CLAIMS

1. Use of a composition comprising mesenchymal lineage precursor or stem cells (MLPSCs) in the manufacture of a medicament for treating Acute Respiratory Distress Syndrome (ARDS) in a human subject in need thereof, in which the subject with ARDS is greater than or equal to 65 years old and in which the composition comprises greater than 4 million MLPSCs per kilogram of body weight (cells/kg), in which the ARDS is caused by a coronavirus.

2. Use according to Claim 1, in which the subject has increased inflammatory biomarkers which indicate:

(a) increased neutrophil and macrophage influx into lungs influx;

(b) increased macrophage inflammation and augmented neutrophil migration to lungs; and/or,

(c) T cell activation/proliferation and apoptotic death.

3. Use according to Claim 1 or 2, in which the subject is on a ventilator.

4. Use according to Claim 2 or 3, in which:

(a) the inflammatory biomarkers which indicate increased neutrophil and macrophage influx into lungs are CCR2- or CXCR3-binding chemokines, in which the CCR2-binding chemokine(s) is CCL2, CCL3, or CCL7, preferably CCL2, in which CXCR3-binding chemokine is CXCL10 or CXCL9, preferably CXCL10;

(b) the inflammatory biomarkers which indicate increased macrophage inflammation and augmented neutrophil migration to lungs are IL-6 or IL-8; and/or

(c) the inflammatory biomarkers which indicate T cell activation/proliferation and apoptotic death are CCL19 or IL-2.

5. Use according to any preceding claim, in which the subject's level of inflammatory biomarker(s) are increased relative to a subject who is less than 65 years old, preferably in which the subject's level of inflammatory biomarker(s) are

increased by at least 2 fold relative to a subject who is less than 65 years old, more preferably in which the subject's level of inflammatory biomarker(s) are increased by at least 5 fold relative to a subject who is less than 65 years old.

6. Use according to any preceding claim, in which the subject has persistent CRP levels after being administered a first dose of MLPSCs which comprises less than 4 million MLPSCs per kilogram of body weight (cells/kg).

7. Use according to Claim 6, in which the subject has persistent CRP levels 3 days after being administered the first dose of MLPSCs.

8. Use according to any of Claims 3 to 7, in which the subject is taken off the ventilator after treatment, preferably in which the subject is taken off a ventilator within 60 days of treatment.

9. Use of a composition comprising mesenchymal lineage precursor or stem cells (MLPSCs) in the manufacture of a medicament for treating or preventing Acute Respiratory Distress Syndrome (ARDS) in a human subject in need thereof, in which the subject:

is greater than or equal to 65 years old; and/or,

has an increased level of one or more inflammatory biomarkers relative to a subject who is less than 65 years old; and/or,

has persistent CRP levels 3 days after being administered a first dose of mesenchymal lineage precursor or stem cells (MLPSCs) which comprises less than 4 million MLPSCs per kilogram of body weight (cells/kg); and

in which the composition comprises greater than 4 million MLPSCs per kilogram of body weight (cells/kg),

in which the one or more inflammatory biomarkers selected from the list comprising: (i) a CXCR3 binding chemokine, preferably CXCL10, and/or CXCL9; (ii) a CCR2-binding chemokine, preferably CCL2, CCL3, and/or CCL7; (iii) IL-6; (v) IL-8; (vi) CCL19; (vii) IL-2; and/or (viii) CRP; and wherein the ARDS is caused by a coronavirus.

10. Use according to any preceding claim, in which treatment decreases the level of at least one inflammatory biomarker(s) relative to baseline, wherein the at least one inflammatory biomarker(s) indicate:

(a) reduced neutrophil and macrophage influx into lungs;

(b) reduced inflammasome;

(c) reduced macrophage activation and neutrophil migration to lungs;

(d) reduced T cell influx and activation; or

(e) reduced circulating biomarkers of macrophage and neutrophil inflammation.

preferably in which the inflammatory biomarker(s) is one or more of the following:

a CXCR3-binding chemokine, preferably CXCL10, and/or CXCL9;

CCR2-binding chemokine, preferably CCL2, CCL3, and/or CCL7;

IL-6;

IL-8;

TNF;

IL-18;

CCL19;

IL-4;

IL-13;

GM-CSF;

CRP; or

Ferritin.

11. Use according to any preceding claim, in which:

treatment reduces CRP and/or ferritin levels within 3 to 14 days of administering greater than 4 million MLPSCs per kilogram of body weight (cells/kg); and/or

treatment improves respiratory function in the subject, preferably in which respiratory function as defined by Berlin criteria is improved at day 14 and/or day 21.

12. Use according to any preceding claim, in which

the composition comprises greater than 5 million MLPSCs/kg, greater than 6 million MLPSCs/kg, or greater than 8 million MLPSCs/kg;

the greater than 4 million MLPSCs/kg is to be administered over at least 2 to 3 doses;

the subject receives greater than 4 million MLPSCs per kilogram of body weight (cells/kg) within 5 to 9 days of being administered a first dose, preferably in which the subject receives greater than 4 million MLPSCs per kilogram of body weight (cells/kg) within 7 days of being administered a first dose; or

the composition comprises between 1 x 10^8 and 2.5 x 10^8 MLPSCs per dose, preferably about 1.6 x 10^8 MLPSCs per dose.

13. Use according to any preceding claim, in which the subject is also taking a corticosteroid, or in which a corticosteroid is to be administered to the subject, preferably in which the corticosteroid is dexamethasone.

14. Use according to any preceding claim, in which the ARDS is moderate or severe and/or in which the coronavirus is Severe Acute Respiratory Syndrome coronavirus (SARS-CoV), Middle East Respiratory Syndrome coronavirus (MERS-CoV) or COVID-19.

15. Use according to any preceding claim, in which

the MLPSCs have been cryopreserved and thawed; and/or

the MLPSCs are culture expanded from an intermediate cryopreserved MLPSCs population, preferably in which the MLPSCs are culture expanded for at least about 5 passages.

16. Use according to any preceding claim, in which the MLPSCs are mesenchymal stem cells (MSCs), optionally in which the MLPSCs are allogeneic and/or the MLPSCs are modified to carry or express an anti-viral drug or thrombolytic agent.

17. Use of a composition comprising mesenchymal lineage precursor or stem cells (MLPSCs) in the manufacture of a medicament for treating Acute Respiratory Distress Syndrome (ARDS) in a human subject in need thereof, in which:

the subject is to be administered with 4 million mesenchymal lineage precursor or stem cells (MLPSCs) per kilogram of body weight (cells/kg);

determining or having determined the subject's level of one or more biomarkers selected from the group consisting of CXCL10, CXCL9, CCL2, CCL3, CCL7, IL-6, IL-8, CCL19, IL-2, ferritin and/or CRP relative to a baseline level of the biomarker(s) prior to administering MLPSCs;

a further dose of MLPSCs is to be administered to the subject if the level of one or more biomarkers does not decrease from baseline, wherein following the further dose, the subject has been administered greater than 4 million MLPSCs per kilogram of body weight (cells/kg).

18. Use according to Claim 17, in which

the biomarker is CRP and/or ferritin, preferably in which the subject's level of CRP and/or ferritin is determined relative to baseline at day 7 and/or day 14; and/or

the further dose comprises 2 million MLPSCs per kilogram of body weight (cells/kg).