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The examination is being carried out on the **following application documents**

**Description, Pages**

1-48 as originally filed

**Sequence listings, SEQ ID NO**

1-14 as originally filed

**Claims, Numbers**

1-15 filed with entry into the regional phase before the EPO

**Drawings, Sheets**

1/4-4/4 as originally filed

1 In respect of the above identified European patent application, only part of the claimed subject-matter has been searched, following an objection of lack of unity of the invention by the European Patent Office acting as International Searching Authority (see Article 17(3)(a) PCT).

In the procedure before the European Patent Office as designated Office, the Examining Division agrees with the finding of lack of unity of the invention for the following reasons:

The application relates to the use of a substance which modulates the expression of MC-R for the preparation of a cosmetic, nutraceutical or pharmaceutical composition and uses thereof for treating e.g ageing of the skin, increase skin pigmentation or prevent skin depigmentation. The specific substances which are modulators of the expression of MC-R are claimed in claim 5. In claim 10 the same substances are claimed for use as an active ingredient in a cosmetic, nutraceutical or pharmaceutical composition without the reference to the modulation of the expression of MC-R. Independent claim 15 is directed to nucleotides which are sense or antisense sequences of MC-1R, MC-2R, mu-opioid receptor or POMC.

The substance or plant extracts which are modulators of the expression of MC-R (see claim 6) and which are subject-matter of independent claim 11 do not share a significant structural element, nor do they belong to a single class of chemical compounds in the art to which the invention pertains.

The common technical feature is the use of modulators of the expression of MC-R for the preparation of cosmetic, nutraceutical or pharmaceutical compositions. This feature is not novel in view of the disclosure of the documents US2003/228658 (see [026], [0126], [0130]) and US2003/0110518 (see [0186]). Pharmaceutical compositions comprising 1 methyl beta carbolin-3-carboxylic acid are also known from the prior art (see Borde et al., Prog. Neuro-Psychopharmacol. & Biol. Psychiat. 1996 vol20, p1379 ; Oakley and Jone, Neuropharmacol. 1982 vol.21 p587).

Consequently, the present application lacks unity of invention, and the different solutions not belonging to a common inventive concept are identified as the different subjects listed below. Each of the inventions listed is a distinct invention, characterised by its own special technical feature, defining the contribution which each of the claimed inventions, considered as a whole makes over the prior art.

In accordance with Rule 164(2) EPC the applicant is invited to limit the application to one invention covered by the international search report.

The subject-matter to be excised may be made the subject of one or more divisional applications. The divisional applications must be filed with the European Patent Office in Munich, The Hague or Berlin and shall be filed in the language of the proceedings relating to the present application (cf. Article 76(1) and Rule 36(2) EPC). The time limit for filing divisional applications (Rule 36(1) EPC) must be observed.

## 2 Prior art:

Reference is made to the following documents; the numbering will be adhered to in the rest of the procedure.

- D1 US 2003/228658 A1 (SHU YOU MIN [US] ET AL) 11 December 2003 (2003-12-11)
- D2 US 2003/110518 A1 (HOUSEKNECHT KAREN L [US] ET AL) 12 June 2003 (2003-06-12)
- D3 WO 97/47316 A (MILLENNIUM PHARM INC [US]) 18 December 1997 (1997-12-18)
- D4 BORDE NATHALIE ET AL: "Effects of methyl beta-carboline-3-carboxylate on memory impairments induced by chronic alcohol consumption in mice",

PROGRESS IN NEURO-PSYCHOPHARMACOLOGY AND  
BIOLOGICAL PSYCHIATRY,  
vol. 20, no. 8, 1996, pages 1377-1387, XP002495557,  
ISSN: 0278-5846

D5 OAKLEY N R ET AL: "DIFFERENTIAL PHARMACOLOGICAL  
EFFECTS OF BETA CARBOLINE-3-CARBOXYLIC-ACID  
ESTERS",  
NEUROPHARMACOLOGY,  
vol. 21, no. 6, 1982, pages 587-590, XP002495558,  
ISSN: 0028-3908

D6 TSATMALI MARINA ET AL: "Skin POMC peptides: Their actions  
at the human MC-1 receptor and roles in the tanning response",  
PIGMENT CELL RESEARCH,  
vol. 13, no. Supplement 8, 2000, pages 125-129, XP009095072,  
ISSN: 0893-5785

D7 HIROBE TOMOHISA ET AL: "The melanocortin receptor-1 gene  
but not the proopiomelanocortin gene is expressed in  
melanoblasts and contributes their differentiation in the mouse  
skin",  
PIGMENT CELL RESEARCH,  
vol. 17, no. 6, December 2004 (2004-12), pages 627-635,  
XP002466465,  
ISSN: 0893-5785

If not indicated otherwise the relevant passages are those mentioned in the search report.

Document D1 discloses the use of compounds which increase or decrease, e.g. antisense oligonucleotides, the expression of MC1-R for preparing compositions for modulating skin pigmentation or preventing freckling.

Document D2 discloses the use of compounds which increase or decrease, e.g. antisense oligonucleotides, the expression of MC5-R for preparing pharmaceutical compositions for treating skin disorders.

Document D3 discloses the use of compounds increasing or decreasing expression of MC4-R for preparing pharmaceutical compositions.

Document D4 discloses pharmaceutical compositions comprising 1 methyl beta carbolin-3-carboxylic acid.

Document D5 discloses pharmaceutical compositions comprising 1 methyl beta carbol-3-caboxylic acid.

Document D6 discloses that MSH/MC1-R are implicated in skin tanning induced by UV.

Document D7 discloses that the expression of MC1 -R gene is implicate din melanocyte differentiation in the skin.

3 Novelty (Art. 54 EPC):

3.1 It is stressed that an intended use is not a characterizing feature in a claim directed to a product as in claims 12 and 13. Claims 1, 12 and 13 lack novelty in view of D1-D5. Dependent claims 2-7 as well lack novelty over D1-D5.

3.2 Claim 10 relates the use of 1-methyl beta carbolin-3-caboxylic acid for preparing a nutraceutical or pharmaceutical composition intended to increase skin pigmentation, exert a tanning effect or prevent depigmentation spots. It is stressed that these uses are not therapeutic uses and are thus not a characterizing feature of claim 10. Claim 10 is thus anticipated by documents D4-D5.

4 Inventive step (Art. 56 EPC):

4.1 In view of D1 it would be obvious to combine a modulator of MCR-1 expression with a compound according to claim 9. Said claim does not involve an inventive step.

4.2 The prior art does not disclose or suggest the cosmetic use of 1-methyl beta carbolin-3-caboxylic acid. An inventive step would thus be acknowledged for claim 14.

5 Art. 84 EPC:

5.1 Claim 1 relates to substance which are modulators of the expression of MC-R. The functional definition of the substances doe snot allow to ascertain the scope of the claim. Moreover, the definition encompasses a large number of compounds and the disclosure is not sufficiently precise for the person skilled in the art to reduce the technical features to practice without undue burden. Claim 1 does not meet the requirement of Article 84 EPC.

5.2 It is not clear which compounds fall in the scope of the functional definitions of claim 9. Claim 9 does not fulfil the requirements of Art. 84 EPC.

5.3 It is not clear which conditions are meant by the functional definitions of the diseases or conditions in claims 2, 12 and 13. Furthermore, these uses are both of cosmetic and therapeutic nature. The scope of claims 2, 12 and 13 is thus unclear contrary to the requirements of Art. 84 EPC.

6 The third-party observation received on 14.07.2010 pursuant to Art. 115 EPC; in particular exhibit 1-7 calls into question the patentability of the subject-matter claimed for the reasons given below. These documents can be relevant for the assessment of inventive step.

7 The applicant is invited to file new claims which take account of the above comments.

In order to facilitate the examination of the conformity of the amended application with the requirements of Article 123(2) EPC, the applicant should clearly identify the amendments carried out, irrespective of whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based.