It is to be understood that if any prior art publication is referred to herein, such reference does not constitute an admission that the publication forms a part of the common general knowledge in the art in Australia or any other country.

SUMMARY

A first example provides a method for treating AAD/ asthma in a subject, the method comprising administering a mesenchymoangioblast mesenchymal stem cell (MCA-MSC) to the subject, wherein the MCA-MSC expresses miR-145-5p, miR-181b-5p, and miR-214-3p, but not miR-127-3p and miR-299-5p.

The first aspect provides use of a mesenchymoangioblast mesenchymal stem cell (MCA-MSC) in the manufacture of a medicament for treating AAD/ asthma in a subject, wherein the MCA-MSC expresses miR-145-5p, miR-181b-5p, and miR-214-3p, but not miR-127-3p and miR-299-5p.

A further alternative or additional example of the first example provides a mesenchymoangioblast mesenchymal stem cell (MCA-MSC) for use in a method of treating AAD/ asthma in a subject, wherein the MCA-MSC expresses miR-145-5p, miR-181b-5p, and miR-214-3p, but not miR-127-3p and miR-299-5p.

In one example, the MCA-MSC has a $CD73^{+}CD105^{+}CD90^{+}CD146^{+}CD44^{+}CD10^{+}CD31^{-}CD45^{-}$ phenotype.

In one example the MCA-MSC is made by a method comprising:

(a) culturing a primitive mesoderm cell in a mesenchymal-colony forming medium (M-CFM) comprising LiCl and FGF2, but excluding PDGF, under normoxic conditions for sufficient time for a mesenchymal colony to form; and

(b) culturing the mesenchymal colony of (a) adherently to produce the MCA-MSC.

In one example, the MCA-MSC is administered intravenously or intranasally. In one example, the MCA-MSC is administered intranasally.

In one example, treating comprises administering about $1x10^{6}$ to about $1x10^{9}$ MCA-MSCs to the subject.

In one example, the subject is mammalian. In one example, the subject is human.

In one example, the subject has previously been administered a corticosteroid or a β agonist for treating asthma. In another example, the subject has not previously been administered a corticosteroid or a β agonist for treating asthma.

In one example, the subject is not administered a corticosteroid or a β-agonist.

In one example, the subject has severe asthma or severe-refractory asthma.

In one example, treating AAD/ asthma or a characteristic feature thereof comprises:

(a) decreasing AI, AWR, airway fibrosis, lung fibrosis, goblet cell metaplasia, epithelial thickening, airway transforming growth factor (TGF)-β1 level, subepithelial myofibroblast density, subepithelial collagen concentration, or total lung collagen concentration; or

(b) increasing lung matrix metalloproteinase (MMP) activity; or

(c) any combination of any one or more feature of (a) or any combination of any one or more feature of (a) and (b).

Use of MCA-MSCs to treat AAD/ asthma or a characteristic feature thereof may provide one or more of the following non-limiting advantages:

- substantial if not complete reversal of aberrant airway TGF-β1 levels, airway/lung fibrosis and AHR
- increased collagen-degrading MMP levels
- no effect on basal expression of the parameters measured, indicating a safe and effective treatment of AAD/ asthma.

The solution provided by the disclosure was unexpected because previous studies showed that ovalbumin (OVA)-induced promotion of subepithelial and total collagen deposition could only be fully reversed when stem cell-based treatments were administered in combination with an anti-fibrotic drug. Therefore, the present disclosure provides a significant improvement in treating AAD/ asthma.

CLAIMS

1. Use of a mesenchymoangioblast mesenchymal stem cell (MCA-MSC) in the manufacture of a medicament for treating allergic airways disease (AAD)/ asthma in a subject, wherein the MCA-MSC expresses miR-145-5p, miR-181b-5p, and miR-214-3p, but not miR-127-3p and miR-299-5p.

2. The use of claim 1, wherein the MCA-MSC has a $CD73^{+}CD105^{+}CD90^{+}CD146^{+}CD44^{+}CD10^{+}CD31^{-}CD45^{-}$ phenotype.

3. The use of claim 1 or 2, wherein the MCA-MSC is made by a method comprising:

(a) culturing a primitive mesoderm cell in a mesenchymal-colony forming medium (M-CFM) comprising LiCl and FGF2, but excluding PDGF, under normoxic conditions for sufficient time for a mesenchymal colony to form; and

(b) culturing the mesenchymal colony of (a) adherently to produce the MCA-MSC.

4. The use of any one of claims 1 to 3, wherein the MCA-MSC is to be administered intravenously or intranasally.

5. The method or use of any one of claims 1 to 4, wherein the MCA-MSC is to be administered intranasally.

6. The use of any one of claims 1 to 5, wherein treating comprises that about $1x10^{6}$ to about $1x10^{9}$ MCA-MSCs is to be administered to the subject.

7. The use of any one of claims 1 to 6, wherein the subject is mammalian.

8. The use of any one of claims 1 to 7, wherein the subject is human.

9. The use of any one of claims 1 to 8, wherein the subject has previously been administered a corticosteroid or a β-agonist for treating asthma.

10. The use of any one of claims 1 to 8, wherein the subject has not previously been administered a corticosteroid or a β-agonist for treating asthma.

11. The use of any one of claims 1 to 10, wherein the subject has severe asthma or severe-refractory asthma.

12. The use of any one of claims 1 to 11, wherein treating AAD/asthma comprises:

(a) decreasing AI, AWR, airway fibrosis, lung fibrosis, goblet cell metaplasia, epithelial thickening, airway transforming growth factor (TGF)-β1 level, subepithelial myofibroblast density, subepithelial collagen concentration, or total lung collagen concentration; or

(b) increasing lung MMP activity; or

(c) any combination of any one or more feature of (a) or any combination of any one or more feature of (a) and (b).

13. The use of any one of claims 1 to 12, wherein the subject is not to be administered a corticosteroid or a β-agonist.