

## ***ABSTRACT***

**BACKGROUND** Pre-gestational endurance training (PGET) with chronic, moderate-intensity is promising method to prevent preeclampsia by improving epithelial-to-mesenchymal transition (EMT) of trophoblasts.

**PURPOSE** The main objective of this study was to demonstrate the effect of PGET on  $\alpha 5$ - and  $\alpha 6$ -integrin expressions as EMT markers of trophoblasts at the end of first week gestation in mice.

**METHODS** Five-to-six weeks old female BALB/c mice ( $n=32$ ) were randomly allocated to PGET ( $n=16$ ) and control ( $n=16$ ) group. In PGET group, mice swam with moderate intensity for 30-minute-limited duration each day in 28 days. Gravid uterus were randomly obtained from six mice each group at the seventh day gestation or embryonic day 7 (E7). The tissue sections were analyzed via immunohistochemistry either for  $\alpha 5$ - or  $\alpha 6$ -integrin expressions at mesometrial region.

**RESULT** In the PGET group, either the count of  $\alpha 5$ -integrin immunostained nuclei cells ( $\alpha 6$ -integrin cytотrophoblasts [CTBs] in human), or the count of  $\alpha 6$ -integrin ones ( $\alpha 5$ -integrin extravillous trophoblasts [EVTs] in human), were significantly lower than control group ( $p<0,01$ ). Higher spatial difference of  $\alpha 6:\alpha 5$  expression ratio in the PGET group compared to control group was demonstrated ( $p=0.014$ ).

**CONCLUSION** The PGET induced more distinguished EMT by changing integrins repertoire of trophoblasts. Meanwhile, smaller gravid uterus indicated by lower overall cell counts in placenta region compared to control group could give relatively less hypoxic condition in the rest of gestation as well as potentially inducing intrauterine fetal growth restriction.

**KEYWORDS** Mice, physical endurance, exercise therapy, integrins, epithelial-mesenchymal transition