CROSSTALK

Last Word from Michael A. Model

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And yet it shrinks!

The discussion of apoptotic shrinkage undertaken within The Journal of Physiology is a very welcome step. It is one of the paradoxes of scientific fashion that shrinkage, which is doubtless one of the strongest markers of apoptosis, evokes relatively little interest within the apoptosis community. This is especially disappointing in view of the strong claims that: (a) cells are aware of their volume (Hoffmann & Pedersen, 2006); (b) shrinkage can be a triggering event in apoptosis (Lang & Hoffmann, 2012); (c) shrinkage can be a necessary step in apoptosis (Maeno et al. 2000); (d) if a dying cell fails to shrink it is likely to swell (Last Word from F. Lang and E. K. Hoffmann), with potentially serious consequences for the organism.

It is natural, and probably a healthy sign, that some diversity of opinion exists on this subject. Lang & Hoffmann (2013) emphasized the essential role of shrinkage, whereas Orlov and coauthors (2013) focused more on alternative possibilities. In their comments on this CrossTalk debate, Y. Okada and I. Levitan brought up the important subject of careful experimentation. It can be added that studies of apoptotic volume decrease (AVD) would benefit from the ability to discriminate between the loss of water and the loss of apoptotic bodies, which cannot be accomplished by volume measurements alone. We have recently published a relatively simple microscopic technique that can accomplish this task (Model & Schonbrun, 2013). In addition to the microfluidics-based methods mentioned by I. Levitan, Shonbrun and colleagues (2014) have developed an optical microfluidics method for volume measurements, which might be adaptable to water measurements as well. Although the role of monovalent ions in apoptosis has been firmly established (Lang & Hoffmann, 2012), the range of discussed mechanisms of shrinkage can be extended beyond activation of monovalent ion channels (Model, 2014). The properties of intracellular water has been a controversial subject; but since apoptotic shrinkage is intrinsically linked to water, it might be necessary at some point to depart from treating cell water as a diluted solution of salts and adopt a more realistic view (Fels et al. 2009; Cameron & Fullerton, 2013). Clearly the subject of water regulation in cell death is far from closed, and one can only hope that more discussions and publications like these will prompt apoptosis researchers to pay more attention to this critical aspect of cell death.

References


Competing interests

None declared.
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