

CLAIMS

1. An *ex vivo* method for detecting a non-adherent endothelial progenitor cell (EPC) comprising determining the level of expression of a nucleic acid encoding Dsg2 or of a Dsg2 protein, or a nucleic acid or a protein having at least about 70% identity thereto, in, on or
5 secreted from a cell, in which an increased level of expression of the nucleic acid or protein thereto compared to another cell type is indicative of an EPC.
2. A method according to Claim 1, in which the nucleic acid or protein is expressed in, on or secreted from EPCs at a level at least 1.5 fold greater or 2 fold greater or 3 fold greater or 4 fold greater or 5 fold greater than in, on or secreted by human umbilical cord vascular
10 endothelial cells (HUVECs).
3. A method according to Claim 2, in which the nucleic acid or protein is expressed in, on or secreted by non-adherent CD133⁺ EPCs at a level at least 1.5 fold greater or 2 fold greater or 3 fold greater or 4 fold greater or 5 fold greater than in, on or secreted by HUVECs.
4. An *ex vivo* method for isolating an endothelial progenitor cell (EPC), the method
15 comprising detecting an EPC by performing the method according to any preceding claim and isolating the detected EPC.
5. An *ex vivo* method for isolating a population of cells enriched for non-adherent endothelial progenitor cells (EPCs), the method comprising contacting a population of cells comprising EPCs with a compound that binds to a Dsg2 protein or a protein having at least
20 about 70% identity thereto for a time and under conditions sufficient for the compound to bind to a cell and isolating cells to which the compound is bound.
6. A method according to Claim 4 or 5, additionally comprising culturing the isolated cells to increase the number of isolated EPCs and/or differentiating the isolated and/or cultured EPCs.
- 25 7. A method according to any of Claims 4 to 6, additionally comprising determining the activity of the isolated and/or cultured EPCs.
8. A method according to any of Claims 4 to 7, additionally comprising formulating the isolated EPCs and/or cells isolated therefrom with a pharmaceutically acceptable carrier or excipient to thereby produce a pharmaceutical composition.

9. A method according to any of Claims 4 to 8, additionally comprising immobilizing the isolated EPCs and/or cells derived therefrom on a solid or semi-solid matrix.

10. A composition comprising a population of cells enriched for non-adherent endothelial progenitor cells (EPCs), in which the population is isolated by performing a method according to any of Claims 4 to 9.

11. A composition comprising a population of cells enriched for non-adherent endothelial progenitor cells (EPCs) expressing Dsg2 encoding nucleic acid or Dsg2 protein.

12. A composition according to Claim 10 or 11, in which the EPCs additionally express one or more proteins selected from the group consisting of CD133, CD117, CD34 CD144, VEGFR2 and CD31.

13. An *ex vivo* method for diagnosing and/or prognosing an endothelial progenitor cell (EPC)-associated condition in a subject, the method comprising performing the method according to any one of Claims 1 to 3 to detect an EPC in a sample from a subject and/or performing the method of Claim 7 to determine the activity of an EPC from a subject in which detection of EPC(s) and/or EPC activity or failure to detect EPCs and/or EPC activity is diagnostic or prognostic of the EPC-associated condition.

14. Use of the population enriched for non-adherent EPCs by performing the method according to any of Claims 4 to 9 in the manufacture of a medicament for treating or preventing a condition associated with reduced endothelial progenitor cell (EPC) numbers or activity, treating or preventing a condition associated with insufficient neovascularization and/or improving grafting and/or improving wound healing in a subject.

15. Use of a solid support or a semi-solid support having immobilized thereon a compound that binds to Dsg2 for a time and under conditions for the compound to bind to non-adherent EPCs from the subject in the manufacture of a medicament for treating or preventing a condition associated with reduced EPC numbers or activity and/or treating or preventing a condition associated with insufficient neovascularization and/or improving grafting and/or improving wound healing in a subject.

16. A use according to Claim 14 or 15, in which the condition is cardiovascular disease or diabetes.

CLAIMS

1. An *ex vivo* method for detecting a non-adherent CD133⁺ endothelial progenitor cell (EPC) prospectively, the method comprising determining the level of expression of a nucleic acid encoding Dsg2 or of a Dsg2 protein in, on or secreted from a cell, in which an increased
5 level of expression of the nucleic acid or protein thereto compared to human umbilical vascular endothelial cells (HUVECs) is indicative of a non-adherent EPC.
2. A method according to Claim 1, in which the nucleic acid or protein is expressed in, on or secreted from EPCs at a level at least 1.5 fold greater or 2 fold greater or 3 fold greater or 4 fold greater or 5 fold greater than in, on or secreted by HUVECs.
- 10 3. A method according to Claim 2, in which the nucleic acid or protein is expressed in, on or secreted by non-adherent CD133⁺ EPCs at a level at least 1.5 fold greater or 2 fold greater or 3 fold greater or 4 fold greater or 5 fold greater than in, on or secreted by HUVECs.
4. An *ex vivo* method for isolating an endothelial progenitor cell (EPC), the method comprising detecting an EPC by performing the method according to any preceding claim and
15 isolating the detected EPC.
5. An *ex vivo* method for isolating a population of cells enriched for non-adherent CD133⁺ endothelial progenitor cells (EPCs) prospectively, the method comprising contacting a population of cells comprising EPCs with a compound that binds to a Dsg2 protein for a time and under conditions sufficient for the compound to bind to a cell and isolating cells to
20 which the compound is bound.
6. A method according to Claim 4 or 5, additionally comprising culturing the isolated cells to increase the number of isolated EPCs and/or differentiating the isolated and/or cultured EPCs.
7. A method according to any of Claims 4 to 6, additionally comprising determining the
25 activity of the isolated and/or cultured EPCs.
8. A method according to any of Claims 4 to 7, additionally comprising formulating the isolated EPCs and/or cells isolated therefrom with a pharmaceutically acceptable carrier or excipient to thereby produce a pharmaceutical composition.

9. A method according to any of Claims 4 to 8, additionally comprising immobilizing the isolated EPCs and/or cells derived therefrom on a solid or semi-solid matrix.
10. A composition comprising a population of cells enriched for non-adherent CD133⁺ endothelial progenitor cells (EPCs) expressing Dsg2 encoding nucleic acid or Dsg2 protein.
- 5 11. A composition according to Claim 10, in which the EPCs additionally express one or more proteins selected from the group consisting of CD133, CD117, CD34 CD144, VEGFR2 and CD31.
12. An *ex vivo* method for diagnosing and/or prognosing cancer, cardiovascular disease, ischaemic event and/or autoimmune disease in a subject, the method comprising performing
10 the method according to any one of Claims 1 to 3 to detect an EPC in a sample from a subject and/or performing the method of Claim 7 to determine the activity of an EPC from a subject in which detection of EPC(s) and/or EPC activity or failure to detect EPCs and/or EPC activity is diagnostic or prognostic of the cancer, cardiovascular disease, ischaemic event and/or autoimmune disease.
- 15 13. Use of the population enriched for non-adherent CD133⁺ EPCs by performing the method according to any of Claims 4 to 9 in the manufacture of a medicament for treating or preventing a condition associated with reduced endothelial progenitor cell (EPC) numbers or activity, treating or preventing a condition associated with insufficient neovascularization and/or improving grafting and/or improving wound healing in a subject.
- 20 14. Use of a solid support or a semi-solid support having immobilized thereon a compound that binds to Dsg2 in the manufacture of a medicament for treating or preventing a condition associated with reduced EPC numbers or activity and/or treating or preventing a condition associated with insufficient neovascularization and/or improving grafting and/or improving wound healing in a subject.
- 25 15. A use according to Claim 13 or 14, in which the condition is cardiovascular disease or diabetes.