

Letter

Nucleus pulposus cells as competent phagocytes to clear apoptotic cells: mission applicable or impossible?

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We have read with interest the research article by Philip Jones and colleagues, in which they studied whether bovine nucleus pulposus (NP) cells were capable of behaving as phagocytes [1]. Collectively, they drew the conclusion that disc cells clearly can undergo phagocytosis, which has implications for the intervertebral disc *in vivo*. We would like to differ from the authors, however, regarding the implications of the role of NP cells *in vivo* in comparison with *in vitro* as competent phagocytes to ingest apoptotic cells.

First, NP cells cultured *in vitro* in a monolayer may not reflect the same physiological status as they showed *in vivo*. In fact, the extracellular matrix of NP cells consists largely of water, collagen type II and aggrecan [2]. The cell concentration within the disc is relatively sparse, making up only about 1% of the disc volume. NP cells *in vivo* therefore distribute sparsely in the intervertebral disc with ample extracellular matrix surrounding. Intercellular communications might pointedly differ from those in cell culture conditions, in which NP cells contact directly and closely. From this point of view, it may appear an impossible mission for NP cells to clear apoptotic cells as phagocytes *in vivo*.

Second, the authors might have omitted one important hallmark of NP cells – that is, immune privilege. In fact, there is accumulating evidence demonstrating that Fas ligand (CD178) is highly expressed in human, rat and rabbit normal NP cells [3,4]. In immune privileged organs, Fas ligand has been shown to act via the induction of apoptosis on invading Fas-positive activated T cells and thus protects the cells from immune attack. The question of whether macrophages take part in the interaction of NP cells with Fas ligand and consequently contribute to clearance of apoptotic cells, however, remains open. Whether the death of NP cells occurs by apoptosis or necroptosis also remains unclear [5]. At present,

therefore, we may not exclude macrophages perhaps playing a role in the clearance of apoptotic cells.

Third, despite the special avascular hallmark of intervertebral discs, cells in the center of the disc exist at low concentrations of oxygen. Oxygen concentrations as low as 1% have been measured in the centers of discs [6]. The oxygen concentration in Jones and colleagues' paper was 21%, however, which may not be consistent with the physiological conditions of NP cells. As a consequence, the conclusion the authors made on the basis of altered oxygen concentration and the subsequently changed cellular physiology may not be reliable.

Taking these points together, a more appropriate NP cell culture system and the role of macrophages in immune privilege of NP cells should be further explored.

Competing interests

The authors declare that they have no competing interests.

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