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DNA demethylation can occur by oxidation or deamination of mCyt, catalyzed by TET dioxygenases and AID/APOBEC deaminases respectively followed by base excision DNA repair. On the other hand, in plants mCyt can be directly removed by specialized bifunctional DNA glycosylases DEMETER and REPRESSOR OF SILENCING 1 (ROS1). However, the exact functions and substrate specificity of these plant DNA glycosylases remain unknown. Furthermore, ROS1 and DEMETER is a potential instrument for epigenome editing. In this study, we cloned and purified a catalytically active fragment of ROS1 from *Nicotiana tabacum*. ROS1 activity was investigated on substrates with a CpG dinucleotide, in which cytosine was methylated, hemimethylated or hydroxymethylated. Besides, we transfected HEK293 cell line by a plasmid coding for wild-type *ROS1* or D1445N to detect of mCyt level variation. It was shown that ROS1 possessed an enzymatic activity to remove hmCyt and mCyt residues from DNA substrates. Moreover, substrates containing mCyt were digested more efficiently then substrates containing hmCyt in both CpG sites with only one modified strand and with fully modified site. ROS1 was expressed in human cells and caused global DNA demethylation. The results obtained in the investigation suggest that plant ROS1 DNA glycosylase can contribute to change of mCyt level in human DNA and can be used as tool for quick and specific epigenome editing.

P-10-003
CMGE complex influences the stability of repetitive DNA sequences in yeast cells

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For years studies of the mechanisms providing high fidelity of DNA replication has been focused mainly on determining the influence of catalytic elements of the replisome. However, recent results show that also noncatalytic proteins could play an important role in maintaining genome stability. One of such elements is the GINS complex -a component of the CMG helicase (Cdc45-Mcm2-7-GINS). GINS is composed of 4 essential subunits: Psf1, Psf2, Psf3, Sld5 and interacts with many replication proteins, including a major DNA replicase- polymerase epsilon. Previously we showed that strains possessing mutated forms of Psf1 subunit exhibit mutator phenotype for base substitution and frameshift mutations. We are interested whether the proper functioning of GINS might be crucial for genome stability, particularly the stability of repetitive DNA sequences. We tested the stability of mono-, di-, tri-nucleotide, and other repetitive sequences in yeast strains carrying the *psf1-1* mutator allele (kindly provided by H. Araki). The Psf1-1 destabilizes interactions within the GINS complex, what may influence the stability of the whole CMGE complex as well as its interactions with DNA polymerase epsilon or DNA. Using 2 different assays, we investigated the mechanism and measured the instability of repetitive tracts in *psf1-1* mutant strains. The obtained data showed that impaired GINS leads to high instability of mono-, di-, tri-nucleotide, and other repetitive tracts. Our current results enhanced our knowledge about the role of the CMGE in the proper functioning of the replication apparatus and its role in ensuring microsatellite stability. These findings are particularly important in the context of a recent report on severe genetic disorders caused by mutations in human homolog of PSF1 gene. This work was supported by the National Science Centre Grant 2015/17/B/NZ1/00850 "Contribution of DNA polymerase delta in the leading strand replication in *Saccharomyces cerevisiae* cells".

P-10-004
Mechanistic insights on the DNA methylation by DNMT3a mutants observed in AML patients

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DNA methylation is an epigenetic modification essential for regulation of cell processes such as chromatin condensation, transcription, gene imprinting and cell differentiation. In mammals, DNA methylation at CpG sites is established by cytosine-C5 DNA methyltransferases (MTases) which form specific DNA methylation patterns. During malignant diseases progression, different multiple changes both in DNA methylation patterns and in MTase genes were observed. Human *de novo* MTase DNMT3A is most frequently mutated in acute myeloid leukemia (AML) with striking prevalence of R882H mutation. R882H has been extensively studied and its potential carcinogenic effect has been suggested. Here, we investigate the role of the other missense mutations in DNMT3A catalytic domain found in AML (S714C, R635W, R736H, R771L, P777R, and F752V) using accordingly mutated murine Dnmt3a catalytic domain and short CpG-containing DNA substrates as model system. The 3-5-fold decrease of initial methylation rates was observed for R181L (R771L), S124C (S714C) and P187R (P777R) with conserved ability to bind DNA. In the case of F152V (F752V), R45W (R635W) and R146H (R736H) a complete loss of the methylation activity was observed accompanied with the loss of DNA binding for R45W and R146H. Strikingly, all the mutations except S124C (S714C) are not located in the DNMT3A catalytic loop. The importance of these amino acids for the proper DNMT3A inner contacts formation was suggested. The ability of the DNMT3A partner protein DNMT3L to restore the methylation activities of S124C (S714C) and R181L (R771L) was revealed. The role of aberrant DNMT3a activity in AML was discussed on the basis of our knowledge of how these mutations affect methylation function and via the computer modelling. This work was supported by the RFBR grant 19-04-00533. *The authors marked with an asterisk equally contributed to the work.

P-10-005
Effects of single-nucleotide polymorphisms in human NEIL2 gene on functional role in DNA repair

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To prevent the consequences of DNA damages all living organisms have protective mechanisms named DNA repair. Base excision repair (BER) is necessary for removal of damaged nucleobases from the genome DNA and initiated by specific enzymes DNA glycosylases. Altering sequence of the DNA glycosylase genes can lead to changing enzyme function, accumulation of DNA damages and association with risk of developing cancer. In mammalian cells DNA glycosylase NEIL2 has unique ability to repair damages from "bubble" structures formed during transcription and replication. There are data on single nucleotide polymorphisms (SNPs) of the *NEIL2* gene are associated with risk of developing cancer, particular, one of the most dangerous – lung cancer. However, the corresponding functional protein variants of NEIL2 are not characterized. Using bioinformatics

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