MOF (Metal-Organic Frameworks) belong to a new group of porous materials with a hybrid organic-inorganic construction. Their structure is a network consisting of metal cations or clusters (acting as metallic centers, nodes) and the organic linkers between nodes. The interest in MOF is primarily associated with the use of their well-developed surface and large porous. Possibility to build MOF of biocompatible components let to use them as potential drug carriers. Furthermore, forming MOF structure from cations possessing paramagnetic properties (e.g. iron cations) allows to use them as MRI (Magnetic Resonance Imaging) contrast agents and monitoring the distribution of the active substance after administration in real time.

Active substances, which will be incorporated into the structure of MOF in the course of the project, are antituberculosis drugs: isoniazid and pyrazinamide. These substances were chosen because of the fact that tuberculosis belongs to the top three infective diseases - together with HIV and malaria - causing morbidity and death worldwide. According to World Health Organization report, about 30% of world's population is infected with *Mycobacterium tuberculosis*. Every year about 10 million of new cases are registered and about 1.5 to 2 millions of deaths are caused by tuberculosis. Standard tuberculosis therapy consists of administering antibiotics for 6 to 9 months. The traditional oral route of administration and long treatment period are responsible for adverse effects, which often leading to therapy discontinuation. After oral administration the distribution of isoniazid, in the lung tissue is uneven. The concentrations of drugs in pulmonary lesions where the pathogen is located have been markedly lower than in the surrounding lung tissue. Additionally, the conventional oral route of isoniazid administration causes periodic decrease of the drug concentration below effective minimum inhibitory concentration (MIC), allowing tuberculosis bacilli to develop resistance. Nowadays multidrug resistance of *Mycobacterium tuberculosis* is more and more frequently observed which makes that the therapy has to prolonged up to 24 months and is associated with pain and numerous side effects.

Therefore, an interesting alternative to oral administration of active substances, which are targeted to the lung, is inhalation. This makes it possible to achieve a therapeutic concentration of active substance in the lung using lower dose compared to general administration, thereby providing increasing the therapy efficacy and reducing the peripheral side effects. In addition, the use of drug carriers allows for sustained and controlled drug release.

The therapeutic effect after inhalation is not solely dependent on the drug dose, but also on the region of the lung deposition. Therefore, there is an interest in the possibility of monitoring the distribution of the drug administered by inhalation, allowing to observe the progress of the disease and the effects of therapy.

An interesting approach is formation of particles that combine the ability to transfer active substance with imaging properties. This concept has been called theranostic (from word combinations therapy and diagnostics). By building MOF structure from iron cations it is possible to use them as theranostic agents.

The scientific goal of the project is to investigate the possibility of applying MOF as carriers of antituberculosis substances: isoniazid and pyrazinamide and analysis of capabilities to monitoring of MOF preparation deposition in a model of lung tissue using magnetic resonance tomography (MRI).

In the course of the project will be assessed stability MOF to investigate the mechanism of their biodegradation. Biological *in vitro* tests will be carried out on human lung epithelial carcinoma cell line, which is a model cell line to test substances administered by inhalation, and the macrophage cell line. The results will be used to assess the possibility of contact MOF with the pulmonary epithelium. Further investigation will concern MOF deposition in the lungs, depending on their particle size. MOF will be also examined in terms of acting as drug carriers. The drug incorporation efficacy and drug release will be assessed. To investigate MOF imaging ability MRI technique will be used and a special model of lung tissue from cellulose sponge will be formed.