Citation: IBMS BoneKEy **10**, Article number: 310 (2013) | doi:10.1038/bonekey.2013.44

www.nature.com/bonekey

MEETING REPORT

Intervertebral disc: a rising star in the skeleton galaxy (ASBMR 2012)

Christophe Merceron[1,2,3] and Ernestina Schipani[1]

[1]Indiana University School of Medicine, Department of Medicine, Division of Endocrinology, Indianapolis, IN, USA. [2]Inserm, UMRS 791-LIOAD, Centre for Osteoarticular and Dental Tissue Engineering, Group STEP 'Skeletal Tissue Engineering and Physiopathology', Nantes, France. [3]Department of Dental Surgery, L'UNAM, Nantes University, Nantes, France.

IBMS BoneKEy **10,** Article number: 310 (2013) | doi:10.1038/ibmsbonekey.2013.44; published online 27 March 2013

Meeting report from the 34th Annual Meeting of the American Society for Bone and Mineral Research, Minneapolis, MN, USA, 12–15 October 2012

The 'skeleton galaxy' has been extensively studied over the past decades, and these studies have led to define in a quite precise way the various entities orbiting in this galaxy and their distribution such as the 'bone and cartilage constellations'. In the 'skeleton galaxy', the intervertebral disc (IVD) has been considered for a long time as belonging to the 'cartilage constellation', and, therefore, has remained in the shadow of the 'chondrocyte system'. However, recent investigations have provided evidence that this 'unidentified skeletal object' is indeed a biological entity clearly distinct from cartilage.[1–3] Not surprisingly, IVD has become the focus of intense research. We will use the ASBMR 2012 Annual Meeting and the *BoneKEy* journal as telescopes to observe this rising star.

The IVD is a key element for spine mobility. It is an amphiarthrosis (or semi-mobile joint), and it is constituted of three distinct parts, the inner element, which is a proteoglycan-rich gelatinous structure called nucleus pulposus (NP), the annulus fibrosus (AF), which is a fibrous ring entrapping the NP and consisting of concentrically organized collagen lamellae, and the cartilaginous endplates, which cap top and bottom NP and AF. NP cells are often referred to as chondrocyte-like cells, but it has become progressively clear that this is indeed an incorrect oversimplification. It has recently been shown that NP, differently from cartilage, derives from notochord[4,5] and is not enriched in collagens.[6]

As the IVD is an avascular structure, NP has a gradient of oxygenation.[7,8] Consistent with these findings, a study has been presented at the ASBMR meeting showing that adult mice with conditional deletion of the hypoxia-inducible transcriptional factor1α (HIF-1α) in notochordal cells (FOXA2-Cre;HIF-1$\alpha^{f/f}$)[9] completely lack the NP, which has been replaced by the inner layer of AF.[10] The virtual disappearance of the NP appears to be the result of altered differentiation of notochordal cells into cells of the NP at earlier stages of development, combined with massive cell death at later time points. This study supports the notion that NP derives from the notochord, and it highlights for the first time the critical role of HIF-1α in NP development.

Moreover, a novel *ex-vivo* model of IVD has been presented that is likely to become a useful tool to study cross-talk signaling between AF and NP.[11] The authors have paid special attention to the Sonic hedgehog signaling pathway, which is known to control many aspects of organogenesis including cell proliferation, differentiation and matrix production.[12] Last, we would like to mention an interesting study that has further highlighted the importance of fibronectin fragments in the degeneration of the NP.[13] In particular, the authors have provided experimental evidence supporting a direct correlation between the increased levels of fibronectin fragments and the severity of disc degeneration.[14]

A few years ago, IVD was only a nebula with vaguely defined contours. But, thanks to the effort and the observations provided by the scientific community, data have started to accumulate around IVD, which has now more consistency. We are currently witnessing a transition phase during which the 'IVD nebula' is being progressively metamorphosed in an independent star within the 'skeleton galaxy', and we will follow its trajectory with the greatest interest.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Clouet J, Grimandi G, Pot-Vaucel M, Masson M, Fellah HB, Guigand L *et al.* Identification of phenotypic discriminating markers for intervertebral disc cells and articular chondrocytes. *Rheumatology (Oxford)* 2009;**48**:1447–1450.
2. Minogue BM, Richardson SM, Zeef LA, Freemont AJ, Hoyland JA. Characterization of the human nucleus pulposus cell phenotype and evaluation of novel marker gene expression to define adult stem cell differentiation. *Arthritis Rheum* 2010;**62**:3695–3705.
3. Lee CR, Sakai D, Nakai T, Toyama K, Mochida J, Alini M *et al.* A phenotypic comparison of intervertebral disc and articular cartilage cells in the rat. *Eur Spine J* 2007;**16**:2174–2185.
4. Choi KS, Cohn MJ, Harfe BD. Identification of nucleus pulposus precursor cells and notochordal remnants in the mouse: implications for disk degeneration and chordoma formation. *Dev Dyn* 2008;**237**:3953–3958.
5. Risbud MV, Schaer TP, Shapiro IM. Toward an understanding of the role of notochordal cells in the adult intervertebral disc: from discord to accord. *Dev Dyn* 2010;**239**:2141–2148.
6. Pattappa G, Li Z, Peroglio M, Wismer N, Alini M, Grad S. Diversity of intervertebral disc cells: phenotype and function. *J Anat* 2012;**221**:480–496.

7. Risbud MV, Guttapalli A, Stokes DG, Hawkins D, Danielson KG, Schaer TP *et al.* Nucleus pulposus cells express HIF-1 alpha under normoxic culture conditions: a metabolic adaptation to the intervertebral disc microenvironment. *J Cell Biochem* 2006;**98**: 152–159.
8. Risbud MV, Schipani E, Shapiro IM. Hypoxic regulation of nucleus pulposus cell survival: from niche to notch. *Am J Pathol* 2010;**176**:1577–1583.
9. Uetzmann L, Burtscher I, Lickert H. A mouse line expressing Foxa2-driven Cre recombinase in node, notochord, floorplate, and endoderm. *Genesis* 2008;**46**:515–522.
10. Mangiavini L, Merceron C, Wilson TL, Robling A, Shapiro I, Risbub M *et al.* HIF-1α is essential for the development of the nucleus pulposus. *J Bone Min Res* 2012;**27**(Suppl 1) (Abstract is available at: http://www.asbmr.org/Meetings/AnnualMeeting/AbstractDetail.aspx?aid=a92e68de-2df3-4a2f-acb4-93c5670cf495).
11. Dahia C, Mahoney E, Wylie C. Cell signaling pathways regulate postnatal intervertebral disc growth and maintenance. *J Bone Min Res* 2012;**27**(Suppl 1) (Abstract is available at: http://www.asbmr.org/Meetings/AnnualMeeting/AbstractDetail.aspx?aid=1b6c014d-79a9-4880-8451-284e5ebc2ded).
12. Dahia CL, Mahoney E, Wylie C. Shh signaling from the nucleus pulposus is required for the postnatal growth and differentiation of the mouse intervertebral disc. *PloS One* 2012;**7**:e35944.
13. Markova D, Ruel N, Chee A, Scanzello C, Anderson DG, Adams S *et al.* Fibronectin fragments in human intervertebral disc tissue and their effects on disc cells. *J Bone Min Res* 2012;**27**(Suppl 1) (Abstract is available at: http://www.asbmr.org/Meetings/AnnualMeeting/AbstractDetail.aspx?aid=1e737c4c-06cc-4690-9907-1264a2ec8e6a).
14. Anderson DG, Markova D, Adams SL, Pacifici M, An HS, Zhang Y. Fibronectin splicing variants in human intervertebral disc and association with disc degeneration. *Spine* 2010;**35**:1581–1588.