Interestingly, IFNλ retains many antiviral properties despite the less inflammatory response compared with type I IFNs. This has spurred development of IFNλ for clinical use as an alternative treatment to IFNα for HCV infection (Muir et al., J. Hepatol. 61 (2014), 1238-1246). More recent developments also indicate that IFNλ treatment could also be utilized to control respiratory viral infections. IFNλ2 and 3 was shown to control IAV pulmonary titers similarly to IFNα or IFNβ treatment (Davidson et al., EMBO Mol. Med. 8 (2016), 1099-1112; Kim et al, Am. J. Respir. Cell. Mol. Biol. 56 (2017), 202-212). Importantly, IFNλ treatment avoided excessive pulmonary inflammation associated with IFNα treatment (Kim et al., Am. J. Respir. Cell. Mol. Biol. 56 (2017), 202-212). Therapeutic applications of IFNλ so far concentrate on the administration of the recombinantly produced protein. However, the use of recombinantly produced protein requires the repeated administration of relatively high doses of protein since the protein is relatively quickly cleared from the system and can, thus, only act for a brief period of time. For example in Dinnon III et al. (Nature https://doi.org/10.1038/s41586-020-2708-8 (2020)) 2 μg of peg-IFNλ1 is administered subcutaneously to mice. Similarly, Davidson et al. (EMBO Mol. Med. 8 (2016), 1099-1112) describe the administration of 2.6 μg/50μl of IFNλ3 to B6.A2G-Mx mice for treating or preventing influenza infection. In Galani et al. (Immunity 46 (2017), 875-890), it was reported that mice were treated with 5 or 10 μg of recombinant mouse pegylated IFNλ2.

Therefore, there is a need to provide means and methods for an efficient way to deliver IFNλ *in vivo* to target tissues, i.e. in a manner which ensures that it is active for an extended period of time and can exert its effect for an extended period of time. This would allow to reduce the amount of IFNλ to be administered to a patient within a given period of time and would also allow to reduce the numbers of administrations to a patient.

The present invention addresses this need by providing the embodiments as recited in the claims.

Summary

In one aspect, the present disclosure provides a use of a pharmaceutical composition comprising an mRNA encoding an IFN-λ polypeptide in the manufacture of a medicament for treating or preventing a viral-induced disorder.

Thus, the present invention relates to a pharmaceutical composition comprising an mRNA encoding an IFN-λ polypeptide for use in treating and/or preventing a viral-induced disorder.

The present invention is based on the finding that mRNA which codes for IFNλ allows for an extremely efficient and long-lasting activating effect on down-stream targets important for antiviral activity of IFN-λ when transfected into cells which serve as a model for alveolar epithelial cells. In particular, in an *in vitro* model using A-549 cells (a model for type II-like pneumocytes/alveolar epithelial cells), even at extremely low doses of mRNA

CLAIMS

1. Use of ~~A~~ a pharmaceutical composition comprising an mRNA encoding an IFN-λ polypeptide ~~for use in~~in the manufacture of a medicament for treating or preventing a viral-induced disorder.

2. The ~~pharmaceutical composition for~~ use of claim 1, wherein said viral-induced disorder is a viral-induced respiratory disorder.

3. The ~~pharmaceutical composition for~~ use of claim 2, wherein the virus which causes said viral-induced respiratory disorder is selected from the group consisting of rhinovirus, influenza virus, parainfluenza virus, metapneumo virus, respiratory syncytial virus, adenovirus and corona virus.

4. The ~~pharmaceutical composition for~~ use of claim 2 or 3, wherein the virus which causes said viral-induced respiratory disorder is a virus which enters cells via the ACE2 receptor.

5. The ~~pharmaceutical composition for~~ use of claim 4, wherein said virus is SARS-CoV, SARS-CoV-2 or HCoV-NL63.

6. The ~~pharmaceutical composition for~~ use of any one of claims 2 to 5, wherein the mRNA is to be administered by delivery into the respiratory system.

7. The ~~pharmaceutical composition for~~ use of claim 6, wherein said delivery into the respiratory system is inhalation.

8. The ~~pharmaceutical composition for~~ use of claim 7, wherein said inhalation is inhalation of an aerosol comprising said mRNA.

9. The ~~pharmaceutical composition for~~ use of any one of claims 1 to 8, wherein the mRNA contains a combination of unmodified and modified nucleotides, wherein 5 to 50% of the uridine nucleotides and 5 to 50% of the cytidine nucleotides are modified uridine nucleotides and modified cytidine nucleotides, respectively, and wherein preferably the modified uridine nucleotides are 2-thiouridine and the modified cytidine nucleotides are 5-methylcytidine.

10. The ~~pharmaceutical composition for~~ use of any one of claims 1 to 9, wherein said IFN-λ polypeptide is selected from the group consisting of IFNλ1, IFNλ2 and IFNλ3 or a combination thereof.

11. The ~~pharmaceutical composition for~~ use of claim 10, wherein the coding region of the mRNA coding for IFNλ1 is as shown in SEQ ID NO: 1, wherein the coding region of the mRNA coding for IFNλ2 is as shown in SEQ ID NO: 3 or wherein the coding region of the mRNA coding for IFNλ3 is as shown in SEQ ID NO: 5.

12. The ~~pharmaceutical composition for~~ use of claim 10 or 11, wherein the mRNA coding for IFNλ1 has a sequence as shown in SEQ ID NO: 13, wherein the mRNA coding for IFNλ2 has a sequence as shown in SEQ ID NO: 14 or wherein the mRNA coding for IFNλ3 has a sequence as shown in SEQ ID NO: 15.

13. The ~~pharmaceutical composition for~~ use of any one of claims 1 to 12 further comprising an mRNA encoding a type I interferon and/or an mRNA encoding a type II interferon.

14. The ~~pharmaceutical composition for~~ use of claim 13, wherein the type I interferon is selected from the group consisting of IFN-α, preferably IFN-α16, and IFN-β, and wherein the type II interferon is IFNγ.

~~15. A DNA molecule having a sequence as shown in any one of SEQ ID NOs: 10 to 12.~~