Comment on Park et al.: High glucose-induced oxidative stress promotes autophagy through mitochondrial damage in rat notochordal cells

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Dear Editor,

Recently, we read with great interest the article by Park et al. [1], who demonstrated that high glucose could impair the transmembrane potential, increase production of reactive oxygen species and activate autophagy in rat notochordal cells. The result of this research is consistent with our previous study, which indicated that autophagy was increased in rats with type I diabetes mellitus [2]. Generally, the appropriate increase of autophagy in the chondrocyte and annulus fibrosus cells is considered to be an adaptive reaction to different types of stresses and play a protective role maintaining the homeostasis within cells. Yet, the authors declared in the discussion that autophagy mediated the disappearance of notochordal cells under the hyperglycemia. On one hand, there was no accurate evidence suggesting that high glucose promoted an excessive level of autophagy named “autophagic cell death” in the research. Instead, the raised autophagy might be a response to the enhanced apoptosis of these cells demonstrated by the authors earlier [3]. On the other hand, whether autophagy could really exert a cell death program or just accompany death in mammalian cells is still elusive. Although an increasing number of researches suggested that autophagy

was involved in the cellular demise, none of them could conceivably demonstrate that the cell killing was exerted by autophagy [4]. As suggested by Kroemer et al. [4], the widespread terminology, “autophagic cell death”, may be a misnomer.

Second, the differentiation of notochordal cells cultured in a monolayer should be considered when the conclusion about these cells was drawn. According to the methods and materials mentioned by the authors, we still could find some polygonal chondrocyte-like cells around the vacuolated notochordal cells in primary cell culture (Fig. 1a). The size of notochordal cells is much larger. Surprisingly, the rare notochordal cells were surrounded by numerous chondrocyte-like cells after passage with trypsin (Fig. 1b). The mechanisms underlying the phenomenon may be the differentiation of notochordal cells and the faster growth speed of chondrocyte-like cells in vitro. Similarly, the differentiation of rabbit notochordal cells has also been detected in 2D culture [5], although the real existence of differentiation of notochordal cells remains controversial. Furthermore, the fluorescence imaging presented by the authors shows that the so-called “notochordal cells” are polygonal and spindle-shaped without any obvious vacuoles, indicating that these cells are more likely to be the chondrocyte-like cells. Therefore, it may be better if the notochordal cell could be named as nucleus pulposus cells or intervertebral disc cells when drawing the conclusion.

In summary, one should be cautious when declaring the participation of autophagy in cell death of mammalian animals. In addition, since the notochordal cells could protect

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Fig. 1 The morphology of notochordal cells and chondrocyte-like cells. The primary cells (**a**) and the first passage cells (**b**) were observed under the phase-contrast microscopy. The *white arrows* indicate the small chondrocyte-like cells around the large notochordal cells

nucleus pulposus from apoptosis and retard disc degeneration, the differentiation of notochordal cells may be involved in the negative effect of high glucose on the cell. Further studies are required to determine the real effect of autophagy on cell death and to explore the differentiation of notochordal cells in vitro.

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Conflict of interest The authors declare that they have no conflict of interest.

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