in various pathologies where all three mechanisms mentioned above do not happen simultaneously. For example, it's established that: during alimentary dyslipidemia, mechanism of regeneration depends on the duration of hepatogenic diet uses and quality of the damage. In cholestatic liver of rat, at initial stage regeneration is only occurs by polyploidization without increasing of cells quantity. In response to trauma, increase of ploidy is also described in different mammalians tissues (heart, liver, and cornea). Based on the above, in some pathologies liver regeneration is achieved by the quantitative increase of ploidy cells, however, it is not known which signaling pathways activation/inactivation provide their appearance in each particular case. Our previous results show that inhibition of HGF receptor (C-Met) doesn't cause the changes of polyploidization of cholestatic liver. ERK 1/2 is involved in HGF activated pathway where MEK 1 and MEK 2 are the key molecules, which can be also activated by avoiding of main receptor - C-Met. The aim of the research is the determination of role of ERK 1/2 signaling pathways in the process of hepatocytes polyplodization in cholestatic liver model. Materials and methods. Experiments were carried out on adult white rats (130-150g). Model of cholestatic liver with common bile duct ligation was used. Animals were divided into three groups: I-control intact animals, II –cholestatic animals (2nd day), III-cholestatic animals with MEK 1/2 (PD98059) inhibitor injection (10mg/kg). Nuclear DNA content was detected by using of computer software ImageJ 1.36b. Determination of colchicine mitotic index was used for assessment of proliferative activity. Results. Hepatocytes mitotic activity significantly increases on the 2nd day from common bile duct ligation in the II group. In addition, the number of diploid (2c) hepatocytes decreases and the polyploid (2c×2, 4c, 4c×2, 8c) cells are increased. In the III group of animals, the number of tetrapoloid cells (4c) has tendency to decreased, while octaploid (8c) and binuclear octoploid (4c×2) cells are not present, which is evidence for suppression of polyploidization. With regard to proliferative activity, there is no difference between the animals from II and III group. Conclusions. Inhibition of formation of high-ploidy (octaploid) cells by blocking of MEK 1/2 proteins indicates that ERK 1/2 signaling pathway is one of the necessary conditions for polyploidization of hepatocytes.

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K-3. Molecular evolution of the histone variant H2A.Z

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Histone variants contribute to the organization of chromatin structures and regulation of genome functions through their deposition into nucleosome. Histone variant H2A.Z, one of the H2A variants, is evolutionarily con-

served. H2A.Z is deposited into nucleosome as H2B-H2A.Z histone heterodimer, and this deposition is mediated by an ATP-dependent chromatin-remodeling complex termed SWR1 in budding yeast and SRCAP in vertebrates. The deposition of H2A.Z regulates transcription, DNA damage repair, and chromosome segregation. While the presence of H2A.Z is conserved among eukaryotes, its functions in eukaryotes have not been analyzed. To approach the molecular evolution of H2A.Z, we firstly expressed vertebrate H2A.Z (vH2A.Z) in yeast H2A.Z (yH2AZ) deletant. However, vH2A.Z was not deposited into yeast nucleosome and did not rescue phenotypic defects in the yH2A.Z deletant. When yH2A.Z and vH2A.Z structure are compared, they are very similar in the sequence recognized by SWR1 and SRCAP. On the other hand, the sequence interacting with H2B histone is not conserved between them. This observation raises a possibility that the intermolecular interaction mode between H2A.Z and H2B, which is required for the deposition of H2A.Z into nucleosome, is not conserved between yH2A.Z and vH2A.Z. To test this hypothesis, we expressed a vH2B-vH2A.Z fusion histone in the yH2A.Z deletant. This vertebrate fusion histone was successfully deposited into yeast nucleosome in a SWR1 complex-dependent manner, and it partly complemented phenotypic defects in the yH2A.Z deletant. This observation suggests that the deposition machinery and functions of yH2A.Z and vH2A.Z are evolutionarily conserved. We expect that the vH2B-vH2A.Z fusion histone contributes to further analysis of epigenetic regulation by H2A.Z and its evolutionary conservation.

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K-4. UVA irradiation strengthened an interaction between UBF1/2 proteins and H4K20 di-/tri-methylation

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Repair of ribosomal DNA (rDNA) is a very important nuclear process due to the most active transcription of ribosomal genes. Proper repair of rDNA is required for physiological biogenesis of ribosomes. Here, we analyzed the epigenetics of the DNA damage response in a nucleolar compartment, thus in the ribosomal genes studied in nonirradiated and UVA-irradiated mouse embryonic fibroblasts (MEFs). Using advanced microscopic techniques, we analyzed the distribution pattern and interactions of transcription factors UBF1/2 and histone modifications H3K9me3, H4K20me2 and H4K20me3. Interactions of these proteins were confirmed by co-immunoprecipitation. Furthermore, we used ChIP-PCR analysis to examine an abundance of UBF1/2, H3K9me3, H4K20me2 and H4K20me3 at the rDNA promotor and rDNA encoding 28S rRNA. We found that the promoter of ribosomal genes is not abundant on H4K20me2, but it is densely occupied by H4K20me3. Ribosomal genes, regulated via UBF1/2 proteins, were characterized by an interaction between UBF1/2 and H4K20me2/me3. This interaction was strengthened by UVA irradiation that additionally causes