

CORRESPONDENCE

Author response to 'Staphylococcus aureus and primary lysis of eosinophils' by Dr Persson

R. Shamri*, Y. Minai-Fleminger*, R. S. Gangwar, H. Migalovich-Sheikhet, M. Seaf and F. Levi-Schaffer

Pharmacology & Experimental Therapeutics, Faculty of Medicine, Institute for Drug Research, School of Pharmacy, The Hebrew University of Jerusalem, Jerusalem, Israel

Dear Editor,

We thank Dr Persson for his interest in our study [1] discussing the role of CD48 in *Staphylococcus aureus* (SA)-mediated eosinophil activation and his thoughtful comments. In this study, we provided evidences for an increase in CD48 expression on human eosinophils in atopic dermatitis lesions. Our *in vitro* studies showed that SA/exotoxins increase CD48 expression on eosinophils and SA mildly induces formation of eosinophil extracellular DNA traps (EETs) by human eosinophils. In addition, CD48 mediates interactions between SA/exotoxins and human and mouse eosinophils and induces signal transduction that leads to eosinophil activation and degranulation. Our *in vivo* experiments in an SEB-induced peritonitis further demonstrated the importance of CD48 in eosinophil recruitment to the site of inflammation.

As mentioned above, our studies observed EETs *in vitro* in SA-eosinophils co-cultures [1]. EET release was further enhanced under blockage of CD48 [1]. This kind of EET has been suggested in previous studies to serve as bacteria traps in antibacterial response [2, 3]. The source of the DNA in Yousefi *et al.* and Ueki *et al.* [2, 3] studies is different: mitochondrial vs. nuclear, respectively. Mitochondrial EETs have been shown to include granule proteins, while nuclear EETs contain free eosinophil granules (FEGs) in addition to granule proteins. While release of mitochondrial EETs is from alive eosinophils [2], release of nuclear EETs is associated with primary lysis, or EETosis, and release of FEGs [3]. Several studies by Persson and others have shown the latter mechanism, that is eosinophil cytolysis and deposition of FEGs at site of inflammation to be common in various human diseases, such as asthma and atopic dermatitis as well as in animal models [4–7].

However, in our experimental settings (using heat-inactivated SA), although EETs were observed, no eosinophil cytolysis was detected (as examined by morphology, viability staining and cell counting) [1]. Interestingly, the presence of blocking anti-CD48 antibodies enhanced EET release without causing cell death. In addition to its involvement in EET formation, we found that CD48 is required for eosinophil SA-/exotoxin-mediated degranulation and cytokine release. Based on previous studies on eosinophils EETs [2, 3], we agree with Dr. Persson's comment that FEGs and granule protein deposition occur upon EET release.

Nevertheless, our current studies [1] focus on the role of CD48 in eosinophil activation and did not address the EET mechanism. Therefore, nor the source of DNA or the existence of FEGs or granule proteins in the EETs were examined in our SA-eosinophil co-cultures. The fact that cell death was not observed in these experiments led us to the assumption that the observed traps are composed of released mitochondrial DNA and not of nuclear DNA. However, further experiments are needed to evaluate this assumption, as well as to understand the exact role of CD48 in EETs.

In conclusion, our studies [1] revealed that CD48 is expressed on eosinophils, is crucial for eosinophil infiltration to the site of inflammation, mediates the interactions between eosinophils and SA and its exotoxins, and is required for eosinophil activation and degranulation, all features essential for eosinophil response against bacterial infection.

Conflict of interest

The authors declare that they have no relevant conflict of interests.

Correspondence:

Francesca Levi-Schaffer, Pharmacology & Experimental Therapeutics, Faculty of Medicine, Institute for Drug Research, School of Pharmacy, The Hebrew University of Jerusalem, POB 12065, Jerusalem 91120, Israel.

E-mail: fls@cc.huji.ac.il

*Equal contributors.

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