

Claims

1. A method of isolating a fetal cell in a maternal blood sample, said method comprising the steps of:

- a. Contacting a maternal blood sample or a fraction thereof with a hybridization probe comprising at least 10 contiguous nucleotides complementary to a gene encoding an endothelial cell marker or a ligand directed to an endothelial cell marker, wherein the endothelial cell marker is selected from the group consisting of CD105, CD146 or CD141, Vimentin, VCAM, ICAM, VEGFR-1, VEGFR-2, VEGFR-3, ITGA5, ITGB5, CDH11 or CDH3 and
 - b. selecting the cells specific for said endothelial cell marker thereby enriching the sample for cells with endothelial phenotype
 - c. Contacting the cells selected in b) demonstrating an endothelial phenotype with a hybridization probe comprising at least 10 contiguous nucleotides complementary to a gene encoding an epithelial cell marker or a ligand directed to an epithelial cell marker, wherein the epithelial cell marker is selected from the group consisting of CK1, CK2, CK3, CK4, CK5, CK6, CK7, CK8, CK9, CK10, CK13, CK14, CK15, CK16, CK17, CK18 or CK19,
 - d. Detecting the cells with endothelial phenotype also binding the epithelial cell marker of step c).
 - e. Optionally, diagnosing and/or predicting the genetic content of the cells detected in d)
- wherein step a)-d) may be performed in any order

2. The method of claim 1, wherein the target of the endothelial marker is located at the surface of the cell to be identified.
3. The method of claim 1, wherein the target of the epithelial marker is located intracellular of the cell to be identified.

4. A method comprising the steps of
 - a. Contacting a maternal blood sample or a fraction thereof with
 - i. a hybridization probe comprising at least 10 contiguous nucleotides complementary to a gene encoding an endothelial cell marker or
 - ii. a ligand directed to an endothelial cell marker

, wherein the endothelial cell marker is selected from the group consisting of CD105, CD146 or CD141, Vimentin, VCAM, ICAM, VEGFR-1, VEGFR-2, VEGFR-3, ITGA5, ITGB5, CDH11 or CDH3

- b. Selecting cells that bind the hybridization probe or the ligand of the previous step and thereby enriching the sample for cells that bind the hybridization probe or the ligand of the previous step

- c. Contacting the (enriched) sample with

- i. a hybridization probe comprising at least 10 contiguous nucleotides complementary to a gene encoding an epithelial cell marker or

- ii. a ligand directed to an epithelial cell marker

, wherein the epithelial cell marker is selected from the group consisting of CK1, CK2, CK3, CK4, CK5, CK6, CK7, CK8, CK9, CK10, CK13, CK14, CK15, CK16, CK17, CK18 or CK19.

5. The method of any claim 4 further comprising a step of identifying fetal cells of the sample.
6. The method of any of claims 4 and 5, wherein identification comprises detecting the presence of the ligand or the hybridization probe on or in the fetal cell.
7. The method any of the preceding claims, wherein the maternal blood sample is whole blood.
8. The method of any of the preceding claims, wherein cells in the sample are subjected to a fixation step after the selection/enrichment step.
9. The method of any of the preceding claims, wherein cells in the sample is permeabilized after the fixation step and before being contacted with the epithelial cell marker directed ligand or hybridization probe.
10. The method of any of the preceding claims, wherein the endothelial cell marker is selected from the group consisting of: CD105, CD146 or CD141.

11. The method of any of the preceding claims, wherein the endothelial cell marker is CD105.

12. The method of any of the preceding claims, wherein the epithelial cell marker is selected from the group consisting of: CK8, CK18, CK19 or CK7.