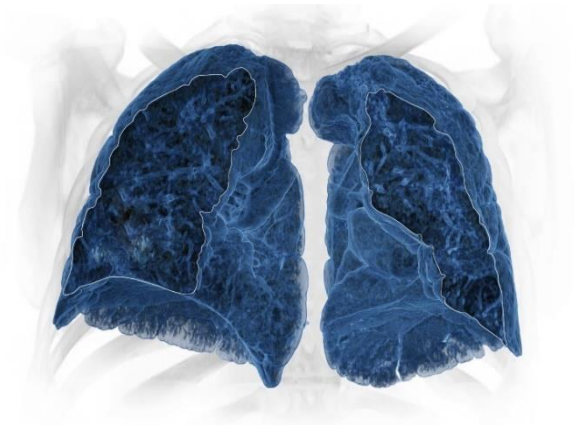
BioLab Assays

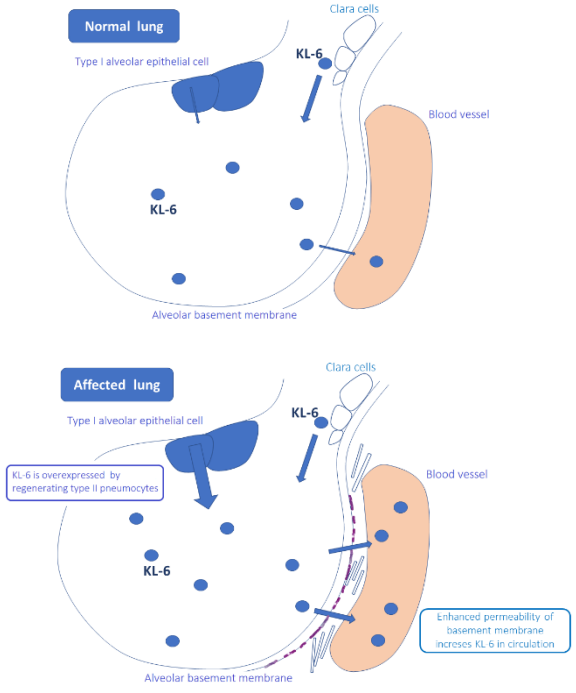
Krebs von den Lungen-6 (KL-6)



Proven marker of Interstitial Lung Disease

BACKGROUND

Krebs von den Lungen-6 (KL-6) is a high-molecular mucin-like glycoprotein, encoded by MUC1 gene. KL-6/MUC1 regulates cell-cell interactions and shows also chemotactic activity. It is distributed mainly on the cell surface of type II alveolar epithelial cells (AECs). During the inflammatory storm, the disulfide bonds on the surface of the epithelial cell membrane may be damaged and KL-6 released into the pulmonary epithelia lining fluid and blood circulation. Increased levels of KL-6 in patients with IPF are due to higher production of KL-6 by regenerating alveolar type II pneumocytes and by its increased release following alveolar damage in the affected lung.



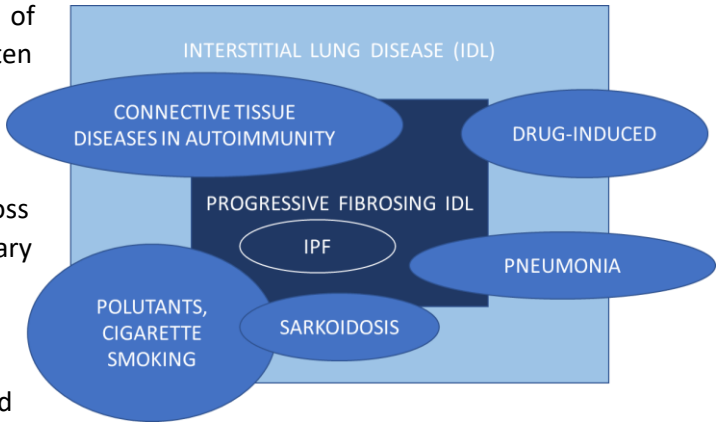
Reference: Ishikawa N, Hattori N, Yokoyama A, Kohno N. Utility of KL-6/MUC1 in the clinical management of interstitial lung diseases. Respir Investig. 2012 Mar;50(1):3-13. doi: 10.1016/j.resinv.2012.02.001. Epub 2012 Mar 8. PMID: 22554854.

PRESENCE OF KL-6 IN THE LUNGS

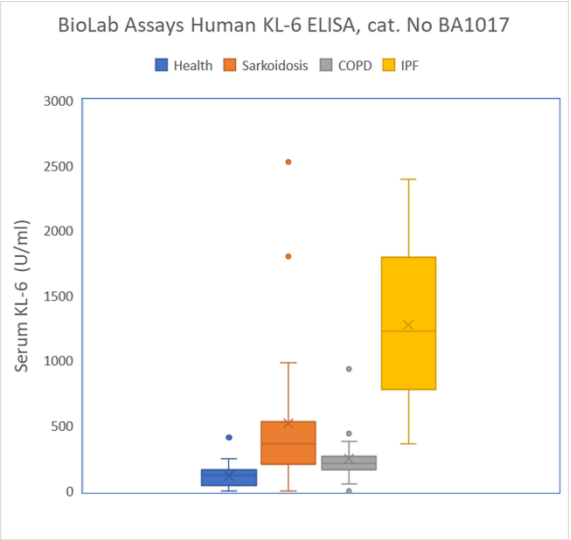
KL-6 is mildly presented in the type II pneumocytes and respiratory bronchiolar epithelial cells and weakly in the basal cells of the bronchiolar epithelium of healthy lungs. No KL-6 expression was observed on type I pneumocytes, goblet cells and mucous cells of the bronchial glands. KL-6 is strongly expressed by the altered and/or regenerating type II pneumocytes in tissue sections obtained from the patients with IPF.

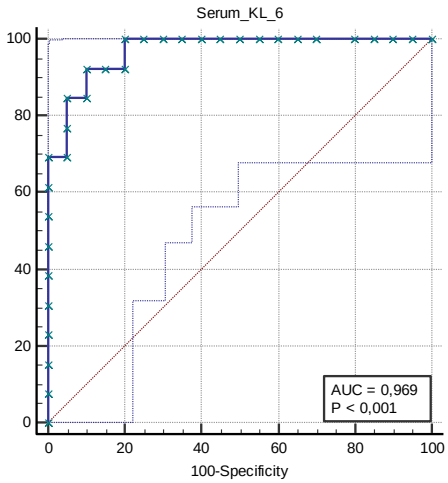
BioLab Assays

KL-6 AND INTERSTITIAL LUNG DISEASE (ILD): DIAGNOSIS AND DISEASE ACTIVITY



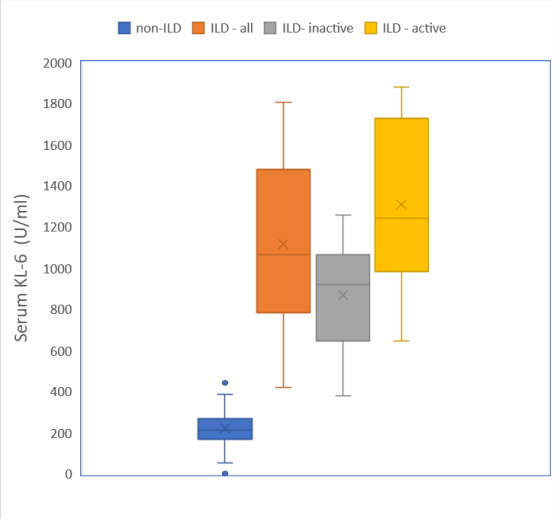
Interstitial lung disease represents a range of heterogeneous difussed parenchymal disorders often characterized by fibrosis of the lungs at advanced stages, and effecting the alveolar space and pulmonary interstitium. Interstitial Pulmonary Fibrosis (IPF) is one of IDLs, that is caused by the loss of function of alveoli, bronchioles and pulmonary interstitium, and its scarring resulting in the decrease of lung capacity. IPF represents progressive fibrosing ILD, which could develop also in the other ILDs. The swiftness of treatment and the disease activity are vital for good patient prognosis. Increased serum levels of KL-6 were observed in IPF patients in many clinical studies. The comparison of serum KL-6 determined by BioLab Assays Human KL-6 ELISA kit in healty individuals, patients with sarcoidosis, COPD and IPF reports serum KL-6 levels typical for the groups (BioLab Assays in-house data).





Risk serum KL-6 values: over 250 U/ml (95percentil of healthy individuals)

ROC analysis COPD vs IPF: cut-off 385 U/ml, clinical specificity 90%, clinical sensitivity 92,3 %, AUC 0,969, 95% confidence interval 0,842 to 0,999



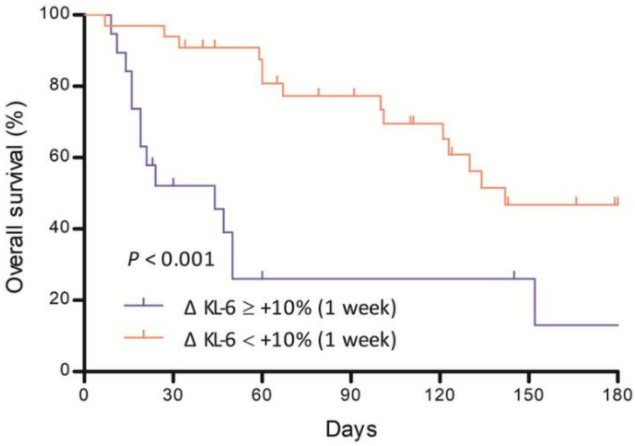
Over differentiation among various IDLs, the challenge is the identification of individuals with extensive lung fibrosis, and progressive fibrosing IDL respectively. The study from He et al. referred comparison among non-Interstitial Lung Disease (non-ILD), Interstitial Lung Disease (ILD-all), and separately non-progressive fibrosing ILD (ILD-inactive) against progressive fibrosing ILD (ILD-active).

Reference: He Q, Tang Y, Huang J, Rao Y, Lu Y. The value of KL-6 in the diagnosis and assessment of interstitial lung disease. Am J Transl Res. 2021 Aug 15;13(8):9216-9223. PMID: 34540037; PMCID: PMC8430136.

KL-6 AND INTERSTITIAL LUNG DISEASE (ILD): MORTALITY IN PATIENTS WITH ACUTE EXACERBATION

The changes in blood KL-6 levels within 1 week hospitalisation were higher in non-survivals. Patients with remarkable increase in KL-6 (≥ 10%) showed significantly worse survival (in-hospital mortality: 63.2 vs. 6.1%, median survival: 42 vs. 142 days; $P < 0.001$) than those without.

Reference: Choi, M.G., Choi, S.M., Lee, J.H. et al. Changes in blood Krebs von den Lungen-6 predict the mortality of patients with acute exacerbation of interstitial lung disease. Sci Rep 12, article 4916 (2022). PMID: 35318424 https://doi.org/10.1038/s41598-022-08965-9



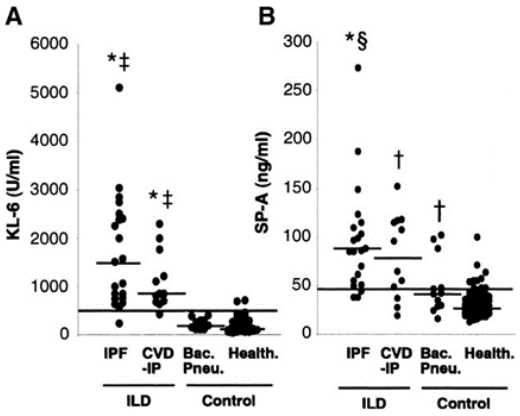
KL-6 AND SURFACTANT PROTEIN A: A COMPARISON AMONG IPF MARKERS

KL-6 and Surfactant protein A (SP-A) are both claimed to be sensitive markers for interstitial lung disease (ILD). The study by Ohnishi et. al. compared these two markers finding out that the sensitivity, specificity, and diagnostic accuracy were 93.9%, 96.3%, and 95.7% for KL-6; 81.8%, 86.6%, and 85.2% for SP-A, respectively. The serum levels of SP-A but not of KL-6 were higher in bacteria pneumonia group than in healthy individuals, which suggests serum SP-A as the sensitive marker in acute respiratory distress syndrome (ARDS), while KL-6 is the most efficient marker for IDL.

BioLab Assays

ILD groups
IPF: Interstitial pulmonary disease; CVD-IP: collagen vascular disease-associated interstitial pneumonitis
Control groups
Bac. Pneu.: Bacterial pneumonia; Health.: Healthy individuals

Reference: Ohnishi H, Yokoyama A, Kondo K, Hamada H, Abe M, Nishimura K, Hiwada K, Kohno N. Comparative study of KL-6, surfactant protein-A, surfactant protein-D, and monocyte chemoattractant protein-1 as serum markers for interstitial lung diseases. Am J Respir Crit Care Med. 2002 Feb 1;165(3):378-81. doi: 10.1164/ajrccm.165.3.2107134. PMID: 11818324.



KL-6

serum KL-6 is the most sensitive and specific serum marker of **interstitial lung disease (IDL),** the release of KL-6 results from alveolar epithelial cell damage and destruction, a recent meta-analysis observed KL-6 diagnostic sensitivity (0.85, 95% CI, 0.77–0.91) and specificity (0.97, 95% CI, 0.90–0.99) for interstitial lung disease

KL-6 levels reflect the severity of **interstitial lung disease** associated with **fibrosing progression** of the disease

KL-6 levels are associated with the presence of connective tissue disease in IDL-related autoimmune diseases: rheumatic arthritis, inflammatory myositis, Sjoengren's syndrome or systemic lupus erythermatosus (SLE)

changes in serum Krebs von den Lungen-6 predict **the mortality** for patients with acute exacerbation in interstitial lung disease, and for patients with IPF

Human KL-6 ELISA

BioLab Assays

Cat.No. BA1017

Sandwich ELISA: capture MAb / detection MAb

Size: 96 wells

Calibration range: 0.156 – 10 U/ml

Sample type: serum, plasma, BALF

Regulatory status: RUO