in a subject. The use of the vector or virion for the preparation of a medicament to prevent or reduce radiation-induced salivary dysfunction in a subject also is provided. In one example, such a vector or virion is useful for protecting a subject from radiation-induced salivary dysfunction.

[0007] In accordance with an example, the disclosure provides a method of preventing or reducing radiation-induced salivary dysfunction in a subject. The method comprises (a) administering a vector encoding an aquaporin (AQP) protein to the subject, and (b) administering ionizing radiation to the subject following (a), thereby preventing or reducing radiation-induced salivary dysfunction in the subject. In one example, salivary gland function can be maintained at a level equivalent to, or at least equivalent to, salivary gland function prior to administration of the ionizing radiation.

[0008] The AQP protein can be any suitable AQP protein including but not limited to an AQP1 protein. For example, in one example, the AQP1 protein is or comprises human AQP1 (hAQP1) protein.

[0009] The vector encoding the AQP (e.g., hAPQP1) can be or comprise any suitable vector including but not limited to a viral vector. For example, in one example, the viral vector is or comprises an adenoviral vector (e.g., serotype 2 or serotype 5 adenoviral vector). In another example, the viral vector is or comprises an adeno-associated viral (AAV) vector (e.g., AAV2, AAV5, AAV6, AAV44.9, or BAAV).

[0010] The viral vector (e.g., AAV vector) can be administered to the subject as a vector or as a virion comprising the vector (e.g., AAV vector). In one example, the virion is or comprises an AAV virion. The vector or virion can be administered to the subject at any suitable location and by any suitable administration route. In example, the vector or virion is administered to a salivary gland of the subject.

CLAIMS:

1. Use of a vector encoding an aquaporin (AQP) protein in the manufacture of a medicament for preventing or reducing radiation-induced salivary dysfunction in a subject, wherein the use comprises:

(a) that the medicament is to be administered to the subject, and

(b) that ionizing radiation is to be administered to the subject following (a),

thereby preventing or reducing radiation-induced salivary dysfunction in the subject.

2. The use of claim 1, wherein the medicament is to be administered to a salivary gland of the subject.

3. The use of claim 1 or 2, wherein AQP protein comprises an AQP1 protein.

4. The use of claim 3, wherein the AQP1 protein comprises human AQP1 protein.

5. The use of any one of claims 1-4, wherein the vector comprises a viral vector.

6. The use of claim 5, wherein the viral vector comprises an adenoviral vector.

7. The use of claim 6, wherein the adenoviral vector comprises serotype 2 or serotype 5.

8. The use of claim 5, wherein the viral vector comprises an adeno-associated viral (AAV) vector.

9. The use of claim 8, wherein the AAV vector comprises AAV2, AAV5, AAV6, AAV44.9, or BAAV.

10. The use of claim 8 or 9, wherein the AAV vector is to be administered as a virion comprising the AAV vector.

11. The use of claim 10, wherein the virion comprises an AAV virion.

12. The use of any one of claims 1-11, wherein salivary gland function is maintained at a level equivalent or at least equivalent to salivary gland function prior to administration of the ionizing radiation.

13. The use of any of claims 1-12, wherein the subject is a human patient.

14. The use of claim 13, wherein the patient has head and neck cancer.