CYTOSKELETAL DYNAMICS IS ALTERED IN THE GROWTH CONES OF DORSAL ROOT GANGLIA NEURONS FROM THE FRIEDREICH ATAXIA YG8R MOUSE

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INTRODUCTION: Friedreich´s Ataxia is an autosomal recessive disorder that affects children and young adults. In most cases, an homozygous GAA trinucleotide expansion causes a deficiency in frataxin, a mitochondrial protein encoded by the nuclear genome. Low frataxin levels lead to changes in mitochondrial and cellular physiology manifested in dysfunction of mitochondrial energy metabolism and oxidative stress in the cell [1]. Some reports suggest that reduced frataxin in fibroblasts and neuronal tissues from FRDA patients results in cytoskeleton anomalies [2]. Here, we report the results of the study of the neurodegeneration in adult sensory neurons of the Friedreich´s Ataxia YG8R mouse model through analysis of the stability of the cytoskeleton. This analysis was focused on the study of axonal growth in frataxin deficient neurons, specifically in the axonal growth cone, and its relationship with the cytoskeleton. Dorsal root ganglion neurons from YG8R mice model (DRG-YG8R neurons) exhibit altered number of growth cones, shorter neurites and abnormal growth cone morphology. In addition, we can see alterations in the actin dynamics.

MATERIAL AND RESULTS: Material used for this study included DRG neuron culture of the Friedreich´s Ataxia YG8R and C57BL/6J (wild type) mice. We performed confocal microscopy studies of immunofluorescence in growth cones of DRG neurons from wild type and YG8R mice. Coverslips were mounted and examined on a *Leica SP8 confocal microscope* at room temperature using a 40x or 63x objective. Images and stacks were processed and quantified using LAS AF Lite version 2.x (Leica).

CONCLUSIONS

- The number and length of neurites in mouse YG8R is decreased significantly. This affects directly the functionality of the growth cones.
- The increase of retracted or collapsed growth cones in YG8R mice implies that morphology of growth cones of mice sensory neurons YG8R is slightly altered.
- There is an increase in F-actin expression in growth cones of DRG-YG8R neurons and that correlates with a reorganization of the actin cytoskeleton and with growth cone morphology changes.

These results suggest that the neurodegenerative process of Friedreich ataxia may be associated with alteration of the cytoskeleton, especially with the dynamics of growth cone.