

## CROSSTALK

**Last Word from Florian Lang and Else K. Hoffmann**Florian Lang<sup>1</sup> and Else K. Hoffmann<sup>2</sup><sup>1</sup>Department of Physiology, University of Tübingen, Germany<sup>2</sup>Department of Biology, University of Copenhagen, Denmark**The many ways to enter cell death**

All three additional comments on this CrossTalk debate (M. Ritter & M. Jakab; I. Levitan; Y. Okada) address important thoughts to the original debate (Lang & Hoffmann, 2013; Orlov *et al.* 2013). Most importantly, it must be considered that alterations of cell volume during apoptosis may not only be due to the suicidal machinery but as well be part of other programmes executed in the dying cell

such as differentiation, or other challenges imposed such as energy depletion. The diversity of cellular signalling, shape and function does not discontinue with the decision to undergo suicidal death but continues to impact on fundamental cellular parameters such as cell volume. Moreover, imposed alterations of cell volume trigger a myriad of cellular reactions which partially interact with the suicidal machinery. Accordingly, the diversity of signalling, shape and function of dying cells is at least in part the reflection of overlapping functional state, cell shape and activated suicidal machinery. In view of the virtually infinite diversity of cellular functions and shapes, we cannot claim that all suicidal cells without any exception do shrink. Nevertheless, in our experience and opinion mechanisms leading to cell shrinkage are an integral part of cellular suicide. In our view ‘successfully’ dying cells counteract swelling to prevent cellular explosion and

try to shrink in order to ease subsequent phagocytosis. For a variety of reasons not all cells are capable to ‘successfully’ execute the full suicidal programme and thus expose the scientists to puzzling observations leading to highly interesting scientific discussions.

**References**

- Lang F & Hoffmann EK (2013). CrossTalk proposal: Cell volume changes are an essential step in the cell death machinery. *J Physiol* **591**, 6119–6121.
- Orlov SN, Model MA & Grygorczyk R (2013). CrossTalk opposing view: the triggering and progression of the cell death machinery can occur without cell volume perturbations. *J Physiol* **591**, 6123–6125.

**Competing interests**

None declared.

Published February 25, 2014