properties. Such damages can be repaired. DNA pol λ is a eukaryotic enzyme belonging to the pol X family. Pol λ consists of two domains: 31 kDa polymerization domain (bearing the three conserved subdomains: fingers, palm, thumb) and 8 kDa domain. Pol λ has a dRP lyase activity, and play an important role in base excision repair (BER). Also, DNA pol λ has been suggested to play a role in meiotic recombination and DNA repair. In order to find out what effect on the localization of the protein in the active center of the enzyme affects the presence of the total number of BPDE-N2-dG residues that are in different regions, we carried out molecular modeling using the molecular dynamics method of the complexes of the enzyme with DNA duplex containing BPDE-N2-dG in the central part of the duplex. The complex also contains dCTP, forming a complementary pair with BPDE-N2-dG; triphosphate coordinated by the Mg^{2+} ion and is in a position of readiness for the reactions of incorporation of the nucleotide into the DNA chain. In summary, we have shown here how a family X polymerase utilizes subtle active site adaptations to carry out a critical repair reaction. The work was supported by RFBR grants (19-34-90052, 18-04-00596).

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Atypical antipsychotic clozapine binds fibrinogen and affects fibrin formation

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Clozapine is an atypical antipsychotic used for the treatment of schizophrenia. Prescribed daily doses of clozapine may reach over 900 mg/day. Some studies reported a connection between clozapine usage and the development of thrombosis. Our *in vitro* study aimed to provide insight into molecular bases of this observation, investigating clozapine binding to isolated fibrinogen, the main protein involved in hemostasis. Fibrinogen/clozapine interaction was confirmed by protein fluorescence quenching, with affinity constant calculated to be 1.7×10^5 M^{-1} and the number of binding sites more than one. Direct interactions do not affect the structure of fibrinogen, as determined by UV-VIS spectrometry and Fourier-transform infrared spectroscopy, nor fibrinogen melting temperature, examined by fluorescence spectroscopy. However, clozapine binding affected fibrin formation, by reducing coagulation speed and thickness of fibrin fibers. This behavior suggests that in the presence of clozapine, fibrinogen may acquire thrombogenic characteristics. Although no difference in fibrin gel porosity was detected, other factors present in the blood may act synergistically with altered fibrin formation to modify fibrin clot, thus increasing the risk for development of thrombosis in individuals on clozapine treatment. By ORAC and HORAC antioxidant assays, we found that clozapine efficiently protects fibrinogen from free-radicals oxidation. Since the effect of clozapine on fibrin formation is dose-dependent, it seems that the dosage of the medication could be the main factor that determines if clozapine will have a more positive or negative effect on fibrinogen and coagulation process *in vivo*.

P-02.5-10
Glucose stimuli prompts insulin secretion by human spermatozoa

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Spermatogenesis is sensitive to metabolic alterations, where insulin is considered one of the most important regulators. Even 100 years upon its discovery, not much is known concerning the role of insulin in the testis. It is hypothesized that insulin plays a major role on human spermatozoa capacitation, a phenomenon where spermatozoa suffer morpho-physiological alterations in order to achieve fertilization capacity. However, the molecular mechanisms remain to be elucidated. Herein, we aimed to evaluate the insulin synthesis and secretion capacity of human spermatozoa, by assessing the expression of enzymes responsible for proinsulin cleavage, PC1/3 and PC2. In addition, our goal was to assess whether insulin secretion was responsive to glucose stimuli. For this purpose, human sperm samples from normozoospermic men were used (n=15). A density gradient protocol was performed and two fractions of spermatozoa were then collected according to its motility condition (high vs low motility). Gene expression of insulin, PC1/3 and PC2 mRNA was evaluated by RT-qPCR in both spermatozoa fractions. Protein expression of insulin, PC1/3 and PC2 in spermatozoa was evaluated by immunofluorescence. The fraction of highly motile spermatozoa was incubated in culture medium under capacitating conditions and supplemented with increasing glucose concentrations (in mM: 0, 5.5, 11 and 22). Insulin concentrations in the medium 6 h later were quantified by ELISA. Our results showed that insulin, PC1/3 and PC2 mRNA, as well as the respective proteins, are expressed in human spermatozoa. The mRNA expression was found to be higher in highly motile spermatozoa. Additionally, human spermatozoa released insulin to the medium in a glucose concentration-dependent manner. This study shows that insulin plays a role in human spermatozoa capacitation though the mechanisms mediated by insulin remain unknown, opening an exciting new line of investigation.

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New potential role of Vps34 kinase in the control of the cell size

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Platelets, the smallest blood cells, are produced in the bone marrow by their precursors, megakaryocytes (MKs). One of the most characteristic features of the MK maturation is a substantial increase in size, together with the polyploidization of the nucleus. At the end of the maturation process, MKs generate prolonged cytoplasmic protrusions, termed proplatelets, which extend through the vascular sinusoids of the bone marrow and release