Understanding the mechanisms of notochord maturation and transformation during intervertebral disc morphogenesis in the mouse

Antoine Henry, Pauline Colombier, Maeva Dutilleul, Florent Autrusseau, Jerome Guicheux, <u>Anne Camus</u> INSERM U1229-RMeS, Laboratory of Regenerative Medicine and Skeleton, Nantes. Université de Nantes, France, UFR Odontologie, Nantes, France, CHU Nantes, PHU4 OTONN, Nantes, France.

Low back pain is one of the most common musculoskeletal disorder and the most common causes of disability in industrialized countries. Although the aetiology of low back pain is unknown, it is often (40%) associated with degeneration of the intervertebral disc (IVD). There is currently no effective treatment for disc degeneration. This is largely due to a lack of basic knowledge of the molecular and cellular controls of disc development, growth, differentiation, and homeostasis, during embryogenesis and at different stages of life.

The notochord (NTC) is composed of large cells packed within a firm connective tissue sheath and is found in all vertebrate embryos at the ventral surface of the neural tube. Notochord cells play major roles both in vertebral column formation and IVD development. Lineage tracing experiments in the mouse demonstrate that notochord cells are the precursor cells that give rise to the nucleus pulposus (NP), the highly hydrated central part of the IVD where degenerative changes are thought to initiate. There is now considerable evidence that notochord cells have a significant influence on the homeostasis of the IVD and their loss has been correlated with aging and degeneration. Our research aims to identify gene networks and signalling pathways associated with notochord maturation into IVD. The present work further investigates the cellular events (apoptosis, proliferation, rearrangement) in combination with the mapping of active SHH signalling during the morphogenesis of IVD at different embryonic stages along the rostro-caudal axis.

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