Pulmonary fibrosis is more and more frequent pathology in ageing global population. Unfortunately, this disorder is characterized by a bad prognosis: no treatment is known and the survival is dramatically low (3 - 5 years). Fibrosis means an excess of fibrous connective tissue production in the area of another type of tissue. In a physiological conditions (tissue repair, regeneration) deposition of fibrous connective tissue enhances the organ structure ensuring its correct functioning. On the other hand, an uncontrolled fibrotic process may lead to the loss of the organ's function. In case of lungs, fibrosis leads to elimination of pathologically changed areas of lung tissue from gas exchange, causing hypoxia and, in the advanced cases, death. Among number of respiratory diseases in the course of which occurs pulmonary fibrosis HP (hypersensitivity pneumonitis) is one of the few with known aetiology. HP is caused by a recurring exposure to organic dust (particles of plant, animal or microbial origin). Worldwide, millions of farmers and workers of many others sectors of industry are occupationally exposed to organic dust. Thus, HP is estimated to be one of the most frequent reasons of pulmonary fibrosis worldwide. HP comprises a number of variants (farmer's lung, bird fancier's lung, thresher's lung, grain handler's disease, malt fever, suberosis, wood chips disease and many others) which show a similar clinical course but are caused by different organic dust components including: thermophilic actinomycetes, fungi, Gram-negative bacteria, bird proteins. Regardless of the causative agent the repeated injuries of epithelium lining airways caused by the recurrent exposure to organic dust observed in HP lead to disorders of tissue repair characterized by mobilization of fibroblasts and their differentiation into myofibroblasts (cells between a fibroblasts and smooth muscle cells) Respiratory epithelium also adds to this process by so called epithelial-mesenchymal transition (EMT), a phenomenon in course of which fully differentiated epithelial cells undergo a phenotypic conversion. They receive an elongated shape and the ability to produce significant amounts of extracellular matrix components. Recent studies have shown that in the case of pulmonary fibrosis the EMT and inflammation drive each other, until fibrotic process reaches the point where fibrosis cannot be attenuated by silencing the inflammation. As the main mechanism of pulmonary fibrosis is a pathology of repair of wounded pulmonary epithelium, we assume that improvement of its regeneration by application the natural enhancer of this process - cathelicidin (antimicrobial peptides, a key component of innate immunity) could prevent or slow down the disease development or perhaps reverse pathological changes.

The aim of the project is to assess the usefulness of inhaled cathelicidin in prevention and treatment of pulmonary fibrosis. In order to achieve the mentioned goal the influence of inhaled cathelicidin on lung tissue in normal and pathological conditions as well as the molecular mechanism of it action will be investigated in the mice model of HP.

The studies will be conducted in the internationally recognized HP mice model, created by our research group, in which pulmonary fibrosis is induced by repeated inhalations of bacteria *Pantoea agglomerans* extract (a potent compound of organic dust widely distributed in the nature, especially on the surface of plants; one of the most important etiological factors of HP) administered to prone to fibrosis mice strain C57BL/6J. Investigated agents (cathelicidin, *P. agglomerans*, PBS) will be provided into the mice respiratory track as aerosol using inhalation challenge set. The research groups were designed to bring the answers to following questions: What is the impact of inhalations with cathelicidin/ *P. agglomerans*/ PBS (solvent for cathelicidin and *P. agglomerans*) on lung tissue? Does pulmonary fibrosis induced by *P. agglomerans* persist after cessation of inhalation? Do inhalations with exogenous cathelicidin prevent pulmonary fibrosis induced by mice exposure to *P. agglomerans*? What is the impact of inhalations with PBS on induced by *P. agglomerans* pulmonary fibrosis? Do inhalations with exogenous cathelicidin are able to reduce or reverse induced by *P. agglomerans* pulmonary fibrosis? Answers for abovementioned questions revealed results of animals respiratory parameters analysis performed during experiments as well as results of assessments on the lung tissue collected from all animals. Lung tissue samples will be subjected to the following analysis: ● histological examination regarding presence of inflammatory changes and fibrotic lesions; ● measurement of fibrosis markers; ● analysis of cell subpopulation in lungs involved in fibrosis development and maintain as well as repair damage caused by organic dust; ● measurement of the levels of cytokines taking part in fibrosis and tissue repair; ● analysis of epithelial-mesenchymal transition markers' genes expression.