Disorders that affect the heart or blood vessels are responsible for 40-50% of mortality and belong to the XXI century civilization diseases. The search for the molecular basis of cardiovascular disease in humans has been ongoing for many years. Unfortunately despite the fact of great progress made in research on the atherosclerosis formation, these mechanisms are still unclear. In particular, little is known about the accelerated development of atherosclerosis during the progression of chronic kidney disease (CKD). CKD is characterized by progressive, irreversible and long-term loss of kidney function and the most common causes of this disease are hypertension and diabetes. The prevalence of CKD in Poland reaches 16% and in the USA and worldwide approximately 11% of the general population. Moreover, CKD patients have increased risk for atherosclerosis and cardiovascular complications, like heart attack or stroke, and this risk increases with disease progression. However, unlike the “classical” atherosclerosis, patients with CKD often do not reveal common risk factors such as obesity or high cholesterol level. In such situations, therapy is extremely difficult because lipid lowering treatments are ineffective in reducing the risk of a heart attack or stroke, especially in patients with the most advanced renal disease. Since both, atherosclerosis and CKD are widely prevalent diseases, and the morbidity is gradually increasing, therefore, understanding of the molecular mechanisms of both diseases is extremely important. The main objective of this project is to clarify the molecular basis of atherosclerosis in CKD and the "classical" atherosclerosis unrelated with renal dysfunction, with particular emphasis on the mechanisms of systemic inflammation and oxidative stress. Proposed research is innovative, and the proposed methodology is based on a very modern techniques.

The proposed study will help us answer to the question of why patients with CKD have accelerated atherosclerosis and increased risk of cardiovascular complications. We hope to gain knowledge whether molecular mechanism of atherosclerosis is the same or different between CKD and "classical" atherosclerosis. We also would like to explain what changes occur in the pathophysiology of both diseases during disease progression. We explain whether the same modulators of inflammation are involved in the pathophysiology of both diseases and what changes occur in the peripheral blood cells and vascular cells due to the development of atherosclerosis, both related and unrelated to kidney disease. We would like to find out how healthy vascular cells react under the increased levels of uremic toxins and other undesirable components present in pathologic serum of patients with CKD or CVD. Finally, we will determine whether the observed changes are reflected in the composition of atherosclerotic plaques in advanced atherosclerosis-related and not related to kidney disease. Obtained results will contribute significantly to our understanding of the molecular mechanisms responsible for the development of atherosclerosis and disturbances in kidney function in CKD and CVD. Additionally, results of the project would allow to search and verification of new, predictive biomarkers supporting CKD diagnostics. The obtained information will help to build a model explaining the signaling pathways and molecular mechanisms of atherosclerosis in CKD.