

CLAIMS

1. An *in vitro* method for obtaining an *ex vivo* model of inflamed skin comprising the following steps:
 - a) injecting, into the dermis of a healthy skin biopsy previously taken from a mammal, a composition comprising an effective amount for activating dermal resident T cells of an anti-CD3 antibody and an anti-CD28 antibody,
 - b) incubating the injected skin biopsy obtained in step a) in the presence of a composition comprising an effective amount, for obtaining the polarization of the T cells activated in step a) into LTh1 and/or LTh17 and the synthesis of inflammation markers, of at least one mixture of IL-1 β , IL-23, and TGF- β .The method according to claim 1, wherein the injected composition further comprises an effective amount of IL-2.
2. The method according to any one of claim 1 or 2, wherein step a) is carried out manually.
3. The method according to any one of claims 1 to 3, wherein the incubation step b) lasts at least 5 days.
4. The method according to any one of claims 1 to 4, which comprises between steps a) and b) an additional step a') of depositing the injected skin biopsy obtained at the end of step a) on a liquid matrix capable of solidifying, said matrix being itself contained in a cell culture insert the bottom of which consists of a porous membrane and said insert being arranged in a container or well, so as to allow, once the matrix has solidified, the 3D integrity of the skin biopsy to be maintained.
5. The method according to any of claims 1 to 5, wherein the concentrations in the composition injected in step (a) of the method are the following ones:
 - between 10 ng/ μ l and 100 ng/ μ l, preferably between 20 ng/ μ l and 80 ng/ μ l, and particularly preferably from 30 ng/ μ l to 70 ng/ μ l for the anti-CD3 and anti-CD28 antibodies, and optionally,
 - between 1 ng/ml and 20 ng/ml, preferably from 2 ng/ml to 15 ng/ml, and particularly preferably from 4 ng/ml to 12 ng/ml for IL-2.

7. The method according to any of claims 1 to 6, wherein the concentrations in the at least one mixture of the composition used in step b) of the method are the following ones:
 - between 1 ng/ml and 50 ng/ml, preferably between 5 ng/ml and 30 ng/ml, and particularly preferably from 7 ng/ml to 15 ng/ml for IL-1 β and TGF β , and
 - between 10 ng/ml and 100 ng/ml, preferably from 20 ng/ml to 80 ng/ml, and particularly preferably from 30 ng/ml to 60 ng/ml for IL-23.
8. The method according to any one of claims 1 to 7, which further aims at evaluating the anti-inflammatory efficacy of a compound and comprises the following additional steps:
 - c) contacting, with a candidate compound, the model of inflamed skin obtained at the end of step b) and comprising LTh1- and/or LTh17-polarized T cells;
 - d) measuring the expression level of at least two inflammation markers of the model of inflamed skin;
 - e) comparing the expression level of said at least two inflammation markers obtained in step d) with their control expression level;
 - f) identifying the anti-inflammatory efficacy of said candidate compound when the expression level of said at least two inflammation markers measured in step d) is lower than their control expression level.
9. The method according to claim 8, which also in step d) includes measuring the expression level of at least three, in particular at least four, preferably at least five, and particularly preferably, at least six inflammation markers selected from the group consisting of IL-8, IL-17A, IL-22, IL-23, IFN γ , TNF α , S100A7, S100A8, S100A9, S100A12, SERPINB3, SERPINB4, SERPINB13, DEFB4, KRT6A, KRT16, KRT17, CXCL9, CXCL10, CCL18, and CCL20.
10. An *ex vivo* model of inflamed skin comprising a dermis, an epidermis, epidermal appendages, a hypodermis and Th1 and/or Th17 cells, which is obtainable by a method according to any one of claims 1 to 7 and is characterized by the expression of at least two inflammation markers, or of at least three or at least four, preferably at least five, and particularly preferably at least six inflammation

markers selected from the group consisting of IL-8, IL-17A, IL-22, IL-23, IFN γ , TNF α , S100A7, S100A8, S100A9, S100A12, SERPINB3, SERPINB4, SERPINB13, DEFB4, KRT6A, KRT16, KRT17, CXCL9, CXCL10, CCL18, and CCL20.

11. A cell culture insert (10), suitable for being contained in a container or a culture box well, and the bottom of which consists of a porous membrane (40), said insert containing the *ex vivo* model of inflamed skin (30) according to claim 10 embedded in a solidified matrix (20), said matrix being in contact with the inner edge of the insert and the porous membrane, the epidermis of the *ex vivo* model of inflamed skin being in contact with the atmosphere and the dermis and the epidermal appendages of the *ex vivo* model of inflamed skin being immersed in the solidified matrix.
12. A use of the *ex vivo* model of inflamed skin according to claim 10 or of the cell culture insert according to claim 11 for identifying anti-inflammatory compounds, in particular anti-psoriatic compounds.
13. A kit for implementing the method according to any of claims 1 to 9 comprising a healthy skin biopsy previously taken from a mammal, a composition A comprising an effective amount of an anti-CD3 antibody and an anti-CD28 antibody, a composition B comprising at least a mixture of IL-1 β , IL-23, and TGF- β , and optionally an injection device.
14. A kit according to claim 13, wherein the composition A comprises IL-2.