Duchenne muscular dystrophy (DMD) is the most common inherited and incurable human muscle disorder caused by lack of dystrophin due to mutations in the gene encoding this protein. As dystrophin gene is located on the chromosome X the DMD sufferers are boys with the estimated prevalence of 1 per 3500-5000 live birth. Dystrophin deficiency is a cause of progressive muscle wasting, which appears at the onset and exacerbates with increased physical activity of a child and is eventually leading to severe disability and premature death. Dystrophin is present in different tissues, however life-threating symptoms of dystrophin deficiency come from a severe muscular dysfunction. Dystrophin-encoding gene (the largest gene in humans) contains seven promotor sequences thus its transcription may start in seven places. Three of them located close to the 3' terminus of the gene encode 427 kDa protein called full dystrophin. Remaining four promotor sequences are responsible for shorter variants of dystrophin synthesis. Their expression as in the case of full dystrophin-encoding gene is tissue specific. The role of shorter dystrophins is still elusive, but they cannot replace 427 kDa protein. This very large protein is synthesized in muscles, brain and Purkinje cells of the cerebellum. Dystrophin localizes to the cytoplasmic face of the sarcolemma and links a group of proteins known as the dystrophin-associated protein (DAP) complex with actin filaments and microtubules. These interactions provide a link between the cytoskeleton, DAP in the membrane of the muscle fibre and the extracellular matrix components bound by DAP, and have a role in mechanical strengthening of the sarcolemma. It stabilizes muscle fibres and prevents sarcolemma damage during the contractile activity. While disruption of this link contributes to the DMD pathology, additional pathogenic mechanisms have also been implicated. DAP serves as a molecular scaffold for many other proteins. Among them there are specific receptors for hormones and growth factors and proteins which are important for a proper cellular calcium homeostasis. Calcium cations play a crucial role in intracellular signaling in all mammalian cells, thus local regulation of their concentration within specific cell compartments is particularly important. De-regulation of calcium homeostasis at least partially explains extra muscular consequences of DMD, including mental retardation and endothelial complications. There is no causative treatment of DMD as it would need a replacement or repairing of mutated gene that is beyond our methodological possibilities. Therefore a symptomatic, supportive therapy gives a chance to improve quality of life of DMD sufferers. A development of efficient therapeutic approaches focused not only muscles but also on other organs affected by DMD should be preceded by understanding basic physiological, biochemical and molecular processes behind systemic complication of DMD. The vascular endothelium plays a crucial role in a regulation of smooth muscle relaxation, vasodilation and eventually regulation of blood flow, so a proper endothelial functioning is of high importance. Endothelial dysfunction which is featured by increased vascular permeability, impairment of NO-dependent function, pro-thrombotic and pro-inflammatory phenotype appears to be a common cause of most cardiovascular diseases. Experimental data available in the literature show that mutations in the dystrophin encoding gene affect endothelial cell function and result in impaired angiogenesis which may limit blood supply to the regenerating muscle. The latter has been considered as an important element of DMD pathophysiology. Endothelial control of the blood flow is to high extent dependent on the intracellular calcium signalling and regulated by factors which induce cellular calcium response. Endothelial cell, like other mammalian cells expresses a plethora of proteins which serve as molecular tools responsible for Ca^{2+} transport across membranes, its buffering, storage and sensing. Also mitochondria, which may transiently buffer cytosolic Ca^{2+}, regulate calcium-dependent processes and shape intracellular calcium signalling. This mitochondrial function is particularly important in endothelial cells as their energy metabolism covering cellular ATP demand is based on glycolysis; mitochondrial input in this matter is relatively small. Previously we showed several abnormalities concerning calcium signalling in mice-derived dystrophic myoblasts, which are mononuclear muscle cells not able to contract because of too early stage of their differentiation. In general, Ca^{2+} signals in these cells were substantially elevated. We found many changes in a spectrum of proteins directly engaged in the maintenance of calcium homeostasis. Furthermore, we also found similar pattern of changes in endothelial cells treated with various pathological stimuli. On a basis of these observations we hypothesize that DMD dependent effects in endothelial cells physiology that have been described in the literature are closely related to an aberrant Ca^{2+} signalling in these cells. We are convinced that an identification of DMD-evoked effects on calcium homeostasis in endothelial cells will shed new light on DMD as a systemic disease. We believe that all experiments which are planned in this project are valuable for fundamental research. However, a potential application of their results would be an additional value in the future. This project seems to be feasible and a risk of underachievement is low. We expect that obtained results will be worthy publishing in prestigious journals.