Claims

1. Method for identifying a cellular target which is involved in a cell phenotype, comprising:
   a) identifying an intrabody comprising a full V_H and/or V_L domain of an immunoglobulin, which can induce, modify or suppress said phenotype when present inside a cell;
   b) identifying a cellular target which is a direct or indirect target of said intrabody in said cell, ; and optionally
   c) isolating said cellular target.

2. Method according to claim 1, wherein step a) comprises the screening of an intracellularly expressed intrabody library, wherein each intrabody comprises a full V_H and/or V_L domain of an immunoglobulin.

3. Method according to claim 1 or 2, wherein step a) comprises:
   i) obtaining a library of molecules, wherein each molecule from the library encodes a different intrabody comprising a full V_H and/or V_L domain of an immunoglobulin;
   ii) transfecting a population of cells with the library of molecules of step i);
   iii) culturing the transfected cells for a time and under conditions sufficient for detectable induction, modification or suppression of said phenotype;
   iv) selecting the cells of step iii) which show an induction, modification or suppression of said phenotype;
   v) optionally repeating steps iii) and iv) on the cells selected from step iv) or on cells recloned from the cells selected from step iv) for one or more additional selection rounds; and
   vi) identifying the intrabody which is responsible for said phenotype induction, modification or suppression.

4. Method according to claim 3, wherein the method comprises a recloning step after at least one selection round, and submitting the recloned cells to one or more selection rounds.

5. Method according to claim 3 or 4, wherein said molecule encoding an intrabody is a vector.

6. Method according to claim 5, wherein said vector is an integrative vector such as a retroviral vector.

7. Method according to claim 2 to 6, wherein said intrabody library and/or said library of molecules is obtained by selecting an intrabody which is functional inside a cell, and then introducing modifications in one or more of its CDR regions.

8. Method according to claim 1 to 7, wherein said direct or indirect target of said intrabody binds to said intrabody or can be immunoprecipitated together with said intrabody.

9. Method according to claim 1 to 8, wherein the intrabody is an scFv, a truncated scFv comprising at least a full V_H or V_L domain, a diabody, a full V_H domain or a full V_L domain.

10. Method according to claim 1 to 9, wherein the full V_H domain and/or the full V_L domain is derived from a human antibody.

11. Method according to any one of claims 1 to 10, further comprising

- a step of target validation using RNA interference technology or a known inhibitor of said cellular target; and/or
- a step of identification of the epitope or the active site of the cellular target; and/or,
- a step of identification of a molecule which competes with the binding of the intrabody identified in step a) to the target identified in step b), and which is capable of modifying said cell phenotype.

12. Method according to any one of claims 1 to 11, wherein said cell is a eukaryotic cell, preferably a mammalian cell such as a human cell.

13. Method according to claim 12, wherein said eukaryotic cell is a cell involved in allergy, inflammation, or both and wherein said phenotype is a phenotype associated with an allergic reaction, an inflammatory reaction, or both.

14. Intrabody comprising the CDR3 sequence “DGGLREGFDC” of the V_H domain of scFv 5H4.

15. Intrabody according to claim 14, further comprising the CDR1 sequence and CDR2 sequence of the V_H domain of scFv 13R4.

16. Intrabody according to claim 14, wherein said intrabody is intrabody 5H4 (SEQ ID NO:3), 5H4-V_H (SEQ ID NO:4) or 5H4-V_L (SEQ ID NO:5).

17. Intrabody comprising the CDR3 sequence “PIAVSDY“ of the V_H domain of scFv 3H2-1.

18. Intrabody according to claim 17, further comprising the CDR3 sequence of the V_L domain of scFv 3H2-1, and preferably the CDR1 sequence and CDR2 sequence of the V_H domain of scFv 13R4, and/or the CDR1 sequence and CDR2 sequence of the V_L domain of scFv 13R4.

19. Intrabody according to claim 18, wherein said intrabody is intrabody 3H2-1 (SEQ ID NO:1).

20. Intrabody comprising the CDR3 sequence “GVRGGYGLDF“ of the V_H domain of scFv 3H2-VH.

21. Intrabody according to claim 20, further comprising the CDR1 sequence and CDR2 sequence of the V_H domain of scFv 13R4.

22. Intrabody according to claim 21, wherein said intrabody is intrabody 3H2-VH (SEQ ID NO:2).

23. Intrabody comprising one of the V_H CDR3 sequences set forth in SEQ ID NO: 7 to SEQ ID NO: 18.

24. Intrabody according to claim 23, wherein said intrabody further comprises one the V_L CDR3 sequences set forth in SEQ ID NO:19 to SEQ ID NO:29 or further comprises a glutamine as V_L CDR3 sequence.

25. Intrabody according to claim 24, wherein said intrabody further comprises the CDR1 sequence and CDR2 sequence of the V_H domain of scFv 13R4, and/or the CDR1 sequence and CDR2 sequence of the V_L domain of scFv 13R4.

26. Intrabody according to claim 14 to 25 for use in therapy.

27. Intrabody according to claim 26 for use in treating allergy and/or inflammation.

28. Use of an intrabody according to any one of claims 14 to 16 for identifying a molecule which is capable of competing with the binding of said intrabody with a protein from the C12ORF4 family, and of modifying a phenotype associated with an allergic and/or inflammatory reaction in a cell involved in allergy and/or inflammation.

29. Use according to claim 28 wherein said protein from the C12ORF4 family is C12ORF4, LOC57102, LOC297607 or LOC28040, preferably is C12ORF4.

30. Use of an intrabody according to any one of claims 17 to 19 for identifying a molecule which is capable of competing with the binding of said intrabody with a protein of the ABCF1 family, and of modifying a phenotype associated with an allergic and/or inflammatory reaction in a cell involved in allergy and/or inflammation.

31. Use according to claim 28 to 30, wherein said molecule is an organic molecule having a molecular weight of 100 to 2500 Da.

32. Inhibitor of a protein from the C12ORF4 family for use in therapy.

33. Inhibitor according to claim 32 for use in treating allergy and/or inflammation.

34. Inhibitor according to claim 32 or 33, wherein said inhibitor is

- an intrabody or an antigen-binding fragment thereof capable of binding to a protein of the C12ORF4 family, preferably an intrabody according to any one of claims 14 to 16 or an antigen-binding fragment thereof;
- an RNA molecule capable of interfering with the expression of a protein of the C12ORF4 family in a cell; or
- an organic molecule having a molecular weight of 100 to 2500 Da which is capable of displacing an intrabody according to any one of claims 8 to 10 from its binding site with a protein of the C12ORF4 family.

35. Inhibitor according to claim 32 to 34, wherein said protein of the C12ORF4 family is C12ORF4, LOC57102, LOC297607 or LOC28040, preferably is C12ORF4.

36. Inhibitor of a protein of the ABCF1 family for use in therapy.

37. Inhibitor according to claim 36 for use in treating allergy and/or inflammation.

38. Inhibitor according to claim 36 or 37, wherein said inhibitor is

- an intrabody or an antigen-binding fragment thereof capable of binding to a protein of the ABCF1 family, preferably an intrabody according to any one of claims 17 to 19 or an antigen-binding fragment thereof;
- an RNA molecule capable of interfering with the expression of a protein of the ABCF1 family in a cell; or

- an organic molecule having a molecular weight of 100 to 2500 Da which is capable of displacing an intrabody according to any one of claims 11 to 13 from its binding site with a protein of the ABCF1 family.

39. Inhibitor according to claim 36 to 38, wherein said protein of the ABCF1 family is ABCF1.

Claims

1. Method for identifying a cellular target which is involved in a predefined cell phenotype, comprising:
   a) screening an intracellularly expressed intrabody library to identify an intrabody comprising a full V_H and/or V_L domain of an immunoglobulin, which can induce, modify or suppress said phenotype when present inside a cell capable of exhibiting said phenotype; and
   b) identifying a cellular target which is involved in said phenotype, wherein said cellular target binds to said intrabody or can be immunoprecipitated with said intrabody; and optionally
   c) isolating said cellular target.

2. Method according to claim 1, wherein step a) comprises:
   i) obtaining a library of molecules, wherein each molecule from the library encodes a different intrabody comprising a full V_H and/or V_L domain of an immunoglobulin;
   ii) transfecting a population of cells with the library of molecules of step i);
   iii) culturing the transfected cells for a time and under conditions sufficient for detectable induction, modification or suppression of said phenotype;
   iv) selecting the cells of step iii) which show an induction, modification or suppression of said phenotype;
   v) optionally repeating steps iii) and iv) on the cells selected from step iv) or on cells recloned from the cells selected from step iv) for one or more additional selection rounds; and
   vi) identifying the intrabody which is responsible for said phenotype induction, modification or suppression.

3. Method according to claim 2, wherein the method comprises a recloning step after at least one selection round, and submitting the recloned cells to one or more selection rounds.

4. Method according to claim 2 or 3, wherein said molecule encoding an intrabody is a vector.

5. Method according to claim 4, wherein said vector is an integrative vector such as a retroviral vector.

6. Method according to claim 1 to 5, wherein said intrabody library and/or said library of molecules is obtained by selecting an intrabody which is functional inside a cell, and then introducing modifications in one or more of its CDR regions.

7. Method according to any one of claims 1 to 6, wherein said cellular target is a protein, a peptide, a carbohydrate, a lipid or a nucleic acid.

8. Method according to any one of claims 1 to 7, wherein said predefined cell phenotype is a morphological feature, a developmental stage, a biochemical property or a physiological property.

9. Method according to claim 1 to 6, wherein the intrabody is an scFv, a truncated scFv comprising at least a full V_H or V_L domain, a diabody, a full V_H domain or a full V_L domain.

10. Method according to claim 1 to 9, wherein the full V_H domain and/or the full V_L domain is derived from a human antibody.

11. Method according to any one of claims 1 to 10, further comprising

- a step of target validation using RNA interference technology or a known inhibitor of said cellular target; and/or
- a step of identification of the epitope or the active site of the cellular target. and/or,
- a step of identification of a molecule which competes with the binding of the intrabody identified in step a) to the target identified in step b), and which is capable of modifying said cell phenotype.

12. Method according to any one of claims 1 to 11, wherein said cell is a eukaryotic cell, preferably a mammalian cell such as a human cell.

13. Method according to claim 12, wherein said phenotype is a phenotype associated with an allergic reaction, an inflammatory reaction, or both.