Long-term elevated blood glucose level (diabetes or hyperglycaemia) lead to serious changes in the kidney, both in the blood vessels and in the tubules, impairing its function, which may lead to complete organ failure (diabetic nephropathy). Kidney dysfunction in *diabetes mellitus* (DM) may be a consequence of, among others, changes in production and activity of local (paracrine) factors e.g. adenosine (Ado, ATP metabolite of ATP), vascular endothelial growth factor (VEGF) or increased release of free radicals (oxidative stress). Moreover, in diabetes there are changes in the expression of Ado-dependent P1 purine receptors, which are involved in maintaining the tone of the renal vascular walls and in the processes of tubular transport. Several studies showed that in pathological conditions there is an increase in the expression of A2B receptors (P1R-A2B), but it has been shown that hyperglycemia can have a variety of effects, also in the opposite way, which can significantly influence the actual role of adenosine on the kidney blood circulation and excretion.

In the project we will use the established model of diabetes induced in primarily normoglycemic rats with streptozotocin, which corresponds to human type 1 diabetes. STZ, to which pancreatic beta cells are particularly sensitive, by causing their damage (DNA destruction), reduces insulin production, causing an increase in blood glucose level. When planning the project studies, we took into consideration the promising results of our preliminary studies in rats with experimentally induced *diabetes mellitus* during acute, short-term intra-renal infusion of an A2B agonist, regarding changes of intrarenal blood flow regulation and renal excretion. We postulate that the long-term application of an P1R-A2B agonist to the kidney of diabetic animals may protect the kidneys from deteriorating their function.

In our research we will use rats breeding with kinship avoidance, i.e. from a diverse population of animals, in which we can expect a response to the stimulus applied in a manner similar to that in the human population (normal distribution, according to the Gauss curve). In these animals, we will investigate the effect of chronic administration of the P1-A2B receptor agonist (a substance that stimulate receptor to action) released from electro-spun fibers, previously implanted on the kidney surface. Prior to implantation, we will prepare a microfiber bundle into which the test substance will be placed during spinning. During the project implementation, the following will be assessed:
(1) the basic metabolism of animals and the excretory function of their kidneys, and urinary excretion of oxidative stress factors and proteinuria (this will allow assessment of damage to the kidneys, especially of the glomeruli); studies in conscious animals;
(2) in animals under anesthesia, surgically prepared for the experiment, the systemic circulation and kidney functions will be assessed simultaneously: changes in the whole blood flow and changes in local blood supply (cortex, renal medulla) and excretion, as well as changes in the concentration of free radicals in the medulla and cortex *in situ* (suitable free radical selective sensors);
(3) the diameter and density of cortical blood vessels will be assessed in the same individuals before and after chronic administration of the agonist of P1R-A2B with a modern technique using *in vivo* confocal laser microscopy of the Cellvizio® Dual Band system;
(4) Using a combination of established techniques to measure changes in blood perfusion (blood flow) and the capabilities of the Cellvizio® Dual Band system, the reactivity (stiffness) of the kidney's blood vessels in response to vasoactive substances (vasoconstrictive or vasodilating) will be assessed.

Renal dysfunction, also that associated with intrarenal haemodynamic disturbances, is postulated to cause many pathological stages including hypertension. Long term exposure to hyperglycemia dramatically increases this risk. It can be expected that examining the role of P1R-A2B (they change in diabetes) will allow to extend the possibilities of treatment of diabetes and hypertension (civilization diseases). The planned research is an opportunity for a better understanding of the pathomechanism of diabetes and a better understanding of the role of P1-A2B receptors. The results obtained in this project will provide knowledge on the effectiveness of early nephroprotective treatment with the P1R-A2B agonist. The results obtained might provide a basis for preclinical research on the treatment of renal malfunction in patients with long term hyperglycemia associated with hypertension.