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SIRT1 is a promising biomarker of the functional accessibility of chromatin in the oocyte follicular cells

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The purpose of the study is to investigate the changes in cytological parameters by changes in the functional state of chromatin of cells of the follicular environment of oocytes under conditions of oxidative stress *in vitro*, as well as under the influence of SIRT-1 activator, PARP (poly(ADP-ribose) polymerase) blocker, NOS substrate and iNOS blocker, which has not been studied before. **Methods.** The experiments were conducted using 89 mature female mice of the CBA line (weighing 18–22 g). *Isolation of oocyte follicular cells* (OFCs) was carried out non-enzymatically (mechanically) from the follicles of the ovaries of mice. *Oxidative stress modeling:* OS was modeled by adding calculated amounts of H_2O_2. *Cytological research of OFCs* (by Fjolgen): 1) chromatization index (ChI) — the ratio of the number of nuclei with a preference for euchromatin to those with a preference for heterochromatin (genome activity); 2) nuclear index (NI) — the proportion of cells with a nucleolus (gene transcription); 3) the index of morphologically changed nuclei (MChN) — the proportion of cells with morphological changes in the karyoplasm and/or karyolemma (integrity of the karyolemma). *Substances used*: resveratrol (RES, Sigma-Aldrich, USA): 2,0 μM — activator of SIRT-1; 4-hydroxyquinazoline (4-G, Sigma-Aldrich, USA): 1,0 mM — PARP-1 inhibitor; L-arginine hydrochloride (L-ARG, Sigma-Aldrich, USA): 0,04 mM — NOS substrate; aminoguanidine (AG, Sigma-Aldrich, USA): 0,02 mM — specific iNOS inhibitor. The results were processed statistically in the Graph Pad Prism version 5.00 for Windows (GraphPad Software, California, USA). After checking for normal distribution, the analysis of data groups was performed using one-way ANOVA followed by multiple comparisons using the Newman-Keuls post-hoc test. Differences were considered statistically significant at $p < 0.05$. The results were expressed as M±m (mean ± standard error). All experiments were performed at $n = 4$ — the number of series of experiments with 4 independent replicates. **Results.** New data were obtained about the effect of H_2O_2 on OFCs, which allowed us to assert that such changes in the values of cytological indicators (chromatization index, nuclear index and morphologically altered nuclei index) reflect damage to the chromatin characteristic of oxidative stress. Under the condition with PARP-1 inhibitor and iNOS inhibitor we obtained the changes that together reflect chromatin damage that can be compared to that occurring under the conditions of OS, which was modeled using H_2O_2. The use of the NOS substrate and the activator of Sirtuin-1, under conditions of exposure to the PARP blocker, the iNOS blocker and, together, the PARP blocker and the iNOS blocker reflect the restoration of chromatin activity. **Conclusions.** Together, the obtained data provide grounds for asserting that both nitric oxide and Sirtuin-1 are involved in maintaining the functional state of chromatin availability in cells of the follicular environment of oocytes.

Keywords: cells of the follicular environment of oocytes, chromatin, oxidative stress, sirtuin-1.