Kraków, similarly to numerous other cities in Poland, belongs to the most polluted cities in the Europe in terms of the levels of particulate matter (PM) in the air.The effect of PM on health depends, among others, on the diameter of a PM particle.PM2.5 (called fine particles) with the diameter less than 2.5 μm, may penetrate the lung alveoli and enter the bloodstream, thus exerting adverse health effects.The presence of PM in blood and internal organs was confirmed by radioisotope methods. Long –time exposure may contribute to the occurrence or aggravate asthma, chronic obstructive lung disease, allergies and some malignancies. The effect of air pollution on health is compared with the effects of smoking. Some epidemiological studies have reported effects PM2.5 on the development of atherosclerosis. The mechanisms linking the exposure to PM with a growing incidence of atherosclerosis have not been fully elucidated. **In our study we hypothesize** that the contact of peripheral blood monocytes (immune system cells with a relatively well-defined role in the development of atherosclerosis) with PM2.5 results in changes to miRNA(small particles of ribonucleic acid that play a crucial role in the regulation of gene expression) that may affect the pathways associated with endothelial dysfunction and the formation of atherosclerotic plaques. Changes in the miRNA expression may affect endothelial function and may help elucidate the mechanisms of systemic effects of PM on the cardiovascular system. We also believe that in humans chronic exposition on PM is associated with changes in miRNA expression depending on the seasonal concentrations of PM2.5.**The aims** of the study were: determination whether in vitro acute exposure of peripheral blood monocytes to different concentration of PM2.5 (with known chemical content) is associated with changes in the miRNA profile. The next we are going to establish which miRNA may affect the development of endothelial dysfunction . In the second part of the study we are going to evaluate the miRNA expression in patients with hypertension and significant coronary artery disease in comparison with patients with hypertension without coronary artery disease, depending on the seasonal (winter-summer) concentrations of PM2.5.(chronic exposition) In our study we also planned to evaluate the elemental and chemical component of PM2.5 as well as assess the contribution of fossil fuel anthropogenic sources to total PM2.5 concentration in Kraków-Krowodrza district and to determine the possible sources of air pollutants.

Methods:Venous blood with monocytes (in vitro study) will be obtained from 3 healthy blood donors. Blood samples will be collected once. Next, peripheral blood monocytes will be exposed to a suspension of PM2.5 at 3 different concentrations, and the changes in the miRNA expression and levels of inflammatory cytokines associated with endothelial dysfunction will be evaluated.

In the second part of our study, blood samples will be collected twice from each study participant during the maximum (winter) and minimum (summer) exposure. The study will include 134 patients (67 patients with arterial hypertension and coronary artery disease and 67 patients with hypertension and without coronary artery disease) recruited from the outpatient cardiac clinic of the John Paul II Hospital in Kraków, Poland. All study patients have lived in the same district of Kraków (Kraków-Krowodrza) for at least 20 years. Seasonal changes in the miRNA expression will be evaluated in all patients.

Evaluation of the chemical composition of PM and determination of the possible sources of pollutants will be possible thanks to scientific equipment provided by the AGH University of Science and Technology in Kraków. Evaluation of the changes in the miRNA expression and assessment of correlations between the changes in the miRNA expression and levels of inflammatory cytokines was possible thanks to scientific experience and equipment of the Department of Molecular Biology and Clinical Genetics of the Jagiellonian University Medical College.

To our knowledge, there have been few studies concerning the molecular mechanisms behind the effect of PM2.5 on atherosclerosis. Therefore, from the medical point of view, it is very important to explore these molecular pathways in vitro. Additionally, assessing the effect of natural seasonal (winter– summer) exposure to PM2.5 among inhabitants of the same Kraków district will elucidate whether higher PM2.5 levels in the autumn and winter seasons result in changes in the gene expression and whether there are any differences in the gene expression between winter and summer when PM2.5 levels are much lower.

We will also attempt to elucidate the effect of PM2.5 on patients with coronary artery disease in comparison with those without the disease, which will have substantial clinical significance.

Another important aspect of our research project is PM2.5 sampling and detailed seasonal analysis of its elemental composition, which will be used in our study. The composition of PM2.5 has a significant effect on health. In Poland, there are few research groups that study the composition of PM. We will also attempt to establish the sources of PM2.5 pollution, which may be important for air pollution reduction measures undertaken in Kraków and other regions of Poland.

This is an interdisciplinary project combining various aspects of medicine, physics, and chemistry.