COMPANION ANIMAL
Research Award

Investigation of nuclear factor kappa B (NF-kB) and Janus kinase- signal transducers and activation of transcription (JAK-STAT) signalling in degenerative spinal disease in dogs

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Introduction

Degenerative lumbosacral stenosis (DLSS) is a common disease in dogs, involving degeneration of the ligamentum flavum (LF). The most common clinical sign of DLSS is back pain. However, degeneration as a stand-alone process does not cause pain. Recent scientific work has shown that tissue inflammation can cause degenerated tissues to become painful, and that nuclear factor kappa B (NF-kB) and Janus kinase – signal transducers and activation of transcription (JAK-STAT) signalling are key inflammatory pathways in this process. However, these pathways have not been investigated specifically for the LF in DLSS patients. The aim of this study was to investigate NF-kB and JAK-STAT signalling in the LF of patients affected by DLSS.

Materials and Methods

LF tissue samples were collected from dogs without spinal disease (control group) and client-owned dogs diagnosed with low back pain and DLSS (diseased group). Western Blot analysis was performed for the following protein targets: NF-kB signalling: P65, Phospho (P)-P65, Inhibitor kappa-B-alpha (IkBa), P-IkBa; JAK-STAT signalling: Signal transducer and activator of transcription 1 (STAT1), P-STAT, STAT3, P-STAT3. The obtained protein signals were quantified and normalized based on total sample protein content. Linear mixed models were used to statistically compare the protein expression between the control and the diseased group. Significance was set to $P < 0.05$.

Results

No significant differences were found between healthy and diseased groups for individual targets of JAK-STAT and NF-kB pathways. Expression of P-IkBa was only found in the degenerated samples. The ratio between the phosphorylated (active) and non-phosphorylated (inactive) targets for P65 protein was significantly higher in the diseased group ($P = 0.018$).

Discussion

Degeneration of the LF in dogs involves an activation of NF-kB signalling. These findings provide new insights in the biomolecular processes underlying degenerative spinal disease and may be implemented in new biomolecular treatment strategies aimed at relieving back pain.

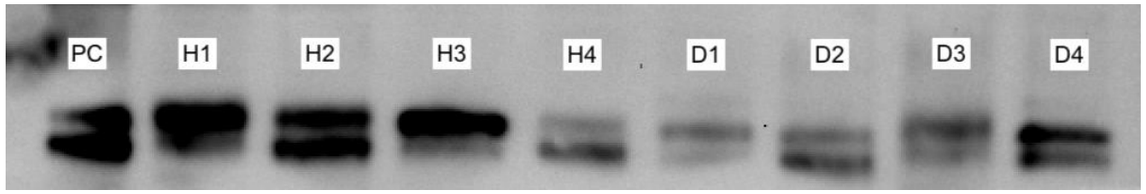

Figure 1: Western Blot of non-phosphorylated (inactive) IkBa in ligamentum flavum (LF), NF-kB signalling. PC: Positive control; H1-4: Healthy LF samples; D1-4 Degenerated LF samples. A stronger expression of IkBa in the healthy samples compared to the degenerated samples can be appreciated.

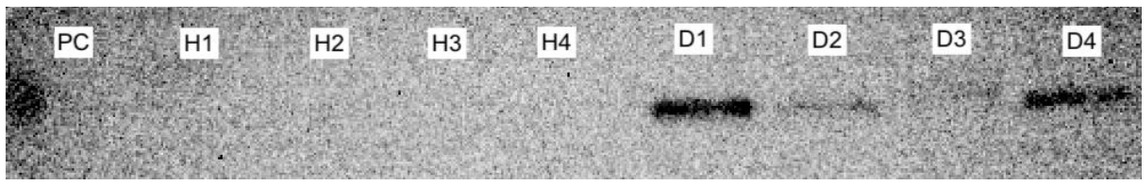

Figure 2: Western Blot of phosphorylated (active) IkBa (P-IkBa) in ligamentum flavum (LF), NF-kB signalling. PC: Positive control; H1-4: Healthy LF samples; D1-4: Degenerated LF samples. Expression of P-IkBa was only found in the degenerated samples.