ER stress in mice prefrontal cortex pyramidal neurons in peripheral tumor growth

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INTRODUCTION

Endoplasmic reticulum (ER) plays an important role in the synthesis, processing and transport of many proteins, the biosynthesis of membrane lipids, the regulation of carbohydrate metabolism, the maintenance of calcium homeostasis and other important cellular processes. Under pathological conditions leading to oxidative stress, including oncology, protein folding is disrupted and ER stress is triggered.

Purpose: to investigate the structure of endoplasmic reticulum of prefrontal cortex pyramidal neurons under conditions of peripheral tumor growth.

Materials and methods

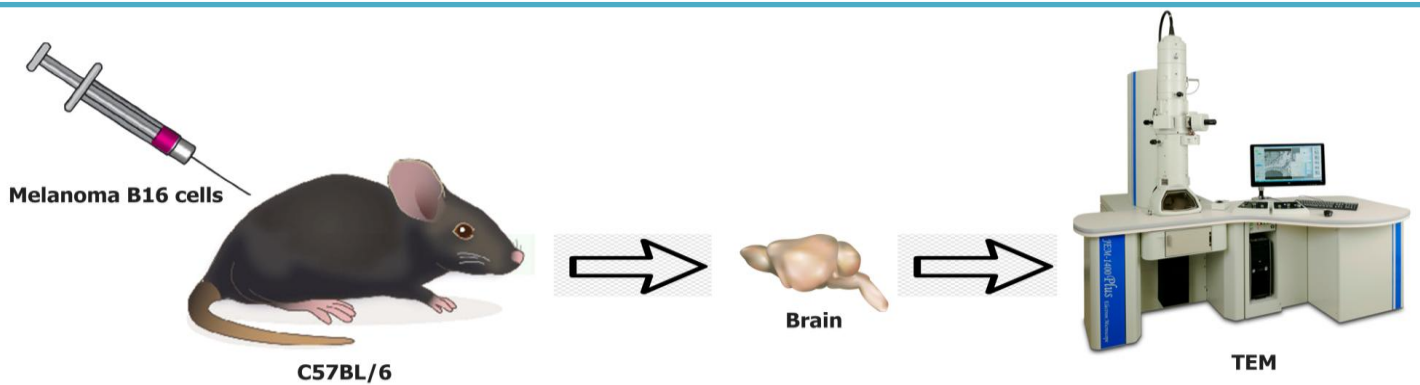
For tumor induction, cultured B16 cells were subcutaneously injected into the right inguinal area of mice. The material was sampled at 7 days.

• Transmission electron microscopy was used to examine the ultrastructural organization of prefrontal cortex pyramidal neurons in brain of C57BL/6 male mice from two groups: a tumor growth model and an intact control. Ultrathin sections thick 70–100 nm were studied using an electron microscope JEM 1400 (Japan). The microscopy was conducted at the Joint Access Center for Microscopy of Biological Objects with the Siberian Branch of the Russian Academy of Sciences.

• Morphometry was performed using Image J software (Wayne Rasband, USA) with an opened test system at x30K magnification.

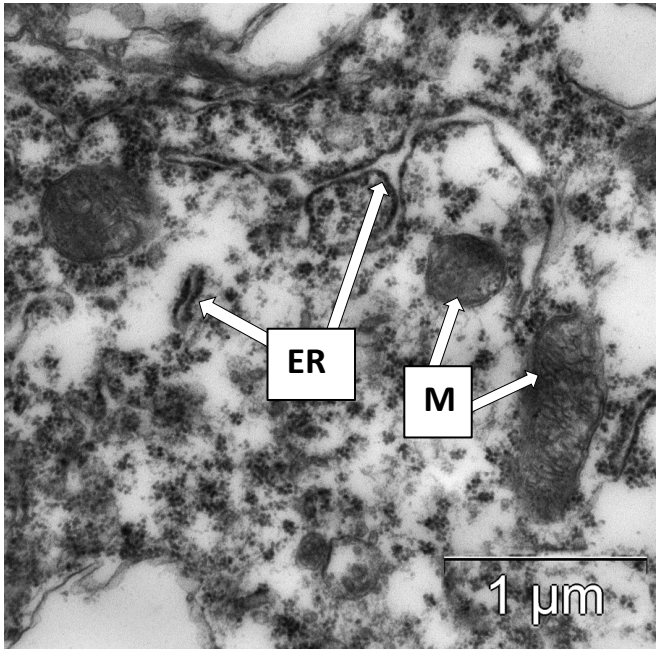
• The mean (M) and standard deviation (SD) were calculated using Microsoft Excel software.

• The significance of differences between the parameters was determined by Statistica 6.0 software (StatSoft, Inc.) with Mann-Whitney U-test. The differences were considered significant at $p<0.05$.

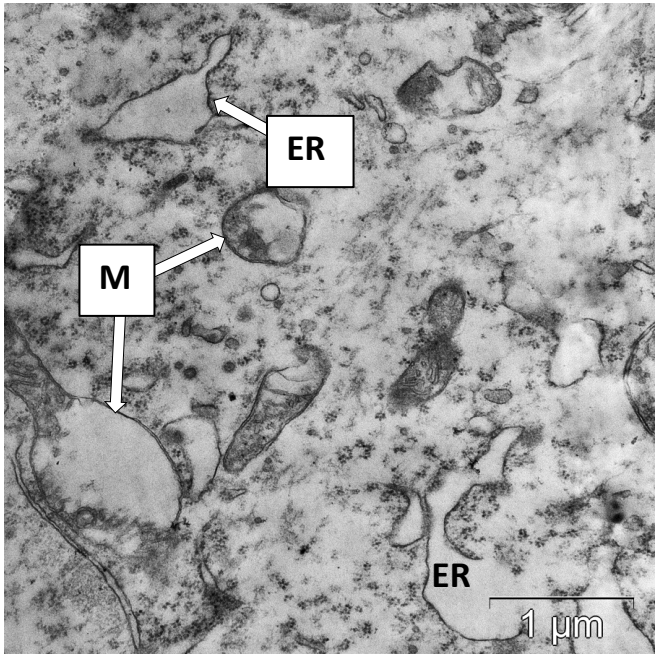


Results

Intact control



Tumor growth model

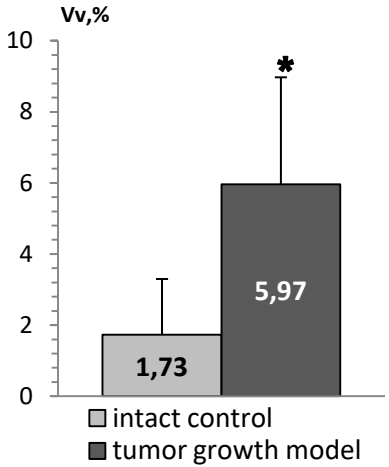


During the study, in the group in tumor growth model, there was an expansion of the ER cisterns and tubules, as well as mitochondria with destructive changes in the cristae.

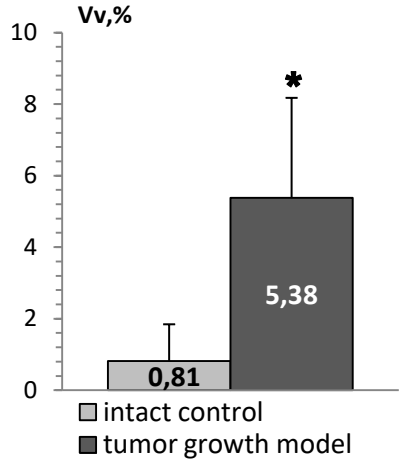
ER – endoplasmic reticulum; M – mitochondria

Results

ER with widening of its cisterns and tubules



Mitochondria with destructive changes of cristae



*p<0.05

Morphometric analysis of neurons in animals with a tumor revealed a significant increase in the volume density of the ER with widening of its cisterns and tubules (V_V=5.97%), which is a structural sign of ER stress. In addition, in the neurons of animals with a tumor, a high level of volume density of mitochondria with destructive changes of cristae was noted (V_V=5.38%), this is 46.6% of the total number of mitochondria.

Conclusions

The data obtained indicate an increase in ER stress in peripheral tumor growth conditions. Further study of the structural features of pyramidal neurons will contribute to a more detailed understanding of the effect of peripheral tumor growth on them and will also help to identify signaling pathways and targets for therapeutic use.