Heart is composed of two types of cells: cardiomyocytes and non-muscular cells such as endothelial cells or fibroblasts. Fibroblasts are the most numerous group and involved in synthesis of extracellular matrix (collagen, proteoglicans). Extracellular matrix of the connective tissue connects cardiomyocytes and allows them work as a pump. Moreover, the shape of the heart chambers is determined by the connective tissue and defines both mechanical and electrical function of heart. The fibroblasts and extracellular matrix may influence on electrical function as well as hypertrophy of cardiomyocytes. Moreover, the collagen accumulation influences on rigidity of the heart walls. Remodeling of heart leads to changes on macroscopic, microscopic and submicroscopic levels and is responsible for dilation of the heart chambers. The alterations of heart structure during remodeling process support hemodynamic disturbances and arrhythmias such as atrial fibrillation. Atrial fibrillation is the most frequent arrhythmia (0.9%) in population of Europe and the USA. Dilation of atria as well as fibrosis are the risk factors of atrial fibrillation. The concept of the submitted research project is focused on finding new mechanisms that would become the basis for pioneering therapies to stabilize the connective tissue in the heart. The obtained knowledge could be used for preparation of a new therapy responsible for inhibition of the atrial fibrosis and remodeling as well as prevention of their complications (atrial fibrillation). Development of a new method stabilizing the connective tissue in heart and inhibiting heart remodeling has been postulated. The matrix metalloproteinases and their inhibitors and renin angiotensin aldosterone system were recommended as the target for this therapy. Moreover, beneficial effect of some medicines (diuretics, betablockers) has been proved.

The purpose of the project is to answer the question whether the integrin α2β1 exerts regulatory effect on metabolism of the connective tissue in atrium. The integrin is involved in mechanotransduction. This process converts mechanical information into understandable for cells biochemical signal. Our preliminary experiments showed that the integrin α2β1 is expressed on fibroblasts isolated from the human atrium. Moreover, we proved that, this integrin is involved in regulation of collagen content in the cells and influences on cell number and proliferation.

The aims of the project are:

- elucidation whether the α2β1 integrin plays role in the collagen metabolism regulation in the atrial heart.
- testing the hypothesis whether the collagen binding integrin α2β1 is making the contribution toward the collagen metabolism through heart fibroblasts cultured on gels with different hardness. In this experiment we would like to refer to physical changes of atrial muscles observed during fibrosis or hypertrophy and possible impact of these parameters on the accumulation of collagen.

The expected results will explain whether the integrin α2β1 may participate in regulation of the collagen metabolism in the heart and whether this knowledge can be used for preparation of a new therapy aimed at stabilization of connective tissue and preventing heart remodeling.