Reviewer's report

Title: Transcriptional regulation of kinases downstream of the T cell receptor: another immunomodulatory mechanism of glucocorticoids

Version: 1  
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Reviewer: Guillaume Darrasse-Jèze

Reviewer's report:

Petrillo et al. describe in this study the effect of dexamethasone treatment on the modulation of expression of Itk, Txk, and Lck, kinases involved in the TCR signaling, in a T cell line and in thymocytes and lymphocytes in different conditions (in vitro, in vivo, at different time points and doses). They conclude that the expression of Itk, and in a lesser extent Txk, is up-regulated following dexamethasone exposure. On the contrary, dexamethasone treatment induces Lck down-regulation in most conditions except in mature lymphocytes activated for 6 hours. The authors observed an increase in cell apoptosis following glucocorticoid treatment in cells deficient for Itk-/- expression compared to normal thymocytes. The article is interesting, as it convincingly documents how T cells may modulate expression of kinases downstream the TCR in order to survive to glucocorticoid induced-cell death, with Itk up-regulation playing a clear protective role in dexamethasone-exposed thymocytes.

Minor Essential Revisions

Results:

Lines 217-218: Authors cannot write that "Lck and Itk were the only kinases downstream of the TCR to be modulated by dexamethasone treatment" as other few kinases are modulated in the previous Bianchini et al. paper (Ref 23), but not Lck. Moreover, Itk appears to be modulated at a level considered significant in the Table 1s of the article. This part should thus be modified/clarified.

Figure 6: Authors should show the flow cytometry dot plots of propidium iodide staining of thymocytes treated or not with dexamethasone

Discussion:

Line 299: Authors claim that their "study demonstrates for the first time that dexamethasone up-regulates Itk expression in thymocytes". But, as Itk appears to be modulated at a level considered significant in the Table 1s of the previous article by Bianchini et al. (Ref 23), authors should better indicate that their study demonstrate clearly that dexamethasone up-regulates Itk expression in thymocytes.

Lines 302-303: In their previous paper (Ref23) Bianchini et al. observed a smaller increase of Itk expression by thymocytes after 3 hours exposure to a similar
dose. This discrepancy should be discussed.

Ref 41: Authors should better cite scientific articles than reviews, to refer to precise scientific results.

OPA Abbreviation should be described.

Discretionary Revisions:

In addition to RPA, it would have been nice to test the kinases expression by nested RT-qPCR.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests