Proinflammatory mediators

Proinflammatory mediators modulate catabolic reactions, resulting in changes in extracellular matrix (ECM) homeostasis and, finally, neural/vascular ingrowth-related chronic intractable discogenic pain. In ECM homeostasis, anabolic protein-regulating genes show reduced expression and changes in ECM production, while matrix metalloproteinase gene expression increases and results in aggressive ECM degradation. The resultant loss of normal IVD viscoelasticity and a concomitant change in ECM composition are key mechanisms in DDDs. During inflammation, a macrophage-related cascade is represented by the secretion of high levels of pro-inflammatory cytokines, which induce inflammation. Aberrant angiogenesis is considered a key initiative pathologic step in symptomatic DDD. In reflection of angiogenesis, vascular endothelial growth factor expression is regulated by hypoxia-inducible factor-1 in the hypoxic conditions of IVDs. Furthermore, IVD cells undergoing degeneration potentially enhance neovascularization by secreting large amounts of angiogenic cytokines, which penetrate the IVD from the outer annulus fibrosus, extending deep into the outer part of the nucleus pulposus. Based on current knowledge, a multi-disciplinary approach is needed in all aspects of spinal research, starting from basic research to clinical applications, as this will provide information regarding treatments for DDDs and discogenic pain [1].

1)
Kim JH, Ham CH, Kwon WK. Current Knowledge and Future Therapeutic Prospects in Symptomatic Intervertebral Disc Degeneration. Yonsei Med J. 2022 Mar;63(3):199-210. doi: 10.3349/ymj.2022.63.3.199. PMID: 35184422.