



# Apoptosis: who was first?

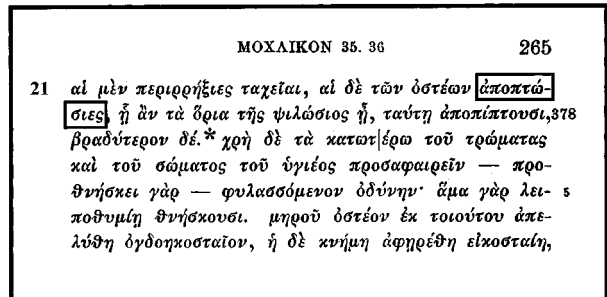
Dear Editor,

With the explosion in the research on apoptosis—at least 5194 PubMed entries in the last year—apoptosis is one of the most used words in biology and medicine today. Seemingly, this word has been introduced as a synonym of programmed cell death by Kerr *et al* (1972). In a footnote they thank a professor of Greek for the suggestion of the term ‘apoptosis’: ‘. . . used to describe the dropping off or falling off of petals from flowers, or leaves from trees’ (Kerr *et al*, 1972). The falling of leaves is the currently accepted etymology of apoptosis in biomedical sciences. But the word was originally coined in medical writings of 2400 years ago! I recently discovered this is in my old Greek dictionary (Rocci, 1945). Remarkably, the word *αποπτωσις* was used for the first time by Hippocrates of Cos, the father of Western medicine (ca. 460-370 BC) in the book *ΜΟΧΛΙΚΟΝ* (Mochlicon, a treatise on the reduction of dislocations). It appears at line 21 of chapter 35:376 (Kuehlewein, 1902) and refers to the ‘falling off of the bones’ (Figure 1). Note that the original text contains the word *αποπτωδιες*, namely the plural of *αποπτωσις* (Figure 1). Subsequently, Galen (129-201 AD) adopted the word *αποπτωσις* not only in the context of bone fractures as used by Hippocrates, but also referring to the ‘dropping of the scabs’.<sup>1</sup> Galen seems to have been very insightful in this, given the role of apoptosis in wound healing and inflammation (Hetts, 1998). Kerr *et al* (1972) were apparently unaware of the classical Authors who used the word apoptosis in medical writings much before them. It is desirable that in the future,

<sup>1</sup>This information has been retrieved by Lara Loreti, my high-school teacher of ancient Greek at Imola (Italy), from the Stephanus’ *Thesaurus Linguae Graecae* (Greek into Latin!).

proper credit will be given to Hippocrates and Galen for the origin and medical use of apoptosis.

Mauro Degli Esposti  
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**Figure 1** Copy of the original text in chapter 35 (376-378) of *ΜΟΧΛΙΚΟΝ*, a book attributed to Hippocrates that deals with the instruments for the reduction of fractures and dislocations, according to the transcription of Kuehlewein (1902). The word corresponding to apoptosis—in the plural case—is boxed. In the translation below, this word is given in italics [\* identifies the end of the translation, line 378 (2)]. [376 (20) In cases of fractured bones,] (21) lines of demarcation form quickly, and the *falling off* of the bones occurs, where the limits of the denudation may happen so that the bones are falling off, but more slowly'

## References

- Hetts SW (1998) To die or not to die. *JAMA* 279: 300–307  
Kerr JFR, Wyllie AH and Currie AR (1972) Apoptosis: a basic biological phenomenon with wide-ranging implications in tissue kinetics. *Br. J. Cancer* 26: 239–257  
Kuehlewein H (1902) *ΜΟΧΛΙΚΟΝ* 35: 376–378. In *Hippocratis opera quae feruntur omnia*, (Leipzig: Teubner Edition), Vol. 2, pp. 265  
Rocci L (1945) *Vocabolario greco-italiano* (Turin: Dante Alighieri)