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The gene expression fluctuation asymmetry as an indicator of development instability in different MHC compatibility models of mother-fetus interactions in mouse strains

Babochkina T.I.*, Gerlinskaya L.A., Anisimova M.V., Kontsevaya G.V., Feofanova N.A., Stanova A.K., Orbant M.O., Moshkin M.P., Moshkin Y.M.
Institute of Cytology and Genetics, SB RAS, Novosibirsk, Russia
** babochkinat@yahoo.com*

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Motivation and Aim: Development destabilization can be indicated by fluctuating asymmetry (FA) of bilateral traits [2, 4].
At the same time, similarity or difference between the mother and the fetus with respect to major histocompatibility complex (MHC) genes play key role in development [1, 3].
The aim of our work is to study the effect of the similarity/difference of the MHC genes of the mother and fetus on the destabilization of prenatal development on models of different MHC gene combinations between mother and fetus organisms which presented the different variants of immunogenetic dialogue between the mother and fetuses. As an indicator of development instability, we used the gene expression FA in bilateral structures of the fetus.
Methods and Algorithms: To model different variants of the MHC compatibility, we transferred two-cell embryos of the C57BL/6J inbred strain to surrogate mothers of either the same or different haplotype for MHC genes. This allowed us to model three variants of mother–fetus immunogenetic dialogue: 1) bidirectional immunogenetic dialogue between C57BL/6J embryos of H2b MHC haplotype and BALB/c surrogate mothers of a distinct H2d MHC haplotype; 2) unidirectional immunogenetic dialogue between C57BL/6J embryos and immunodeficient NOD SCID surrogate mothers of H2g7 MHC haplotype; and 3) reduced immunogenetic dialogue between same genotype C57BL/6J mother and fetuses.
We utilized the FA analysis of gene expression and PLGF, VEGF concentration and fetoplacental indexes and body weight of the embryos as indicators of development destabilization.
For gene expression FA analysis, an analytical algorithm was developed based on the decomposition of dispersions by the method of principal components (PCA).
Results: It was found that the highest level of FA occurred during intra line transplantations, that is in the absence of an immunogenetic dialogue between the fetus and mother, and the least when transferring C57BL/6J embryos to BALB/c mothers, that is full-fledged dialogue in the mother-fetus system. The transfer of allogeneic embryos to immunodeficient mothers (C57BL/6J in NodScid) gave an intermediate result.
At the same time, intra-individual gene expression FA variations as an indicator negatively correlated with the body weight of the embryos and the content of the Placental Growth Factor (PlGF) in the placenta.
The second important result is that the body mass of fetuses and the level of PLGF were negatively correlated to the values of the expression development noise.

Conclusion: The same inbred mouse strain carried by surrogate mothers (syngeneic pregnancies) with the same MHC haplotypes (histo-MHC-compatible pregnancies) demonstrated higher internal expression noise. On the contrary, the different inbred mouse strain carried by surrogate mothers (allogeneic pregnancies) with distinct MHC haplotypes demonstrated the lower internal expression noise and an advantage in the conditions of early embryo development. And the individual variations in internal genetic noise correlated with indicators reflecting the growth of embryos (body mass of fetus) and the functioning of the fetal-placental complex (PLGF concentration).
Thus, the gene expression FA in the bilateral structure of the fetus associated with developmental conditions depends significantly on MHC compatibility between fetus and surrogate mothers.
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