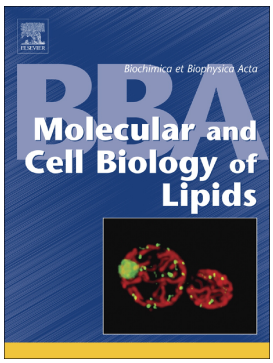

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PII: S1388-1981(18)30072-6
DOI: doi:10.1016/j.bbalip.2018.04.010
Reference: BBAMCB 58278

To appear in:

Received date: 7 December 2017
Revised date: 7 March 2018
Accepted date: 15 April 2018

Please cite this article as: Patrick Drücker, Simon Bachler, Heidi Wolfmeier, Roman Schoenauer, René Köffel, Viktoria S. Babiychuk, Petra S. Dittrich, Annette Draeger, Eduard B. Babiychuk , Pneumolysin-damaged cells benefit from non-homogenous toxin binding to cholesterol-rich membrane domains. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Bbamcb(2018), doi:10.1016/j.bbalip.2018.04.010

Pneumolysin-damaged cells benefit from non-homogenous toxin binding to cholesterol-rich membrane domains

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Abstract

Nucleated cells eliminate lesions induced by bacterial pore-forming toxins, such as pneumolysin via shedding patches of damaged plasmalemma into the extracellular milieu. Recently, we have shown that the majority of shed pneumolysin is present in the form of inactive pre-pores. This finding is surprising considering that shedding is triggered by Ca^{2+}-influx following membrane perforation and therefore is expected to positively discriminate for active pores versus inactive pre-pores.

Here we provide evidence for the existence of plasmalemmal domains that are able to attract pneumolysin at high local concentrations. Within such a domain an immediate plasmalemmal perforation induced by a small number of pneumolysin pores would be capable of triggering the elimination of a large number of not yet active pre-pores/monomers and thus pre-empt more frequent and perilous perforation events. Our findings provide further insights into the functioning of the cellular repair machinery which benefits from an inhomogeneous plasmalemmal distribution of pneumolysin.