CLAIMS

1. Use of a composition comprising a population of culture expanded mesenchymal lineage precursor or stem cells (MLPSCs) or extracellular vesicles obtained therefrom in the manufacture of a medicament for treating an inflammatory disease in a subject, in which the MLPSCs have been culture expanded in a cell culture medium comprising at least one pro-inflammatory cytokine, preferably in which the extracellular vesicles are exosomes.

2. Use according to Claim 1, in which the MLPSCs have been culture expanded in media containing:

IFN-gamma and/or TNF-alpha; and/or

one or more pro-inflammatory cytokines selected from the group consisting of IL-6; IL-8; IL-17A; MCP-1; MIP-1-alpha; MIP-1-beta; IP-10.

3. Use according to Claim 1 or 2, in which the media contains three or more pro-inflammatory cytokines.

4. Use according to Claim 1 or 2, in which the media contains two or more pro-inflammatory cytokines selected from the group consisting of IL-6; IL-8; IL-17A; MCP-1; MIP-1-alpha; MIP-1-beta; IP-10.

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

the level of IFN-gamma is < 1 ng/ml, preferably < 500 pg/ml, more preferably < 100 pg/ml; and/or

the level of TNF-alpha is < 1 ng/ml, preferably < 750 pg/ml, more preferably < 400 pg/ml.

6. Use according to any preceding claim, in which the media is characterised by one or more or all of the following:

(i) a level of IFN-gamma greater than 1 pg/ml;

(ii) a level of TNF-alpha greater than 2 pg/ml;

(iii) a level of IL-6 greater than 3 pg/ml;

(iv) a level of IL-8 greater than 500 pg/ml;

(v) a level of IL-17A greater than 0.2 pg/ml;

(vi) a level of MCP-1 greater than 3 pg/ml;

(vii) a level of MIP-1-alpha greater than 0.5 pg/ml;

(viii) a level of MIP-1-beta greater than 3 pg/ml;

(ix) a level of IP-10 greater than 500 pg/ml.

7. Use according to any preceding claim, in which the media contains serum which comprises the pro-inflammatory cytokines.

8. Use according to Claim 7, in which:

the media comprises a non-foetal serum;

the serum is a newborn mammalian serum;

the serum is newborn calf serum (NBCS);

the serum is obtained no more than 21 days after birth;

the serum is obtained between the day of birth and 21 days after birth; between the day of birth and 14 days after birth; between the day of birth and 10 days after birth; or, between the day of birth and 7 days after birth; or

the serum is obtained between the day of birth and 10 days after birth.

9. Use according to Claim 7 or 8, in which:

the media comprises at least 5% (v/v) NBCS;

the media comprises 5% non-foetal serum; or

the media comprises 5% non-foetal serum and 5% foetal serum.

10. Use according to any of Claims 1 to 6, in which the media is serum free and/or xeno free.

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

the inflammatory disease is mediated by T-cell activation;

the inflammatory disease is refractory to steroid immunosuppressant and/or ruxolitinib;

the inflammatory disease is hyperinflammation;

the inflammatory disease is hyperinflammation, in which the hyperinflammation is caused by a coronavirus infection, preferably in which the coronavirus is coronavirus (SARS-CoV), Middle East Respiratory Syndrome coronavirus (MERS-CoV) or COVID-19;

the inflammatory disease is multi-system inflammatory syndrome (MIS) or acute respiratory distress syndrome (ARDS);

the inflammatory disease is selected from the group consisting of graft versus host disease (GvHD), pruritus, skin inflammation, psoriasis, multiple sclerosis, rheumatoid arthritis, osteoarthritis, systemic lupus erythematosus, Hashimoto's thyroidis, myasthenia gravis, type I or II diabetes, diabetic nephropathy, asthma, inflammatory lung injury, inflammatory liver injury, inflammatory glomerular injury, atopic dermatitis, allergic contact dermatitis, irritant contact dermatitis, seborrhoeic dermatitis, Sjoegren's syndrome, keratoconjunctivitis, uveitis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, an inflammatory disease of the joints, skin, or muscle, acute or chronic idiopathic inflammatory arthritis, myositis, a demyelinating disease, chronic obstructive pulmonary disease (COPD), interstitial lung disease, interstitial nephritis and chronic active hepatitis;

the inflammatory disease is diabetes or an associated condition or symptom of diabetes selected from the group consisting of abnormal wound healing, kidney failure, blindness, neuropathy, nephropathy, retinopathy, inflammation, impotence or nonalcoholic steatohepatitis (NASH);

the inflammatory disease is type II diabetes, rheumatoid arthritis or diabetic nephropathy; or

the inflammatory disease is pain, in which the pain is chronic pain and/or lower back pain, preferably in which the lower back pain is associated with a degenerated disc.

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

the MLPSCs or extracellular vesicles obtained therefrom are formulated for systemic and/or intravenous administration;

the MLPSCs or extracellular vesicles obtained therefrom are administered over multiple doses; and/or

the composition comprises between 1 x 10^7 and 2 x 10^8 cells.

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

the mesenchymal lineage precursor or stem cells are mesenchymal precursor cells (MPCs), optionally in which the MPCs are isolated from bone mononuclear cells with an anti-STRO-3 antibody before culture expansion; or

the mesenchymal lineage precursor or stem cells are mesenchymal stem cells (MSCs).

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

the MLPSCs or extracellular vesicles obtained therefrom are allogeneic;

the MLPSCs or extracellular vesicles obtained therefrom have been cryopreserved prior to administration;

the cells have been cryopreserved prior to culture expansion in a cell culture medium comprising non-foetal serum; and/or

the MLPSCs have been culture expanded in a cell factory, optionally in which the cell factory is passively primed with CO2 before seeding cells.

15. Use according to any preceding claim, comprising selecting for use in treatment culture expanded MLPSCs or extracellular vesicles obtained therefrom that have increased level(s) of one or more angiogenic markers selected from the group consisting of:

the level of VEGF, angiogenin and/or SDF-1α expressed by the MLPSCs under culture conditions; and/or

the level of endothelial network formation, endothelial network length, endothelial branch length measured after treating a population of endothelial cells with conditioned media obtained from the MLPSCs,

preferably in which an increased level of the one or more angiogenic markers is determined relative to a population of MLPSCs that have been culture expanded in a cell culture medium comprising 10% foetal serum.