January 13, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 7469-review.doc).

Title: Biomarkers of psoriasis severity and therapy monitoring

Author: Susana Coimbra, Alice Santos-Silva

Name of Journal: *World Journal of Dermatology*

ESPS Manuscript NO: 7469

The manuscript has been improved according to the suggestions of reviewers:
1 Format has been updated

2 Revision has been made according to the suggestions of the reviewers

(1) Reviewer 00646460

The alterations suggested were now introduced in the manuscript:

"**CONCLUDING REMARKS**

For most of the potential biomarkers there are studies with divergent results, …. **Moreover, the use of some of these biomarkers must consider other inflammatory comorbidities that may be misleading, as they are not specific for psoriasis."**

"PENTRAXINS

C-reactive protein (CRP), a short-chain pentraxin produced in the liver, is a positive acute phase protein that increases rapidly in the presence of inflammation, a hallmark of psoriasis. …..

We must emphasize that CRP and PTX3 evaluation, although sensitive, lacks specificity, as they are also increased in different types of inflammatory diseases. Therefore, the presence of inflammatory comorbidities should be considered when using these biomarkers to assess psoriasis."

(2) Reviewer 00646519

As suggested, CCR6 is now referred in the manuscript: "As referred, the IL-23/Th17 axis is believed to be crucial in psoriasis pathogenesis [48]. … **The expression of CC chemokine ligand 20 (CCL20) and its receptor CC chemokine receptor 6 (CCR6) is up-regulated in psoriasis [49,50], which may be related to the disease pathogenesis. Indeed, Hedrick et al. found that CCR6 has an important role in IL-23-related responses and identified CCR6 as a potential therapeutic target in psoriasis [51]. In opposition to the therapy with calcipotriol, camptothecin or tazarotene, clobetasol treatment inhibited the CCR6 expression in a imiquimod-induced psoriasis-like mouse model [52]."**

(3) Reviewer 00382448

As recommended, a minor linguistic revision was made.

(4) Reviewer 00646502

We thank the reviewer for his kind commentaries.

(5) Reviewer00504152

As recommended, the DLQI questionnaire was added: "The Psoriasis Area and Severity

Index (PASI) is the prototype **to** measure psoriasis severity, … There are other approaches to asses psoriasis severity, such as **the** percentage of involved body surface area, the Physician's Global Assessment, the Lattice System Physician's Global Assessment, **and** the National Psoriasis Foundation Psoriasis Score. **There are also more specific instruments, focusing on aspects of quality of life that are affected by skin disease, such as the Dermatology Life Quality Index (DLQI)** [7] , but **they** are **all** clinical tools.**"**

As far as we know, there is no data reporting associations between levels of sTNF-R1 and TNF-α in psoriasis patients. There are studies concerning the relationship of TNF-α-converting enzyme (TACE) concentration in peripheral blood mononuclear cells with plasma concentration of sTNF-R1, which is now referred in the manuscript: "**TNF-α-converting enzyme from peripheral blood mononuclear cells may contribute to the up-regulation of sTNF-R1 in psoriasis. The raised concentrations of sTNF-R1 in psoriasis were correlated with PASI and were diminished after NB-UVB therapy, suggesting that it may be a marker of the disease severity** [30]**."**

In this review, we only intended to debate published data concerning biomarkers of severity and/or monitor treatment of psoriasis vulgaris without arthritis, we did not pretended to consider biomarkers in psoriatic arthritis, which was now clarified in the manuscript ("Considering that any attempt to identify these biomarkers should be encouraged, we intend to review and debate published data concerning the proposal of biomarkers to evaluate the severity and the response to treatment of psoriasis vulgaris. **To avoid a length and complex manuscript, we will only consider biomarker evaluation in psoriasis vulgaris without arthritis.**"). Biological markers of psoriatic arthritis, an inflammatory arthritis that occurs in the presence of psoriasis vulgaris, is an intricate topic that we believe that needs an individualized and especial approach.

3 References and typesetting were reviewed

Thank you again for publishing our manuscript in the *World Journal of Dermatology*.

Sincerely yours,

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