

CLAIMS

1. A process for the manufacturing of a composition of Extracellular Vesicles (EVs) derived from mesenchymal stromal cells (MSCs), said method comprises:
 - 5 - culturing and expanding MSCs in a serum-free and xeno-free medium comprising human albumin and human transferrin;
 - collecting cell supernatant, said cell supernatant comprises EVs;
 - filtering said cell supernatant to obtain EVs; and
 - 10 - concentrating said EVs, wherein said human albumin concentration in said medium is between 1 g/L and 5 g/L.
2. Process according to claim 1, wherein said human albumin and human transferrin are purified from human plasma or are recombinant albumin and recombinant transferrin.
3. Process according to any of the previous claims, wherein the human transferrin
15 concentration in said medium is between 55 mg/l and 100 mg/l, preferably between 55 mg/l and 70 mg/l.
4. Process according to any of the previous claims, wherein said filtering of cell supernatant is an at least two-step filtration process.
5. Process according to claim 4, wherein said filtering in a two-step filtration
20 process is performed through a first filter having a mesh size of between 1 and 5 μm , and subsequently through a second filter having a mesh size below 1 μm .
6. Process according to any of claims 4 to 5, wherein said concentration step is a tangential flow filtration step, thereby concentrating the filtrate of the filtration process.
- 25 7. Process according to claim 6, wherein at least 0.25×10^9 particles/ml cell medium are produced in a time span of 18 to 24 hours of culturing said MSCs, wherein at least 90% of said particles with particle size of between 0.05 and 0.22 micron are EVs.
8. A composition comprising Extracellular Vesicles (EVs) derived from
30 mesenchymal stromal cells (MSCs), wherein said EVs have a size below 1 μm , wherein said composition has a human albumin concentration of between 10 and 30 g/l, and wherein at least 90% of said human albumin present in said composition is associated with said EVs.
9. The composition according claim 8, wherein said composition comprises human
35 transferrin, preferably in a concentration of between 60 mg/l to 600 mg/l.

10. The composition according to claim 8 or 9, wherein said composition comprises human transferrin and human albumin at a ratio of between 2 and 60 mg transferrin per g albumin.
11. The composition according to any of claims 8 to 10, wherein said EVs have a size of between 50 and 300 nm.
12. The composition according to any of claims 8 to 11, wherein the composition is further formulated and/or processed.
13. The composition according to any of claims 8 to 12, for therapeutic or prophylactic use.
14. The composition according to any of claims 8 to 12, for use in the prevention or treatment of lung disorders.
15. The composition for use according to claim 14, wherein said lung disorder is inflammatory lung disease, lung vascular disease, or acute lung injury.
16. The composition for use according to claim 15, wherein said inflammatory lung disease is pulmonary hypertension, asthma, bronchopulmonary dysplasia (BPD), allergy, pneumonia, or idiopathic pulmonary fibrosis.
17. The composition for use according to claim 15, wherein said acute lung injury is associated with sepsis or is acute respiratory distress syndrome (ARDS).
18. The composition for use according to claim 15, wherein said inflammatory lung disease is associated with a viral infection, preferably associated with influenza, SARS-CoV-1, MERS, or SARS-CoV-2.
19. The composition according to any of the claims 8 to 12, for use in the treatment of COVID-19, preferably for use in the treatment of COVID-19 induced or acute pneumonia.
20. The composition according to any of claims 8 to 12, for use in the prevention or treatment of inflammatory bowel disease such as Crohn's Disease.
21. The composition for use according to any of claims 13 to 20, wherein a therapeutically effective amount of said composition is to be administered to a patient, said patient may be an adult, an infant or a neonate.
22. The composition for use according to claim 21, wherein said composition is to be administered at a dose of 10^9 EVs/kg to 10^{12} EVs/kg of said patient or for each administration.