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The influence of different temperature IVF conditions on development destabilization of CD1 mice

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Motivation and Aim: The organism development program is determined by the coordinated expression of genes. In multicellular bilateral organisms it is expected that the gene expression in the left/right structures of the body will be symmetrical. However, all stages of the implementation of genetic information are subject to stochastic fluctuations. These stochastic fluctuations may generate fluctuating asymmetry (FA), which can indicate developmental destabilization. Traditionally, this FA can be evaluated on the basis of morphometric measurements of bilateral structures. We proposed to use the evaluation of FA in bilateral structures at the molecular level – at the level of gene expression.

The FA of gene expression in the organism's bilateral structures in a variable environment remains an area of active research. The establishment of the gene expression pattern, including FA, may depend on many environmental factors during early development, including temperature. The temperature can influence the gene expression pattern via epigenetic changes soon after fertilization. This epigenetic modification might be important for the establishment of gene expression patterns in bilateral structures of the organism, which create the FA in adult phenotypes.

The aim of our work is to investigate the effects of different IVF temperature conditions on developmental destabilization (the forming of gene expression patterns, which affect the gene expression FA in bilateral structures) by analyzing the FA gene expression in left\right bilateral organs of adult mice.

Methods and Algorithms: The mice zygotes were subjected to two different developmental temperatures, 35 °C and 37 °C, in the first 24 h after *in vitro* fertilization with subsequent transfer to the recipient female. For the control group, we used *in vivo* fertilization with subsequent transfer to the recipient female. The temperature influence on FA gene expression was studied in 36-week-old adult mice by the RT-PCR method. The 11 – gene "diagnostic set" was used for expression in left\right forelimbs. The data was analyzed via traditional calculation of asymmetry coefficient (K_{FA} =|L-R|\|L+R|) and by an analytical algorithm based on the decomposition of dispersions by the method of principal components (PCA). To study the development destabilization of adult mice we analyzed the FA indicators of gene expression and correlated them with the body weight of mice in aged 3, 8, 18, and 24 weeks.

Results: The weight of mice depends significantly on the IVF temperature conditions and on the age of the mice. The body mass of mice in aged 3, 8, and 18 weeks in the 37 °C group differs from that in the 35 °C group. Also, it was different from the mass of mice in the control group aged 8 weeks.

The levels of FA gene expression are different in the 35 °C and the 37 °C IVF temperature and control groups. The traditional coefficient of symmetry K_{FA} in mice in the 37 °C group was significantly different from that of the mice from the control group. The quantitative estimation of gene expression of 11 genes in the left/right forelimbs of the males by real time PCR and following PCA decomposition demonstrated the left\right forepaw patterns' different gene expression in experimental 35 °C and 37 °C IVF conditions and in control groups.

Conclusion: We propose that the temperature conditions of the period before implantation play a significant role in development, contributing to the fitness of the adult offspring.

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