arthritis research&therapy

LETTER

# Response to 'TNF/TNFR signal transduction pathway-mediated anti-apoptosis and anti-inflammatory effects of sodium ferulate on IL-1β-induced rat osteoarthritis chondrocytes *in vitro*'

Jing Ma[1], Ang Li[1], Shu Zhu[2], Xiao-Rui Cao[2] and Guo-Xian Pei*[2]

See related research by Qin *et al.*, http://arthritis-research.com/content/14/6/R242, and related letter by Qin *et al.*, http://arthritis-research.com/content/15/3/409

We read with great interest the research article by Qin and colleagues, in which they addressed, on the basis of their previous work, the underlying mechanisms for the protective effect of a small component of traditional Chinese herbs, sodium ferulate (SF), on osteoarthritis (OA) [1]. Utilizing the classical *in vitro* OA chondrocyte model induced by IL-1β, they provided lines of evidence that SF does make a big difference to the OA model in a dose-dependent manner. Furthermore, the underlying mechanisms of the effects were owing to the regulative role of SF on the apoptotic machinery. However, we would like to supplement as well as applaud the authors' findings with particular reference to the apoptotic machinery regulation.

First, the caspase cascade signaling pathway only represents the extrinsic pathways of apoptotic signaling [2]. In fact, it is well established that there are mainly two types of apoptotic signaling pathways: the aforementioned extrinsic pathway, and the intrinsic pathway originating from the mitochondria and involving activation of the Bcl-2 family [3]. Both the extrinsic and intrinsic pathways play important roles in the apoptosis of human OA as well as the chondrocyte-like cells, nucleus pulposus cells [4]. Despite the authors addressing the caspase-8 and caspase-3 pathway, they might have neglected the intrinsic apoptotic pathway characterized by the Bcl-2 family. The integration of the entire apoptotic pathways might strengthen the basis of the conclusion they drew.

Second, the authors might have omitted one important regulatory molecular family; that is, miRNAs. Indeed, there is accumulating evidence demonstrating that miRNAs play critical regulatory roles in a variety of physiological and pathological processes, including cell growth, migration and apoptosis [5,6]. Specifically, the apoptotic machinery and inflammation process are regulated by miRNAs. Wang and colleagues noted that miR-155 targets *FADD* and *CASP3* as the underlying mechanisms for the increase of apoptosis in human disc degeneration [7]. Given that nucleus pulposus cells are similar to chondrocytes in histology and cell markers, we might reasonably deduce that miRNAs could play roles in apoptosis in OA. At this point, SF might exert its influence by altering the expression of miRNAs. Such a beneficial investigation is promising with the hope of providing novel insights into the molecular mechanisms for the effects of SF on OA.

Third, the authors claimed that different concentrations of SF have no effect on normal chondrocyte viability in the first section of Results. However, SF concentrations of 500 and 1,000 μmol/l significantly increase chondrocyte viability compared with the control group, which was shown as Figure 1 in their article.

Taken together, the role of the intrinsic apoptotic signaling pathway and miRNAs in the impact of SF might enhance the persuasive capability of the article and further expand our understanding of OA.

**Abbreviations**
IL, interleukin; miRNA, microRNA; OA, osteoarthritis; SF, sodium ferulate.

**Competing interests**
The authors declare that they have no competing interests.

**Author details**
[1]School of Stomatology, Fourth Military Medical University, 15 Changle Western Road, Xi'an 710032, PR China. [2]Department of Orthopaedics, Xijing

*Correspondence: nfperry@163.com
[2]Department of Orthopaedics, Xijing Hospital, 127 Changle Western Road, Fourth Military Medical University, Xi'an 710032, PR China
Full list of author information is available at the end of the article

Hospital, 127 Changle Western Road, Fourth Military Medical University, Xi'an 710032, PR China.

Published: 24 May 2013

**References**

1. Qin J, Shang L, Ping A-s, Li J, Li X-j, Yu H, Magdalou J, Chen L-b, Wang H: **TNF/TNFR signal transduction pathway-mediated anti-apoptosis and anti-inflammatory effects of sodium ferulate on IL-1β-induced rat osteoarthritis chondrocytes *in vitro*.** *Arthritis Res Ther* 2012, **14:**R242.
2. Nagata S: **Apoptosis by death factor.** *Cell* 1997, **88:**355-365.
3. Krammer PH: **CD95's deadly mission in the immune system.** *Nature* 2000, **407:**789-795.
4. Tschoeke SK, Hellmuth M, Hostmann A, Robinson Y, Ertel W, Oberholzer A, Heyde C-E: **Apoptosis of human intervertebral discs after trauma compares to degenerated discs involving both receptor-mediated and mitochondrial-dependent pathways.** *J Orthop Res* 2008, **26:**999-1006.
5. Bartel DP: **MicroRNAs: genomics, biogenesis, mechanism, and function.** *Cell* 2004, **116:**281-297.
6. Selbach M, Schwanhausser B, Thierfelder N, Fang Z, Khanin R, Rajewsky N: **Widespread changes in protein synthesis induced by microRNAs.** *Nature* 2008, **455:**58-63.
7. Wang HQ, Yu XD, Liu ZH, Cheng X, Samartzis D, Jia LT, Wu SX, Huang J, Chen J, Luo ZJ: **Deregulated miR-155 promotes Fas-mediated apoptosis in human intervertebral disc degeneration by targeting FADD and caspase-3.** *J Pathol* 2011, **225:**232-242.

doi:10.1186/ar4226
**Cite this article as**: Ma J, *et al.*: Response to 'TNF/TNFR signal transduction pathway-mediated anti-apoptosis and anti-inflammatory effects of sodium ferulate on IL-1beta-induced rat osteoarthritis chondrocytes *in vitro*'. *Arthritis Research & Therapy* 2013, **15:**408.