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New Horizons in Spine Research: Disc Biology, Spine Biomechanics and Pathomechanisms of Back Pain

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Low back pain and neck pain are the first and fourth leading causes of years lived with disability, respectively.¹ The widespread prevalence of back pain makes it among the most costly healthcare conditions, yet, it is surprisingly not among the top ten health conditions receiving research funding.² This funding discrepancy was noted by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) with a Roundtable on the Role of Disc Degeneration in Neck and Back Pain highlighting the need for novel research and partnerships to overcome some of these challenges.³ To advance novel spine science and collaborations, the 3rd International Spine Research Symposium, co-sponsored by the Philadelphia Spine Research Society (PSRS), NIAMS/NIH and the Orthopaedic Research Society (ORS), was held to enhance understanding of the clinical problems associated with degenerative disc disease, and to highlight cutting-edge scientific research in areas of basic biology, epidemiology, disease mechanisms, biomechanics, tissue engineering and imaging of the intervertebral disc (IVD).⁴ This special issue on 'New Horizons in Spine Research' and a second issue to follow at a later date are outcomes from that meeting, with articles selected from the strong response to the 'call for papers'. This issue focuses on the fundamental topics of disc ageing and cell biology, spine biomechanics, anatomy and imaging, and pathomechanisms of spine pain. A second special issue will focus on repair and regeneration. This growing passion for advancing spine research and improving spinal health has ignited the spine research community to coalesce within the Orthopaedic Research Society as the newly formed Spine Section (<http://www.ors.org/spinesection/>) in order to enhance communication and collaboration.

DISC AGEING AND CELL BIOLOGY

Vo et al. review important IVD ageing changes⁵ that are distinct from but interact with IVD degeneration since aged IVDs are more susceptible to injury with inferior repair responses. This review follows the consensus review on nucleus pulposus phenotype of the ORS Spine Research Interest Group (now Spine Section).⁶ Improved functional nucleus pulposus cell markers are reported that highlight notochordal markers,^{7,8} clarify their distinction from articular chondrocytes, and include novel molecular phenotypic changes that also occur with ageing and degeneration.⁹ Defining markers of annulus fibrosus phenotype remains a young field and important functional cellular behaviours of annulus cells are described.^{10,11}

SPINE BIOMECHANICS, ANATOMY AND IMAGING

Novel features of IVD structure and their functional roles are still being identified and the role of the inter-lamellar matrix is clarified by Tavakoli et al.¹² Identifying early degenerative changes requires advanced imaging methods, their quantitation,¹³ and their validation in animal models.¹⁴ Effects of degeneration on human motion segment functional biomechanics are clarified in papers using advanced multi-degree-of-freedom biomechanical testing methods,^{15,16} and Muruiki et al. further identifies biomechanical changes with spinal level and sex.¹⁶ The endplate is receiving increasing attention and papers by Kishimoto et al. and DeLucca et al., describe novel findings regarding their anatomy and changes with degeneration.^{17,18}

PATHOMECHANISMS OF SPINE PAIN

Chronic inflammation is a known source of spine pain and novel methods are described to longitudinally track structural and inflammatory changes following injury.¹⁹ Neuroimmune cellular activation in response to whole body vibration can also induce spine injury and persistent pain.²⁰ Bacterial infection in immune-privileged IVDs can induce inflammation, induce IVD degeneration and result in modic-like changes in the adjacent marrow in a model system²¹ providing some evidence for this provocative and intriguing back pain mechanism. Nerve ingrowth²² and vascularization²³ of IVDs are also attributed to discogenic pain, and spine pain can be associated with pathology surrounding structures including facet joints²⁴ and ligamentum flavum.²⁵

CONCLUSIONS

This issue includes papers that improve understanding of disc biology, degeneration and pain, and it is our hope that these advances will stimulate further research to impact spine science for many years. The next issue in this series will focus on translational research with a focus on innovations in repair and regeneration.

REFERENCES

1. Murray CJ, Atkinson C, Bhalla K, et al. The state of US health, 1990–2010: burden of diseases, injuries, and risk factors. JAMA. 2013; 310:591–608. [PubMed: 23842577]
2. The Burden of Musculoskeletal Diseases in the United States: Prevalence, Societal and Economic Cost. American Academy of Orthopaedic Surgery; 2008. <http://www.boneandjointburden.org/>

3. NIAMS/NIH Roundtable on the Role of Disc Degeneration in Neck and Back Pain. National Institute of Arthritis and Musculoskeletal and Skin Diseases; 2014 Oct 27. http://www.niams.nih.gov/News_and_Events/Meetings_and_Events/Roundtables/2014/disc_degeneration.asp#cit3
4. Orthopaedic Research Society Philadelphia Spine Research Society: ORS PSRS 3rd International Philadelphia Spine Research Symposium. Philadelphia, PA: Thomas Jefferson University; 2015 Nov 9–12. <http://www.ors.org/philaspinemeeting/>
5. Vo NV, Hartman RA, Patil PR, et al. Molecular mechanisms of biological aging in intervertebral discs. *J Orthop Res.* 2016; 34:1289–1306. [PubMed: 26890203]
6. Risbud MV, Schoepflin ZR, Mwale F, et al. Defining the phenotype of young healthy nucleus pulposus cells: recommendations of the Spine Research Interest Group at the 2014 annual ORS meeting. *J Orthop Res.* 2015; 33:283–293. [PubMed: 25411088]
7. Fujita N, Suzuki S, Watanabe K, et al. A chordomaderived cell line U-CH1-N recapitulates the biological properties of notochordal nucleus pulposus cells. *J Orthop Res.* 2016; 34:1341–1350. [PubMed: 27248133]
8. Rodrigues-Pinto R, Berry A, Piper-Hanley K, et al. Spatiotemporal analysis of putative notochordal cell markers reveals CD24 and keratins 8, 18 and 19 as notochord-specific markers during early human intervertebral disc development. *J Orthop Res.* 2016; 34:1327–1340. [PubMed: 26910849]
9. Tang X, Jing L, Richardson WJ, et al. Identifying molecular phenotype of nucleus pulposus cells in human intervertebral disc with aging and degeneration. *J Orthop Res.* 2016; 34:1316–1326. [PubMed: 27018499]
10. Gruber HE, Riley FE, Hoelscher GL, et al. Human annulus progenitor cells: analyses of this viable endogenous cell population. *J Orthop Res.* 2016; 34:1351–1360. [PubMed: 27249627]
11. Nakai T, Sakai D, Nakamura Y, et al. CD146 defines commitment of cultured annulus fibrosus cells to express a contractile phenotype. *J Orthop Res.* 2016; 34:1361–1372. [PubMed: 27273299]
12. Tavakoli J, Elliott DM, Costi JJ. Structure and mechanical function of the inter-lamellar matrix of the annulus fibrosus in the disc. *J Orthop Res.* 2016; 34:1307–1315. [PubMed: 27208689]
13. Pandit P, Talbott JF, Pedroia V, et al. T1rho and T2-based characterization of regional variations in intervertebral discs to detect early degenerative changes. *J Orthop Res.* 2016; 34:1373–1381. [PubMed: 27227485]
14. Gullbrand SE, Ashinsky BG, Martin JT, et al. Correlations between quantitative T2 and T1rho MRI, mechanical properties and biochemical composition in a rabbit lumbar intervertebral disc degeneration model. *J Orthop Res.* 2016; 34:1382–1388. [PubMed: 27105019]
15. Amin DB, Sommerfeld D, Lawless IM, et al. Effect of degeneration on the six degree of freedom mechanical properties of human lumbar spine segments. *J Orthop Res.* 2016; 34:1399–1409. [PubMed: 27291789]
16. Muriuki MG, Havey RM, Voronov LI, et al. Effects of motion segment level, Pfirrmann intervertebral disc degeneration grade and gender on lumbar spine kinematics. *J Orthop Res.* 2016; 34:1389–1398. [PubMed: 26990567]
17. DeLucca JF, Peloquin JM, Smith LJ, et al. MRI quantification of human spine cartilage endplate geometry: comparison with age, degeneration, level, and disc geometry. *J Orthop Res.* 2016; 34:1410–1417. [PubMed: 27232974]
18. Kishimoto M, Akeda K, Sudo A, et al. In vivo measurement of vertebral endplate surface area along the whole-spine. *J Orthop Res.* 2016; 34:1418–1430. [PubMed: 27346338]
19. Abraham AC, Liu JW, Tang SY. Longitudinal changes in the structure and inflammatory response of the intervertebral disc due to stab injury in a murine organ culture model. *J Orthop Res.* 2016; 34:1431–1438. [PubMed: 27273204]
20. Zeeman ME, Kartha S, Winkelstein BA. Whole-body vibration induces pain and lumbar spinal inflammation responses in the rat that vary with the vibration profile. *J Orthop Res.* 2016; 34:1439–1446. [PubMed: 27571442]
21. Dudli S, Fields AJ, Samartzis D, et al. Pathobiology of modic changes. *Eur Spine J.* 2016
22. Gruber HE, Hoelscher GL, Bullock L, et al. Human annulus signaling cues for nerve outgrowth: in vitro studies. *J Orthop Res.* 2016; 34:1456–1465. [PubMed: 27155444]

23. Pohl PH, Lozito TP, Cuperman T, et al. Catabolic effects of endothelial cell-derived microparticles on disc cells: implications in intervertebral disc neovascularization and degeneration. *J Orthop Res.* 2016; 34:1466–1474. [PubMed: 27246627]
24. Netzer C, Urech K, Hugle T, et al. Characterization of subchondral bone histopathology of facet joint osteoarthritis in lumbar spinal stenosis. *J Orthop Res.* 2016; 34:1475–1480. [PubMed: 27147479]
25. Qu X, Chen Z, Fan D, et al. Notch signaling pathways in human thoracic ossification of the ligamentum flavum. *J Orthop Res.* 2016; 34:1481–1491. [PubMed: 27208800]