cells. The use of SICM showed the dependence of the nucleus mechanical properties on the amount of lamin A and its isoforms. Therefore, the mechanical properties of the NE have tight relationship with molecular composition of NL. Thus, the cell nuclei expressing the additional lamin A gene were found to be 1.3 times more rigid than the wild-type cell nuclei, and changes in the structure of lamin A lead to improper organization of the nuclear skeleton. These may be due to the polymerization abnormality of dimers and decreased network stability and/or sequestration of normal protein.

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L-2. Irradiation by γ-rays reduces the level of H3S10 phosphorylation and weakens the G2 phase-dependent interaction between H3S10 phosphorylation and γH2AX

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A mutual balance between specific histone markers is essential for optimal DNA repair. For example, the epigenetic factors HDAC1 and HDAC2 play a crucial regulating role in the DNA damage response [1]. To show how HDAC1 depletion in mouse embryonic stem cells (mESCs) can affect the histone signatures after being exposed to γ-rays, we used mass spectrometry, western blotting, immunohistochemistry, and advanced confocal microscopy. We mainly compared the epigenetic profiles of histones H3 and H4 in wild-type (wt) and HDAC1 double-knockout (dn) ES cells exposed to γ-rays. We observed that a decrease in H3S10 phosphorylation is a hallmark of γ-irradiated mESCs. However, radiation-induced changes in H3S10 phosphorylation (H3S10ph) were not affected by HDAC1 depletion. We found, as well a decrease in H3K9me3 induced by γ-irradiation but no difference at the level of HP1β. These results fit well with the work published by [2] showing that all HP1 isoforms are recruited to UV-induced DNA lesions independently of H3K9me3. Changes in H3S10ph were likely caused by a γ-radiation-induced decrease in the number of cells in the G1 phase, characterized by no interaction between H3S10ph and γH2AX. However, an interaction of such modified histones we found in the G2 phase of the cell cycle. Together, our data show that even though H3S10ph is not directly involved in DNA repair, radiation-induced changes in the cell cycle can affect the function of H3S10ph.

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L-3. Design and development of new thiazolidinone-based drug-like molecules

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4-Thiazolidinones as privileged heterocycles are in focus since 60th. Main achievements are related to glitazones and set of drug-candidates with antidiabetic, antimicrobial, antiviral and anticancer activities. They are confirmed ligands toward various biotargets as well as compounds with unknown mechanism of actions. Combination of several reactive centers of main core and variety of its synthetic routs led do different 4-thiazolidinone subtypes. Among them 5-ene-thiazolidinones are of special interest due to chemical properties and pharmacological profiles. While, they are considered as frequent hitters or PAINS, which are useless because of possible low selectivity. This is argued by Michael acceptor property of 5-ene-4-thiazolidinones. Such thesis is discussed, and requires further investigation following the usefulness properties of Michael acceptors. The main goal of the project is the search for new 4-thiazolidinone-based drug-candidates. Methods: Drug design; synthesis; biological activity assays; SAR. Results and conclusions: The diverse in-house library have been designed and synthesized. Biological assays were focused on the search for anticancer, anti-inflammatory, antiparasitic/antimicrobial agents. Following polypharmacological approach and the multi-target drugs concept, the compound with several pharmacological effects were regarded as an advantage. Thus, the main directions for 4-thiazolidinones optimization were outlined: complication of C5 and modification of N3 positions; isosteric replacement; combination with other scaffolds; thiazolidinones-based synthesis of thiopyrano[2,3-d]thiazoles, thiazolo[4,5-b]pyridines, isothiocoumarines, *etc* and "simplified" derivatives. It was shown that thiopyranothiazoles are fixed "biomimetics" of starting 5-substituted-4-thiazolidiones without Michael acceptor properties. Study of the active anticancer thiazolidinones reveled the PPAR-mediated, ROS-dependent and pro-apoptotic mechanisms of action. Based on the biological activity data, 4-thiazolidinones can be considered as pro-drugs with efficient characteristics. The similarity of 4-thiazolidinones with H2S donors and preliminary results open new oportunities to design of new 4-thiazolidinone-based H2S releasing agents. Additionally, Michael functionality of thiazolidinones should be used in the useful way – search for Nrf2-modulatos, covalent inhibitors, ROS modulators.

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