Sequential proteomic profiling of patients with Stevens Johnson-Syndrome or Toxic Epidermal Necrolysis

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May 8, 2023

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Funding sources: The study was funded by the University Zurich.

Conflicts of interest: The authors have no conflict of interest to declare.

Word count text: 507

To the editor:

It is a pleasure to see that sequential proteomic profiling of Stevens-Johnson Syndrome / Toxic Epidermal Necrolysis (SJS/TEN) patients is gaining attention and we thank the authors of this commentary for their interest in and reflections on our work. SJS and TEN are the rarest types of delayed-type drug hypersensitivity reactions, with an estimated incidence of about 1.53-6 cases per million in western Europe [1, 2]. The aim of our study [3] was to perform the first comparative study of sequential proteomic profiles of SJS/TEN

patients receiving different types of adjuvant therapies and thereby create a rationale and basis for further investigations.

In their commentary, the authors emphasize the limitations of our study: notably the number of patients (16 overall), the differences in baseline characteristics (affected body surface area, SCORTEN, ethnicity), the type of sampling (serum but not sequential skin biopsies) and type of study (not a prospective, randomized controlled clinical trial). We fully agree with all these points raised by the authors and consider them important for interpreting our findings. Therefore, all of them are mentioned and either discussed / thoroughly described in the methodology of our paper and/or accounted for in proteomic sub-analyses that we performed.

More specifically, we did a baseline analysis of the serum proteomic profiles depending on the affected BSA (i.e. SJS vs TEN cases), which was mentioned in our manuscript and, in addition, is shown in the Figure 1a. This analysis did not show significant differences between the treatment groups. In the subgroup analysis of ethnicities, we found only one differentially expressed protein (CNTNAP2), as displayed in Figure 1b. Although our study was not designed to primarily address the question of ethnicity- or severity-related proteomic expression differences, these analyses allowed us to exclude a baseline bias. As addressed and shown in our manuscript (Table 1 of the original paper), there were no significant differences in terms of other factors (SCORTEN, age, gender) between the treatment groups.

On a clinical level, we agree that an ideal setting to further explore and understand the efficacy of different adjuvant / supportive treatment approaches of SJS/TEN is a randomized prospective clinical trial. Given the rare incidence of SJS/TEN, there is, to the best of our knowledge, so far no published prospective interventional randomized clinical trials in the area and it was also for our setting not possible to perform such a study. Our study was not designed to address this question and we clearly did not draw any conclusions or claim the preferential use of any SJS/TEN treatment. Of note, the ongoing Canadian*NATIENS* study (NCT02987257), a phase III randomized study comparing cyclosporine versus etanercept versus supportive care, may provide important answers regarding adjuvant treatments in the management of SJS/TEN.

Finally, as also brought up by the authors, we discuss in our paper that future studies should aim at consolidating and expanding our results with concurrent analyses of skin and blood. We see our work as providing a rationale for such investigations and look forward to further progress in the field.

References

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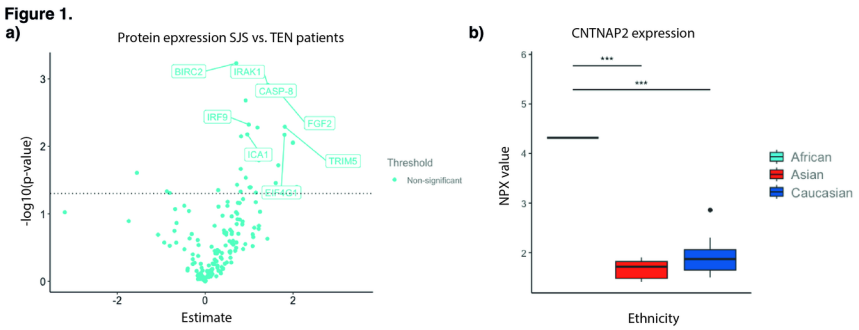
Figure legends.

Figure 1. Protein expression in serum in different severity grades and ethnic groups.

(a) Volcano plot of expressed serum proteins in SJS, SJS/TEN (n=10) vs. TEN (n=6) at baseline (day 0). Protein expression was measured by OLINK high-throughput targeted proteomics (inflammation and immune response panels), as described in our manuscript. (b) Box plots showing the serum levels of CNTNAP2, the only protein differentially expressed between ethnic subgroups (African: n=1; Asian: n=5; Caucasian: n=10), at baseline (day 0).



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