pigmentation changes, indeterminate leprosy, tuberculoid leprosy, borderline leprosy, lepromatous leprosy.

The following examples are given by way of illustration of the present invention and therefore should not be construed to limit the scope of the present invention.

EXAMPLE 1

Cultures of normal human epidermal melanocytes (NHEM) (procured from Lonza, or established from epidermis) were maintained in M254 medium containing PMA-free supplements (Invitrogen), at 37°C, in 5% CO_2. To study the effect of IFN-γ on melanocytes, early passage cultures of melanocytes were grown in the presence or absence of recombinant human IFN-γ (Peprotech) at a dose of 100 U/ml and the cells were observed after 8 days of treatment. Decreased pigmentation could be observed in the cell pellets treated with IFN-γ, confirming the presence of a mechanism for the induction of hypopigmentation (Fig 1). To understand the molecular targets of human IFN-γ (henceforth referred to simply as IFN-γ) in melanocytes and the mechanism by which the cells are hypopigmented further studies were carried out.

Melanosome maturation status in the cells and visible pigmentation are tightly linked together. The process of melanin synthesis is sequestered in the late stages of melanosome maturation and requires a proper targeting of multiple proteins to early stages of melanosomes for initiation. The status of melanosomal receptivity for the synthesis of melanin and the content of melanin within each melanosome could therefore be considered as cellular endpoint of pigmentation program. Since melanin is an electron dense substance, visualization of melanosomes is classically carried out using electron microscopy. The technique allows identification of distinct stages of melanosomes I to IV based on the organelle architecture and melanin content. IFN-γ treated cells (as mentioned above) were subjected to electron microscopy and confocal imaging using HMB45 and melanin antibody. Electron microscopic evaluation was carried out on control and IFN-γ treated cells. Analysis of the micrographs suggested that fewer stage III and IV melanosomes were detected in IFN-γ treated cells, whereas several could be distinctly identified in control cells. For finer and quantitative analysis of the status of melanosomes immuno-cytochemical approach was adopted. Control and IFN-γ treated primary melanocytes were stained with Human melanoma Black 45 (HMB45) from (Dako Cytomation) and anti-melanin antibody (rabbit polyclonal raised against synthetic melanin, raised in the laboratory). Nuclei were counterstained with DAPI (4',6-diamidino-2-phenylindole) (Invitrogen) and the cells observed

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CLEAR VERSION OF CLAIMS

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We claim:

1. A method to reversibly alter melanosóme maturation occurring in stage I and II in an epidermal melanocytes in a subject by contacting or withdrawing IFN- γ and its derivative, mimic, antagonist thereof with said melanocytes in a controlled manner,

   wherein the IFN- γ and derivative, mimic, antagonist thereof modulate the expression of IFN-γ pathway components selected from a group comprising IFNGR1, JAK1 and STAT1.

2. The method as claimed in claim 1 wherein IFN- γ, or its derivative, or its mimic, or an antagonist, or components of IFN-γ pathway are contacted with melanocytes in the range of 100 – 500 U/ml for a period in the range of 1 to 10 days.

3. The method as claimed in claim 1 wherein IFN-γ or its derivative, or a mimic or an antagonist of IFN-γ reversibly alters the levels of TYR, and TYRP2/DCT, CNO, HPS4, GPR143, OCA2, SLC7A11 and MCOLN3.

4. The method as claimed in claim 1 wherein the transfer of melanosome to keratinocytes is altered by targeting components of IFN-γ pathway selected from the group comprising of IFNG, IFNGR1, JAK1 and STAT1.

5. Use of IFN-γ and its components and its agonists and antagonists in modulating pigmentation in humans for clinical or cosmaceutical purposes.

6. A method of treating skin pigmentation by administering to a subject IFN-γ or its derivative, or a mimic or antagonist of IFN-γ.

7. The method as claimed in claim 6 wherein IFN-γ or its derivative, or a mimic or an antagonist of IFN-γ is administered to the subject by topical delivery or by sub-cutaneous delivery.

8. The method as claimed in claim 7 wherein the topical delivery or sub-cutaneous delivery is in a dosage form selected from the group comprising, a powder, a solution, an emulsion, a fluid emulsion, a suspension, a fluid suspension, a semi-

solid, an ointment, a paste, a cream, a gel, a jelly, a foam, an implant, an injection, a patch and a spray.

9. The method as claimed in claim 6 useful for treating skin disorders selected from the group comprising of hyperpigmentation, hypopigmentation, uneven pigmentation, post inflammatory pigmentation, sun-damaged skin, pigmented birthmark, acanthosis nigricans and solar lentiges, age-related pigmentation changes, indeterminate leprosy, tuberculoid leprosy, borderline leprosy, lepromatous leprosy.

10. IFN- γ and its derivative, mimic, antagonist thereof for use in reversibly altering melanosome maturation occurring in stage I and II in an epidermal melanocytes in a subject

wherein the IFN- γ and derivative, mimic, antagonist thereof modulate the expression of IFN-γ pathway components selected from a group comprising IFNGR1, JAK1 and STAT1.

11. IFN- γ and its derivative, mimic, antagonist thereof for use as claimed in claim 10 wherein IFN- γ, or its derivative, or its mimic, or an antagonist, or components of IFN-γ pathway are contacted with melanocytes in the range of 100 – 500 U/ml for a period in the range of 1 to 10 days.

12. IFN- γ and its derivative, mimic, antagonist thereof for use as claimed in claim 10 wherein IFN-γ or its derivative, or a mimic or an antagonist of IFN-γ reversibly alters the levels of TYR, and TYRP2/DCT, CNO, HPS4, GPR143, OCA2, SLC7A11 and MCOLN3.

13. IFN- γ and its derivative, mimic, antagonist thereof for use as claimed in claim 10 wherein the transfer of melanosome to keratinocytes is altered by targeting components of IFN-γ pathway selected from the group comprising of IFNG, IFNGR1, JAK1 and STAT1.

14. IFN- γ and its derivative, mimic, antagonist thereof for use in treating skin pigmentation by administering to a subject IFN-γ or its derivative, or a mimic or antagonist of IFN-γ.

15. IFN- γ and its derivative, mimic, antagonist thereof for use as claimed in claim 14 wherein IFN-γ or its derivative, or a mimic or an antagonist of IFN-γ is administered to the subject by topical delivery or by sub-cutaneous delivery.

16. IFN- γ and its derivative, mimic, antagonist thereof for use as claimed in claim 15 wherein the topical delivery or sub-cutaneous delivery is in a dosage form selected from the group comprising, a powder, a solution, an emulsion, a fluid emulsion, a suspension, a fluid suspension, a semi-solid, an ointment, a paste, a cream, a gel, a jelly, a foam, an implant, an injection, a patch and a spray.

17. IFN- γ and its derivative, mimic, antagonist thereof for use as claimed in claim 14 for treating skin disorders selected from the group comprising of hyperpigmentation, hypopigmentation, uneven pigmentation, post inflammatory pigmentation, sun-damaged skin, pigmented birthmark, acanthosis nigricans and solar lentiges, age-related pigmentation changes, indeterminate leprosy, tuberculoid leprosy, borderline leprosy, lepromatous leprosy.

pigmentation changes, indeterminate leprosy, tuberculoid leprosy, borderline leprosy, leprematous leprosy.

EXAMPLE 1

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We claim:

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   wherein the IFN- γ and derivative, mimic, antagonist thereof modulate the expression of IFN-γ pathway components selected from a group comprising IFNGR1, JAK1 and STAT1.

2. The method as claimed in claim 1 wherein IFN- γ, or its derivative, or its mimic, or an antagonist, or components of IFN-γ pathway are contacted with melanocytes in the range of 100 – 500 U/ml for a period in the range of 1 to 10 days.

3. The method as claimed in claim 1 wherein IFN-γ or its derivative, or a mimic or an antagonist of IFN-γ reversibly alters the levels of TYR, and TYRP2/DCT, CNO, HPS4, GPR143, OCA2, SLC7A11 and MCOLN3.

4. The method as claimed in claim 1 wherein the transfer of melanosome to keratinocytes is altered by targeting components of IFN-γ pathway selected from the group comprising of IFNG, IFNGR1, JAK1 and STAT1.

5. Use of IFN-γ and its components and its agonists and antagonists in modulating pigmentation in humans for clinical or cosmaceutical purposes.

6. A method of treating skin pigmentation by administering to a subject IFN-γ.

7. The method as claimed in claim 6 wherein IFN-γ is administered to the subject by topical delivery or by sub-cutaneous delivery.

8. The method as claimed in claim 7 wherein the topical delivery or sub-cutaneous delivery is in a dosage form selected from the group comprising, a powder, a solution, an emulsion, a fluid emulsion, a suspension, a fluid suspension, a semi-solid, an ointment, a paste, a cream, a gel, a jelly, a foam, an implant, an injection, a patch and a spray.

9. The method as claimed in claim 6 useful for treating skin disorders selected from the group comprising of hyperpigmentation, hypopigmentation, uneven pigmentation, post inflammatory pigmentation, sun-damaged skin, pigmented birthmark, acanthosis nigricans and solar lentiges, age-related pigmentation changes, indeterminate leprosy, tuberculoid leprosy, borderline leprosy, leprematous leprosy.