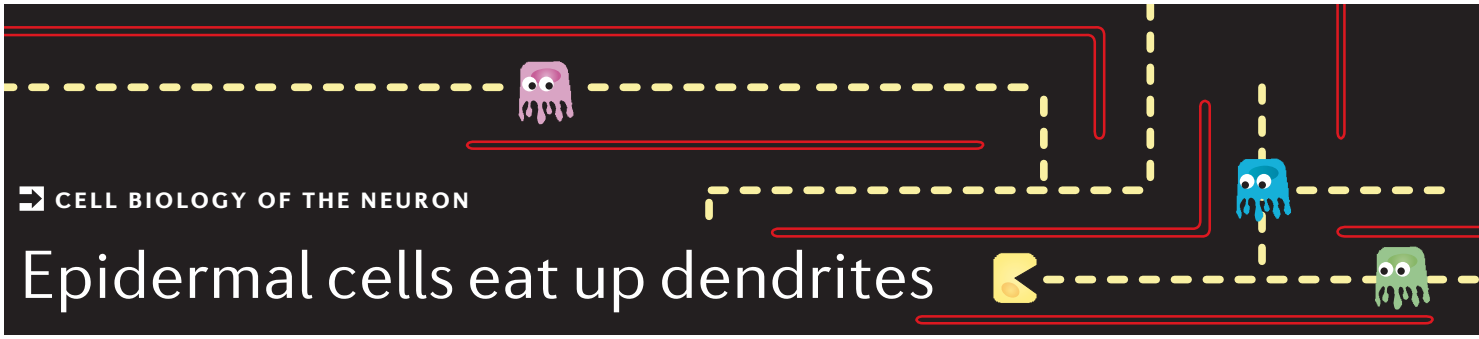
Nature Reviews Neuroscience | AOP, published online 29 January 2014; doi:10.1038/nrn3688

J. Vallis/NPG



CELL BIOLOGY OF THE NEURON

Epidermal cells eat up dendrites

Neuronal dendrites degenerate as a result of injury or developmental pruning, and rapid removal of the resulting debris is vital for the maintenance of tissue homeostasis. In the CNS, glial cells act as phagocytes to clear dendritic debris; however, the identity of the cells that carry out this task in the peripheral nervous system (PNS) is unknown. Jan and colleagues now show that degenerating dendrites in the *Drosophila melanogaster* PNS are engulfed and degraded by epidermal cells, rather than by the phagocytic haemocytes that had generally been presumed to do this job, and uncover some of the key molecules involved.

D. melanogaster larval dendritic arborization sensory neurons provide a good model of dendrite degeneration: their dendrites degenerate during metamorphosis or after an injury and can be labelled by the expression of membrane-targeted fluorescent proteins that are coupled to a specific marker protein. Using *in vivo* time-lapse imaging, the authors showed that most of the labelled debris of degenerating dendrites dispersed into the epidermal layer during metamorphosis and after an injury. Furthermore, inhibition of a key phagocytic protein, Shibire, specifically in epidermal cells prevented dendrite clearance, confirming that these cells are the main site of dendrite phagocytosis in the *D. melanogaster* PNS.

Debris engulfed during phagocytosis is contained in vesicles known as phagosomes, which subsequently mature and fuse with endosomes and lysosomes to enable degradation of their contents. By monitoring the disappearance of fluorescently labelled dendritic debris and the pH of phagosomes, which become more acidic with maturation, the authors tracked phagosome maturation after dendrite engulfment and examined the role of various molecules in this pathway.

First, the authors examined the roles of two proteins that had previously been implicated in the clearance of apoptotic neurons in the CNS. They showed that epidermal cell-specific knockdown of the receptor Draper blocked the earliest stage of the pathway: engulfment. By contrast, knockdown of the CD36 family member Croquemort did not affect engulfment but halted phagosome maturation at a stage just after the initial acidification and promoted phagosome fusion. Finally, the authors showed that knockdown of a previously uncharacterized CD36 family member CG1887 (subsequently named Debris buster) blocked late stages of phagosome maturation.

This study adds to our understanding of the ways in which epithelial and epidermal cells can influence nervous system development and function, and confirms the importance of the relationship between the two tissues.

Katherine Whalley

ORIGINAL RESEARCH PAPER Han, C. *et al.* Epidermal cells are the primary phagocytes in the fragmentation and clearance of degenerating dendrites in *Drosophila*. *Neuron* http://dx.doi.org/10.1016/j.neuron.2013.11.021 (2014)

> “most of the labelled debris of degenerating dendrites dispersed into the epidermal layer”