

## Introduction

- Human bronchorrhea is defined by an excessive sputum production (>100 ml/day) with neoplasms being the most frequent underlying cause.
- Shiroshita and colleagues at the 2019 ACVIM, reported clinical features of 18 cats with rattling sounds and airway watery hypersecretion and coined the term feline bronchorrhea (FB) for the syndrome.
- Lobectomized samples from 5 FB cats revealed histologic features consistent with idiopathic pulmonary fibrosis (IPF), a human lung disease of unknown etiology with poor prognosis.
- A minority of human IPF patients with hypersecretion have a worse prognosis but the mechanism of hypersecretion is unknown.

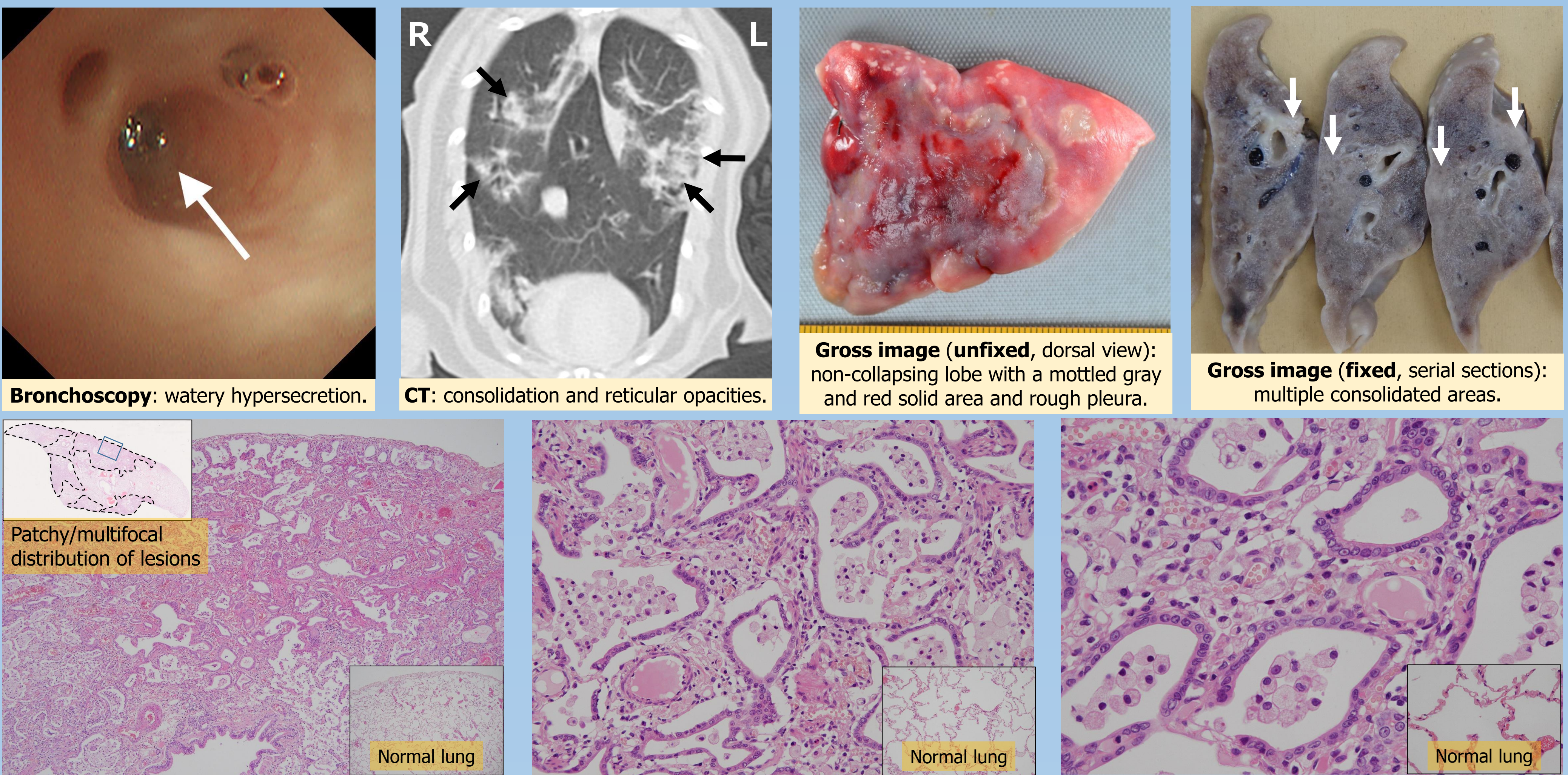
## Objective

To determine the cause/source of FB hypersecretion.

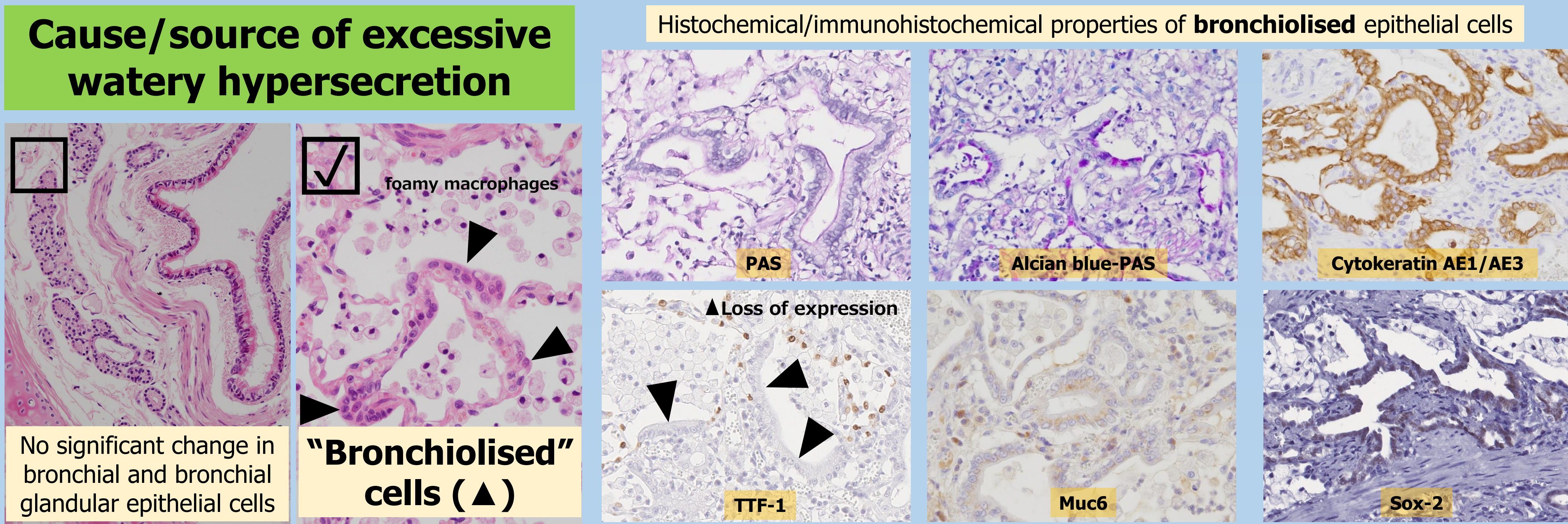
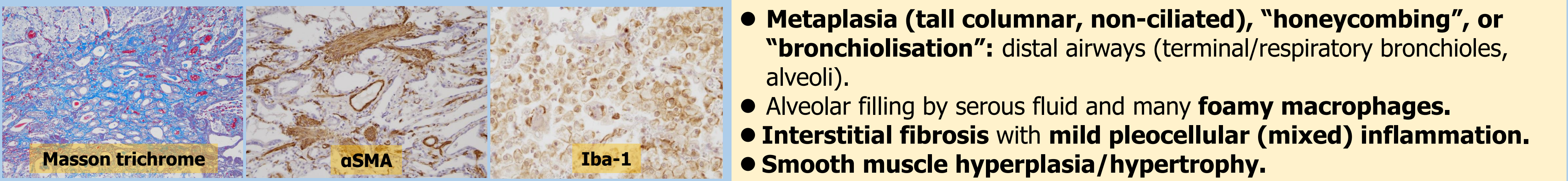
## Materials and methods

The patient is a 10-year-old castrated male Scottish Fold. Histopathology, histochemistry, and immunohistochemistry were performed for the lobectomized left caudal lobe.

Timeline	Description
-3 month	➤ Intermittent rattle (observed by the owner).
-1 month (regional veterinarian)	➤ Anorexia, lethargy, tachypnea, no cough, “abnormal” chest radiographic findings. ➤ Symptomatic therapy ineffective.
Day 0 (veterinary respiratory specialist, the same applies hereafter)	➤ Physical exam: tachypnea, labored breathing, coarse crackles. ➤ Blood gas: hypoxemia (PaO <sub>2</sub> 73mmHg). ➤ X-ray: diffuse patchy infiltrates in both caudal lobes. ➤ Bronchoscopy: excessive clear watery fluid. ➤ BAL: foamy macrophages and neutrophils. No bacteria were cultured. ➤ PCR of laryngeal swab: negative for FHV-1, FCV, H1N1 Influenza, <i>Chlamydomphila felis</i> , <i>Mycoplasma felis</i> , <i>Bordetella bronchiseptica</i> .
Day 7	➤ Radiographic abnormality diminished by prednisolone (1mg/kg).
Day 36	➤ CT: irregular reticular pattern in both caudal lobes.
Day 44	➤ Right caudal lobe surgically excised and showed histologic features of IPF. ➤ Significant clinical improvement achieved.
Day 118	➤ The left caudal lobe was surgically excised (the present specimen).
Day 709	➤ The cat's condition remains stable.

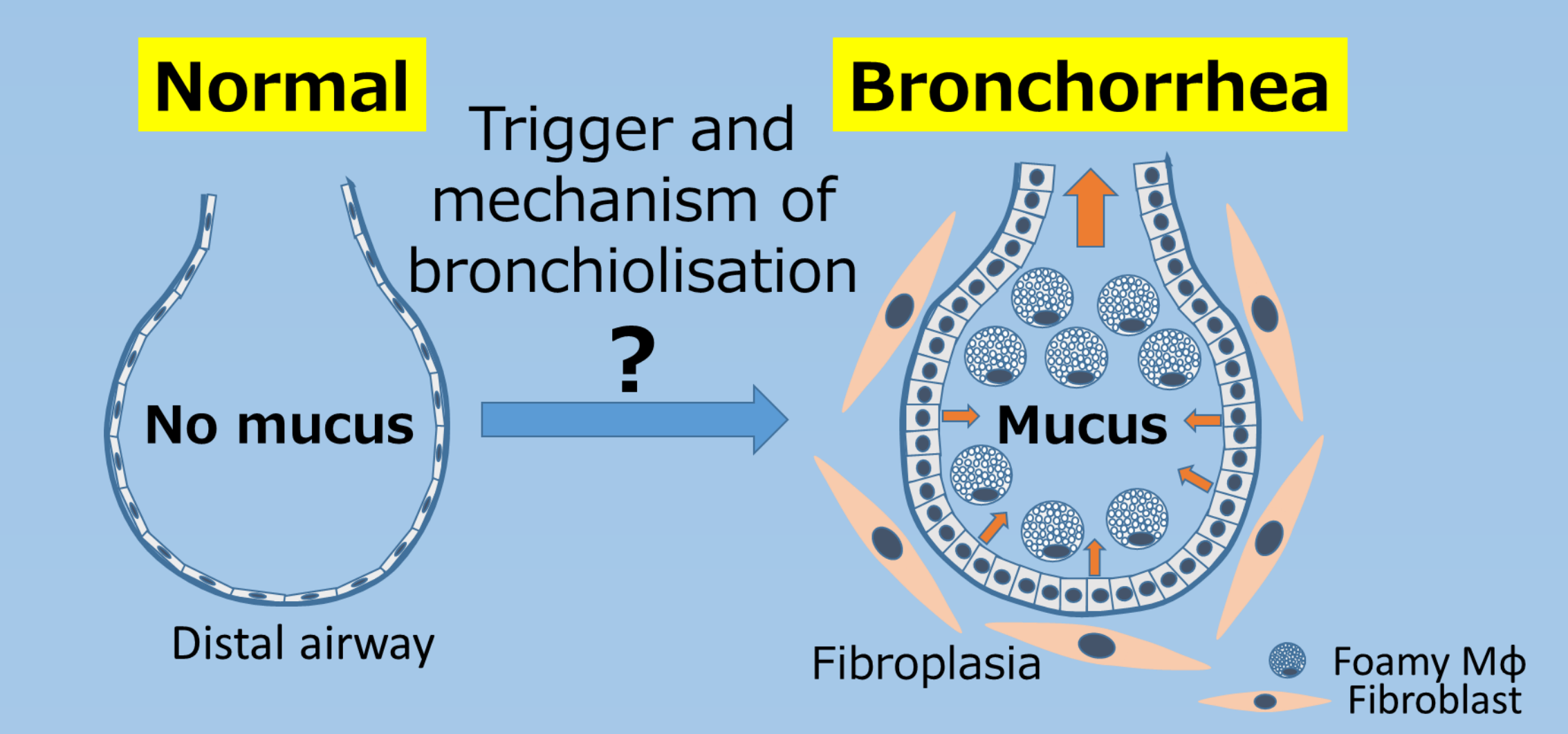


Histologic features are consistent with **human/feline idiopathic pulmonary fibrosis**.



	Histochemistry			Immunohistochemistry			
	PAS	AB pH2.5	AB/PAS	CK AE1/AE3	TTF-1	Muc6†	Sox-2‡
Bronchial NC-EC*	+ (mainly GC)	+ (GC only)	+ (GC only)	+	+	±	+
Bronchial gland EC*	±	–	±	+	+	±	+
Bronchiolar NC-EC*	+ (mainly GC)	+ (GC only)	+ (GC only)	+	+	±	+
Metaplastic (“bronchiolised”) EC	±	–	+	+	Often –	Often +	+
Alveolar EC*	–	–	–	+	+	±	–

NC: non-ciliated, EC: epithelial cell, GC: goblet cell  
\*: internal control (cells in the unaffected part of the patient’s lung).  
†: IHC for Muc1, Muc2, and Muc5AC yielded equivocal results likely due to lack of antibodies’ cross reactivity to feline tissues.  
‡: Sox-2: transcription factor expressed selectively in conducting airway epithelial cells but not in alveoli.



## Results

No hyperplastic or hypersecretory changes were observed in the bronchial epithelium or submucosal glands. Instead, metaplastic distal airway epithelial cells showed active secretion of acid mucin demonstrated by Alcian blue-PAS stain with subsequent macrophage engulfment. The metaplastic cells showed loss of typical airway epithelial cell marker (TTF-1). Reaction to Muc-6, which is secreted by gastric mucosa in humans, was detected by IHC in the metaplastic cells.

## Discussion

Abnormal programming of airway epithelial cells has been suggested for minority of human IPF cases with mucus hypersecretion. The seemingly analogous correlation between human and feline bronchorrhea and IPF lesions can be clarified by further detailed clinicopathological and genotypic investigation of FB cohorts. Cats could be a useful model for the investigation of human bronchorrhea and IPF.

## Conclusion

Metaplastic (“bronchiolised”) distal airway epithelial cells are the cause of watery hypersecretion in FB.

## Acknowledgments

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- Kyodo Byouri Co. Ltd. (Kobe, Japan) for histochemistry and immunohistochemistry.
- Canine-Lab. Inc. (Tokyo, Japan) for PCR.

## Selected references

- Cohn LA et al, Identification and characterization of an idiopathic pulmonary fibrosis-like condition in cats, *Journal of Veterinary Internal Medicine* 2004;18:632-641.
- Plantier L et al, Ectopic respiratory epithelial cell differentiation in bronchiolised distal airspaces in idiopathic pulmonary fibrosis, *Thorax* 2011;66:651-657.
- Shiroshita Y et al, Feline bronchorrhea: a retrospective study of 18 cases (2012-2017). E-Poser presentation at 2019 ACVIM annual conference, Phoenix, Arizona.
- Williams K et al, Identification of spontaneous feline idiopathic pulmonary fibrosis, *Chest* 2004;125(6):2278–2288.