Author's response to reviews

Title: Signal transduction mechanisms involved in S100A4-induced activation of the transcription factor NF-kappaB

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Author's response to reviews: see over
Dear Editor,

We sincerely appreciate the favorable comments from the reviewers, and the comments made by reviewer #1 are addressed below.

The reviewer is concerned that H-7 and staurosporine only indirectly inhibit IKK activity. Since IKKγ is not cleaved upon treatment with H-7/staurosporine in our cell system (see figure in previous cover letter), this concern is based on two observations: (i) the ratio of P-IκBα/total-IκBα is similar in H-7/staurosporine-treated cells as in cells only exposed to S100A4. (ii) Only a marginal induction of IKK activity by S100A4 was observed in the kinase assay.

The latter is partly due to a technical artifact (a non-specific spot in the control lane in Figure 5B), and seems less relevant due to the fact that H-7/staurosporine reduce S100A4-induced IKK-activity to approximately 40% in the kinase assay (Figure 5). Based on this we argue that H-7/staurosporine most likely inhibit IKK directly. The levels of P-IκBα/total-IκBα in H-7/staurosporine-treated cells are discussed in the present version of the manuscript (pages 15, lines 19-23 and page 16, lines 1-9).

Thus, we believe that the present discussion covers the comments raised by the reviewer, and we think that it would be more confusing than clarifying to further elaborate this issue.

Hoping the manuscript will be accepted for publication, I look forward to receiving your decision.

Sincerely,

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