IMPACT OF GENOME DUPLICATIONS ON MULTIPOTENCY SIGNALING ACTIVITY IN MAMMALIAN CELLS

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Polyploidy, that is also known as genome duplication, creates selective advantages for various species and individual somatic cells under normal conditions and transformation. One possible reason for this phenomenon may be an increase in biological plasticity due to the activation of developmental programs. To promote understanding of the nature of this relationship, we investigated the effect of genome duplications on the activity of signaling pathways related to early development. For this propose we analyzed the activity of the molecular pathways of the BioSystems data base related to the regulation of multi- and pluripotency in homologous organs of humans and mouse with different degrees of polyploidization. Using method of pairwise cross-species transcriptome comparison, we investigated the difference of pathway activity in the human heart — mouse heart and mouse liver — human liver. The obtained results revealed the highly significant induction of different branches of the WNT embryonic pathway and the synergistically regulated pathways of Hippo, NOTCH, TGFb, PI3K and Hedgehog signaling, which was associated with polyploidization. The analysis of protein interaction network for genes implicated in the induced pathways confirmed the results of functional gene module analysis and discovered a close connection between the WNT network (receiving the signals from the cell surface) and the activation of proteasome genes, that points to the attractor (stable state) of the proteome when these multipotency pathways are activated in polyploid cells. Thus, our data indicated that polyploidy, associated with embryonalization and coordinated induction of the main multipotency pathways in response to changes in environmental conditions, is ensured by the stability of the proteome homeostasis of the cell. The obtained data explain one of the important reasons for the selective advantage created by genomic duplications, which can be used in the development of new antitumor therapy approaches.

K e y w o r d s: polyploidy, selective advantages, transcriptome analysis, embryonalization, multipotency