Baranov V S Yarmolinskaya M I, Asian J Biomed Pharmaceut Sci 2018, Volume 8 | DOI: 10.4066/2249-622X-C3-008

DEVELOPMENTAL GENETICS OF ENDOMETRIOSIS

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Over 100 years the problem of endometriosis (EM) a common disabilitating female disease remains very urgent with no efficient prevention, prediction or treatment known so far. For many decades EM was in the focus of complex studies in our institute. The report highlights major advances in molecular genetic studies of endometriosis, its pathogenomics, as well as some recent hypothesis in this area. Spectacular progress in this area could be attributed to the systems genetic view of EM which implies identification of many (over 100) EM genes, analysis of their functional allelic variants, comparative gene expression studies in euthopic and ectopic endometrium, gene interactions within relevant (about 30) metabolic pathways, as well as complex epigenetic damages due to abnormal methylation pattern and miRNA deregulation. Endometrial stem cells (eSC) which reside in the borderline of endometrium and myometrium I within junction layer (eSC niche), or mesenchymal stem cells - the products of epithelial/mesenchymal cells transition (EMT) was shown play a major role in the origin of endometriosis. Also, the peculiarities of personal genetic background, unique "epigenetic landscape" of genetically and epigenetically predisposed to EM stem cells underlie the origin of pathological process which soon becomes canalized and irreversible and proceeds to final clinical manifestation. Novel data on the molecular, genetic and epigenetic mechanisms governing EM suggests the existence of endometriosis development genetic program (EMDP) mitigated with at least three tentative r sensitive periods (SP). The origin of genetically or epigenetically modified stem cells potentially destined to give rise to endometriosis (SP1), endometrial epithelium cells transition (metaplasia) into mesenchymal SCs through EMT) (SP2), and their invasion into peritoneum with subsequent progression into endometriotic lesions (SP3). Feasible origin of EM from the embryonic stem cells disseminated throughout the pelvic lining during female urogenital system embryogenesis should not be considered as well. Complex genomic and epigenetic interactions at different stages of EMs progression result in different forms of the disease, with their specific traits and clinical manifestations. The EMDP and especially its highly vulnerable sensitive periods might be of major significance in elaboration a new strategy of EM prediction, prevention, and treatment.

Note:

BIOGRAPHY

Baranov V S Yarmolinskaya M I Born in 1940, graduated from the State Medical Institute in Lvov (Ukraina), took postgraduate courses and received a PhD degree in Saint-Petersburg (Russia) in 1976 . The Chief of laboratory for prenatal diagnosis of inherited and inborn diseases at the Ott's Institute of Obstetrics, Gynecology & Reproduction. Interested in genetic and cytogenetic aspects of early development, gene testing of inherited predisposition to common disorders , personalized predictive medicine, gene therapy. Professor, Corresponding Member of Russian Academy of Sciences, Honorary Scientist, Chief City Expert in Medical Genetics, , The author and co-author of 29 books and over 400 scientific papers.

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