Assessment of SPP1 and FN1 in serum, bronchoalveolar lavage fluid and lung tissue samples from dogs affected with canine idiopathic pulmonary fibrosis

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Background:

Canine idiopathic pulmonary fibrosis (CIPF) is a chronic disease affecting West Highland white terriers (WHWTs)[1,2]. Osteopontin (SPP1) and fibronectin (FN1) are associated with pulmonary fibrosis in men[3-6] and are overexpressed in bronchoalveolar lavage fluid (BALF) macrophage clusters in CIPF[7].

Study premise:

The aim is to investigate whether these molecules are potential disease markers. SPP1 and FN1 serum and BALF concentrations were measured using canine ELISA kits in CIPF WHWTs (n=24), healthy aged-matched WHWTs (n=13) and healthy terriers (n=15). Proteins were also localized in lung tissue by immunohistochemistry.

Results:

SPP1 serum concentrations were higher in CIPF compared with healthy WHWTs and terriers, and in healthy WHWTs compared with terriers. There were negatively correlated with PaO_2 in WHWTs. Higher SPP1 BALF concentrations were found in CIPF and healthy WHWTs compared with terriers. Intense labelling was reported in all groups in ciliated epithelial cells, smooth muscular cells surrounding large vessels and some macrophages. Moreover, in all CIPF WHWTs, the pneumocytes II and the extra cellular matrix were labelled, while it was the case in only 57% of healthy WHWTs and not present in terriers.

FN1 serum concentrations were lower in CIPF and healthy WHWTs compared with terriers. No difference was found between groups in BALF. There was no evidence of differences in FN1 labelling.

Conclusions:

The results suggest that SPP1 is involved in CIPF pathogenesis and could predispose that breed to the disease. However, further studies are required to determine its interest as biomarker or potential therapeutic target.

References:

1. Clercx C, Fastrès A, Roels E. Idiopathic pulmonary fibrosis in West Highland white terriers: An update. Vet J (2018) 242:53–58. doi:10.1016/j.tvjl.2018.10.007
2. Laurila HP, Rajamäki MM. Update on canine idiopathic pulmonary fibrosis in West Highland white terriers. Vet Clin North Am - Small Anim Pract (2020) 50:431–446. doi:10.1016/j.cvsm.2019.11.004
3. Morse C, Tabib T, Sembrat J, Buschur KL, Bittar HT, Valenzi E, et al. Proliferating SPP1/MERTK-expressing macrophages in idiopathic pulmonary fibrosis. Eur Respir J (2019) 54:1802441. doi:10.1183/13993003.02441-2018

4. Upagupta C, Shimbori C, Alsilmi R, Kolb M. Matrix abnormalities in pulmonary fibrosis. Eur Respir Rev (2018) 27:180033. doi:10.1183/16000617.0033-2018
5. Rennard SI, Hunninghake GW, Bitterman PB, Crystal RG. Production of fibronectin by the human alveolar macrophage: Mechanism for the recruitment of fibroblasts to sites of tissue injury in interstitial lung diseases. Proc Natl Acad Sci USA (1981) 78:7147–7151. doi:10.1073/pnas.78.11.7147
6. Adams TS, Schupp JC, Poli S, Ayaub EA, Neumark N, Ahangari F, et al. Single-cell RNA-seq reveals ectopic and aberrant lung-resident cell populations in idiopathic pulmonary fibrosis. Sci Adv (2020) 6:eaba1983. doi:10.1126/sciadv.aba1983
7. Fastrès A, Pirottin D, Fievez L, Tutunaru AC, Bolen G, Merveille AC, et al. Identification of pro-fibrotic macrophage populations by single-cell transcriptomic analysis in West Highland white terriers affected with canine idiopathic pulmonary fibrosis. Front Immunol (2020) 11:611749. doi:10.3389/fimmu.2020.611749