initiation zones. Our data verify the previously proposed model of the spatio-temporal organization of replication in Drosophila chromosomes (Kolesnikova *et al.*, 2018) and indicate that the multi-stranded nature of PCh provides a unique opportunity to visualize in one chromosome the stochastic initiation of replication in some regions of the chromosomes, as well as the effective initiation of replication in other sites.

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Workshop IV Nuclear organization in disease

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Polyploidy reprograms regulatory pathways towards unicellular mode: the role in stress response, drug resistance, growth and cancer

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Polyploidy (PLD) is a common event in development and aging [1]. Also, it may be induced by physiological and pathological stresses [2]. Currently, PLD attracts much attention because of its links to regeneration, tumor initiation and drug resistance [3-5]. Aim: To understand the evolutionary nature of these links, we investigated the effects of PLD on transcriptome in homologous human and mouse tissues differed by PLD (heart, liver and placenta). Methods: The methods of bioinformatic data analysis and analysis of principal components (PCA), cross-species transcriptome comparison (TC), phylostratigraphy, protein interaction network (PIN) and gene module investigation were used. Results: We show that polyploidy exerts common effects on various cell types. The main PLD-related effects were the up-regulation of gene modules and PIN clusters increasing adaptation and transformation, including oncogene signaling, growth, development, drug metabolism, adaptation to stress and hypoxia and epithelial to mesenchymal transition. PLD-inhibited gene modules were involved mainly in differentiation and immunity. To find out whether PLD activates molecular programs of unicellular organisms that can trigger cancer, we applied the method of phylostratigraphy. The analysis revealed the enrichment of PLD-induced genes with genes from evolutionary ancient phylostrates (from procaryota, eucaryota, and opistokontha). In particular, these genes were implicated in drug resistance and ABC transporters. Accordingly, PLD-inhibited genes were

enriched in evolutionary young phylostrates (bilateria, chordata, amniota and mammalia). These genes participated mostly in immunity, multicellular organism processes and differentiation. Conclusion: PLD causes de-speciation by restructuring transcription towards the up-regulation of the early phylogenetic unicellular strates (cellular organisms to opistokonta) and down-regulation of the multicellularian complexity strates from (bilateralia to mammalia) indicating together with literature data concerning cancer [1, 2, 3] that cancer-induced phylogenetic shift is associated with polyploidy component.

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Pericentromeric tandem DNA transcription in malignant cells and tumour microenvironment in mice NSLC model.

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In higher primates, only about 1-5 % of DNA is made up of protein-coding genes; the other 99 % is noncoding. Most of the genome consists of repetitive DNA elements, dispersed and tandem repeats. Tandem repeats (TR, satellite DNA) are located mainly in the centromere and pericentromeric regions of the chromosomes and are the DNA component of constitutive heterochromatin. In some tumours, the TR DNA decondenses and goes into a transcriptionally active state. However, it is not clear yet, what are the cells of the tumour (the stroma, malignant cells) where transcription occurs. The aim of the work was to study the transcription of TR DNA in K-rasG12D –induced carcinogenesis in mouse lung. Methods. Cancer cells and cancer-associated macrophages and fibroblasts were obtained from non-small-cell lung carcinoma (NSLC) of K-rasG12D mice. Transcription of mouse pericentromeric TR DNA (major satellite, MaSat) was analysed by qPCR, RNA-DNA FISH, immunohistochemistry methods. Results. The level of long non-coding MaSat (lncRNA) RNA in a tumour was lower than in the adjacent tissue and normal lung tissue of a healthy mouse. In the culture of NSLC epithelial tumour cells, the content of MaSat lncRNA was lower than in cancer-associated mouse fibroblasts (CAF). An increase in MaSat transcription in NSLC tumour cells occured only when apoptosis was induced by a cytotoxic drugs cisplatin, or after heat exposure. In the tumour microenvironment, the transcription was increased only in CAF but not in cancer-associated macrophages. The increase of MaSat transcription was shown both in histological specimens and in cell cultures, where CAF phenotype was induced either by co-cultivation with cancer cells or by TGFb treatment. The MaSat transcription was acoompanied with the appearance of markers of a CAF phenotype, including markers of cellular senescence. Transcripts were detected only in