substrate having stiffness of about 1 kPa to 100 kPa and not coated with a matrix protein.

The method may be *in vitro*.

In one example, the stiffness is about, 1 kPa, 10 kPa, or 40 kPa.

In one example, the matrix protein is a collagen, fibronectin, or laminin.

In one example, the substrate has stiffness of about 10 kPa and is coated with fibronectin.

In one example, the substrate has stiffness of about 1 kPa or 10 kPa and is coated with fibronectin and collagen.

In one example, the substrate is coated with a matrix protein at about 25 µg/mL.

In one example, the substrate comprises polyacrylamide.

In one example, the MSC is produced according to WO2017/156580.

In one example, the method further comprises cryopreserving the MSC after culturing the MSC on the substrate.

In one example, the method further comprises thawing the cryopreserved MSC, wherein improved angiogenic potential persists after cryopreservation and thawing.

In one example, improved angiogenic potential is measured using a tubulogenesis assay.

A second aspect provides a mesenchymal stem cell (MSC) having angiogenic potential when improved by the method of the first aspect.

A third aspect provides a composition comprising a mesenchymal stem cell (MSC) when prepared by a method comprising culturing the MSC on a substrate having stiffness of about 1 kPa to 100 kPa and coated with a matrix protein, wherein the MSC has improved angiogenic potential when compared with a MSC cultured under identical conditions except not cultured on a substrate having stiffness of about 1 kPa to 100 kPa and not coated with a matrix protein.

In one example, the composition of the third aspect is a pharmaceutical composition comprising a pharmaceutically acceptable carrier, diluent and/or excipient.

A fourth aspect provides a container comprising the MSC of the second aspect or the composition of the third aspect.

A fifth aspect provides a kit comprising the MSC the second aspect or the composition of the third aspect, or the container of the fourth aspect.

In another example, the present disclosure provides a method for treating coronary artery disease (CAD) or peripheral artery disease (PAD), the method comprising administering to a subject having CAD or PAD the MSC of the second aspect.

Additionally or alternatively, the sixth aspect provides use of the MSC of the second aspect in the manufacture of a medicament for treating coronary artery disease (CAD) or peripheral artery disease (PAD) in a subject having CAD or PAD.

In another aspect, the present disclosure refers to the MSC or the composition as disclosed herein for use in treating coronary artery disease (CAD) or peripheral artery disease (PAD) in a subject having CAD or PAD. In another example, the present disclosure provides the MSC of the second aspect for use in a method for treating coronary artery disease (CAD) or peripheral artery disease (PAD) in a subject having CAD or PAD.

BRIEF DESCRIPTION OF FIGURES

Figure 1 is a schematic representation of the experimental design investigating matrix biological and physical composition influence in stem cell proangiogenesis.

Figure 2 is a schematic representation of the experimental design testing the persistence of the pro-angiogenic effects in primed MSCs after cryopreservation.

Figure 3 is a schematic representation of the tubulogenesis assay analyses. Master segments are shown in yellow and consist in pieces of tree delimited by two junctions none exclusively implicated with one branch, called master junctions. Master junctions are junctions linking at least three master segments. Optionally, two close master junctions can be fused into a unique master junction. Master junctions are shown in red. Meshes are areas enclosed by segments or master segments. Meshes are shown in blue.

CLAIMS

1. A method for improving angiogenic potential of a mesenchymal stem cell (MSC), the method comprising culturing the MSC on a substrate having stiffness of about 1 kPa to 100 kPa and coated with a matrix protein, wherein the MSC has improved angiogenic potential when compared with a MSC cultured under identical conditions except not cultured on a substrate having stiffness of about 1 kPa to 100 kPa and not coated with a matrix protein.

2. The method of claim 1, wherein the stiffness is about, 1 kPa, 10 kPa, or 40 kPa.

3. The method of claim 1 or claim 2, wherein the matrix protein is a collagen, fibronectin, or laminin.

4. The method of any one of claims 1 to 3, wherein the substrate has stiffness of about 10 kPa and is coated with fibronectin.

5. The method of any one of claims 1 to 3, wherein the substrate has stiffness of about 1 kPa or 10 kPa and is coated with fibronectin and collagen.

6. The method of any one of claims 1 to 5, wherein the substrate is coated with a matrix protein at about 25 µg/mL.

7. The method of any one of claims 1 to 6, wherein the substrate comprises polyacrylamide.

8. The method of any one of claims 1 to 7, wherein the MSC is produced according to WO2017/156580.

9. The method of any one of claims 1 to 8, further comprising cryopreserving the MSC after culturing the MSC on the substrate.

10. The method of claim 9, further comprising thawing the cryopreserved MSC, wherein improved angiogenic potential persists after cryopreservation and thawing.

11. The method of any one of claims 1 to 9, wherein improved angiogenic potential is measured using a tubulogenesis assay.

12. A mesenchymal stem cell (MSC) having angiogenic potential when improved by the method of any one of claims 1 to 11.

13. A composition comprising a mesenchymal stem cell (MSC) when prepared by a method comprising culturing the MSC on a substrate having stiffness of about 1 kPa to 100 kPa and coated with a matrix protein, wherein the MSC has improved angiogenic potential when compared with a MSC cultured under identical conditions except not cultured on a substrate having stiffness of about 1 kPa to 100 kPa and not coated with a matrix protein.

14. The composition of claim 13, wherein the composition is a pharmaceutical composition comprising a pharmaceutically acceptable carrier, diluent and/or excipient.

15. A container comprising the MSC of claim 12 or the composition of claim 13 or claim 14.

16. A kit comprising the MSC of claim 12, the composition of claim 13 or claim 14, or the container of claim 15.

17. Use of the MSC of claim 12 or the composition of claim 13 or claim 14 in the manufacture of a medicament for treating coronary artery disease (CAD) or peripheral artery disease (PAD) in a subject having CAD or PAD.

18. The MSC of claim 12 or the composition of claim 13 or claim 14 for use in treating coronary artery disease (CAD) or peripheral artery disease (PAD) in a subject having CAD or PAD.