P3.23
Therapeutic potential of murine mesenchymal stem cells (MSC) from different origins in the treatment of muscular dystrophy
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As no effective treatment options are still available for muscular dystrophies, cell therapy is a strong hope. Mouse models for these diseases are an important tool for testing putative therapies. Mesenchymal cells derived from bone marrow (bMSC) and from adipose tissue (aMSC) are multipotent and can lead to other tissues such as bone, cartilage, connective and muscle tissues, in vivo and in vitro.

The main objective of this study was to evaluate the therapeutic potential of MSC from different origins in the treatment of muscular dystrophy in murine models: mdx (dystrophin deficient), Lama2<sup>2<sub>4<sub>/</sub>J</sub> (laminin-α2 deficient) and Large<sup>myd</sup> (defect in glycosilation of α-DG).

We compared the results with injected normal mice to study the homing and behavior of these cells in non-dystrophic conditions. We isolated and characterized the bMSC and aMSC from eGFP mice by flow cytometry and by in vitro differentiation. Than, these cells were transplanted in the different strains by systemic injections repeated for 4 weeks.

We could find the cells in some of the treated animals, tracking the eGFP gene by PCR. We also were able to find the expression of eGFP protein in the muscle of some of the injected animals. The maintenance of the cells, however, was very variable among the treated animals, suggesting that the critical features to the success of the therapy remains unknown as individual variation. Comparative studies of the potential of different stem cells injected into different animal models are important to improve the effectiveness of stem cells in neuromuscular therapies. Financial support: FAPESP-CEPID, CNPq-INCT, FINEP, ABDIM.

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P3.24
Therapeutic potential of murine mesenchymal stem cells (MSC) from adipose tissue in the treatment of muscular dystrophy in the new double mutant mouse model for the genes Dystrophin and Large
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Mesenchymal stem cells derived from adipose tissue (aMSC) are multipotent and can lead to bone, cartilage and muscle cells, in vivo and in vitro. Therefore, they may be a relevant source of cells for therapies for muscle diseases, mainly using animal models. Among them, two well known models are the mdx mouse with deficiency of dystrophin but a mild phenotype, and the large<sup>myd</sup> mouse with defect of glycosylation and severe muscle weakness.

We recently generated in our lab a new dystrophic model, double mutant for dystrophin and large proteins. This mdx/large<sup>myd</sup> mouse presents a significant weakness and deficiency of dystrophin in the muscle being therefore a very good model for testing cell therapies. The injected cells can be tracked both through DNA analysis for the wild allele of the large gene, as well as through the study of the presence of normal dystrophin protein in the muscle. Additionally, functional evaluation can show possible clinical benefit. We performed the transplantation of normal murine adipose MSC, previously characterized, in this double mutant by systemic injections in the caudal vein, repeated for 3 weeks. In the fourth week, the animals were sacrificed, a necropsy was done, and several muscles and tissues were studied.

The DNA of the injected cells was found in heart, stomach, quadriceps and diaphragm of the injected animals, suggesting that these cells were properly engrafted to the muscles. Furthermore, we were able to identify the presence of traces of dystrophin in some of the muscles studied suggesting the ability of adipose derived mesenchymal stem cells to differentiate into muscle. However, additional studies are necessary to improve the amount of expressed muscle proteins leading to a better therapeutic effect. Financial support: FAPESP-CEPID, CNPq-INCT, FINEP, ABDIM.