Stem cells have been identified in many tissues building adult organism. These cells are responsible for the tissue renewal and regeneration. The ones which reside within the skeletal muscles, so called satellite cells (SCs), are localized between muscle fibers and basal lamina, i.e. extracellular protein network. Under physiological conditions SCs remain quiescent what means that they do not divide. However, after injury they become activated and convert into rapidly proliferating myogenic precursor cells (MPCs), which then cease to divide and fuse with each other forming myotubes. Finally, they mature to form large, containing multiple nuclei, skeletal muscle fibers, i.e. myofibers, that are equipped with "protein apparatus" responsible for the contraction. Importantly, in order to be fully functional, muscle fibers have to be innervated, surrounded by basal lamina and extracellular matrix proteins, such as laminin, and to interact with microvasculature. Unfortunately, with aging or in consequence of disease, such as Duchenne's muscular dystrophy (DMD), the pool of SCs may become limited or even exhausted. As a result skeletal muscles lose their ability to regenerate and function properly. In worst case scenario, as it happens in DMD patients, such muscle dysfunction might be fatal. For this reason various therapies to support regeneration of malfunctioning skeletal muscles have been tested. Among therapeutic approaches are cell based ones, that involve endogenous cells as well as exogenous, i.e. transplanted ones, possessing ability to differentiate into MPCs, myotubes, and myofibers. Next, many protocols test different factors or biomaterials/scaffolds as potential tools supporting cells transplanted in order to improve muscle regeneration.

In our project, in order to achieve the best therapeutic results, we plan to combine the use of hydrogel functionalized with the synthetic peptides, i.e. fragments of SDF-1 and IL-4 with cell based therapies. We have chosen the hydrogels, since they have been shown in our previous studies to support the healing of wounded skin. We functionalized them with the active fragments of either SDF-1, which is the factor stimulating cell migration and homing to injured tissues or IL-4 which is the factor enhancing differentiation of MPCs. Our cells of choice are induced pluripotent stem cells (iPSCs) which are pluripotent, i.e. able to form any given cell type and tissue. Importantly, the protocols to stimulate myogenic differentiation of iPSCs are currently available, so we can generate MPCs for the current study. Thus, by combining these reagents, we aim to analyze their effect at the mouse skeletal muscle regeneration. We will follow the impact of hydrogel scaffolds at skeletal muscle resident cells, such as endothelium building blood vessels, fibroblasts synthesizing extracellular matrix, and also exogenous ones, i.e., MPCs generated either from human iPSCs or SCs and transplanted to injured mouse muscles. We will use two animal models of skeletal muscle injury and regeneration. We will study reaction of chemically injured skeletal muscles and also of those one affected by muscular dystrophy. To this point we will use *mdx* mice which are the model of patients suffering from DMD. Our study will involve variety of molecular, cellular, histological techniques as well as functional tests, altogether allowing to check the RNA and protein levels and localization as well as cell characteristic, tissue structure, functionality of skeletal muscles subjected to the transplantation of peptide functionalized hydrogels with or without MPCs. Our working hypothesis states that peptide hydrogels functionalized with SDF-1 or IL-4 fragments support both the skeletal muscle regeneration and also therapeutic potential of human MPCs to improve this process. If regeneration will be improved using our experimental protocols they could be used in the future to treat injured skeletal muscles, which lost their regenerative ability, and to support their healing and regaining of functionality.