Nanoparticles (NPs) have been in the center of interest of nano(bio)technologies for the last two decades. In particular, titanium oxide (TiO_2), silver (Ag) and gold (Au) NPs due to their unique electronic, photonic, catalytic and therapeutic properties belong nowadays to the most commonly used nanomaterials. They are applied in cosmetic, paint, textile, food or pharmaceutical industries as well as in various medical fields. However, the vast range of these NPs used in our everyday life induces especially high exposure of humans to their action. They are mainly accumulated in the urban area (in atmosphere, hydrosphere, lithosphere and biosphere). Ultrafine NPs (< 100 nm) may easily infiltrate human body and accumulate in many organs. TiO_2, Ag and Au NPs, once ingested, inhaled, administered topically or injected, can reach the bloodstream and interact with red blood cells (RBCs = erythrocytes) through their span life. However, the knowledge of the degree to which RBCs are damaged due to their exposure to NPs is still limited. Recent epidemiological studies have shown a high correlation between exposure to these NPs and the incidence of life-threatening cardiovascular events. Only a few reports on erythrocyte rheological toxicity of TiO_2, Ag and Au NPs are available. These NPs have been found to cause hemolysis, deformability and aggregation of isolated RBCs and to alter microcirculation and proper oxygen delivery to tissues. NPs concentrations at which no hemolysis is observed are currently assumed as non-hazardous.

The influence of NPs on human health is a big concern. The action of NPs on erythrocytes may underlie many so-called diseases of civilization (e.g. circulatory diseases or type 2 diabetes) which are not related to the longevity or lifestyle. They appear at greater rates in young population living in the developed, more industrialized countries and the reasons for these cases are not recognized. Based on our preliminary studies we postulate that NPs interactions with RBCs could be responsible for acute development of primary hypertension in young people. This aspect has never been discussed in relation to risk related to NPs but calls for a systematic examination. Untreated hypertension may lead to risk factors for transient ischemic attack and stroke, so an increase of young people mortality. We found that TiO_2 NPs at concentrations much lower than those reported in the literature as nontoxic did not alter the shape of RBCs but they influenced the sodium and potassium ion transport through their membranes and disrupted the ability of hemoglobin to bind reversibly O_2. As far as we know these phenomena have not been studied before. We postulate that these phenomena, if present in vivo, are prone to cause hypoxemia which, in turn, by sympathetic activation, may further increase blood pressure in patients. Significance of this observation prompts us to expend our analysis to different types of nanoparticles, especially those that are already in common use, and to compare the effects that they have on RBCs from healthy individuals and patients with type 2 diabetes.

The aim of the studies is to establish a direct cellular and molecular impact of TiO_2, Ag and Au NPs, to which our environment is permanently exposed, on RBCs functioning. We are going to concentrate on ion transport through the cell membrane, stability of the membrane skeleton and hemoglobin oxygen affinity. In our investigations we will use TiO_2 NPs - white TYTANPOL pigment in the most hydrophilic phase, anatase (A-11) from the chemical plant in Police, Poland (the sixth biggest TiO_2 producer in Europe) and Ag and Au NPs provided by GoldenGevity Inc. (the USA) as a dietary supplement: Pure Colloidal Silver 4000 ppm and Pure Colloidal Gold 4000 ppm. The superfine size of these NPs with diameters of about 1nm ensure their easy penetration to erythrocytes.

To reach the goal we plan *in vitro* investigations of physicochemical properties of isolated RBCs treated with different concentrations of TiO_2, Ag or Au NPs at different time periods of incubation. We will exploit RBCs from healthy donors and patients with type 2 diabetes at the known stage of disease, distinguishing cases with and without hypertension. We plan to investigate RBCs from patients with type 2 diabetes because it has been proven that glucose can enhance NPs penetration into the cells and we want to check how the surface modifications of diabetic erythrocytes would affect the action of TiO_2, Ag and Au NPs. We will apply many complementary biochemical and biophysical techniques. We hope that the studies carried under this project will allow us to estimate upper limit of TiO_2, Ag and Au NPs concentrations which remain harmless for humans. Results will be very important for respective protective regulations on potential health risks of titanium oxide, silver and gold nanoparticles.