экспрессии фосфатазы Wip1 через активацию транскрипции гена проапоптотического белка Bax (Goloudina et al., 2012; Eren et al., 2021).

Предложенная нами модель сенсибилизации трансформированных клеток к ДНК-повреждающим воздействиям с помощью фосфатазы Wip1 через дефосфорилирование и инактивирование репарационного белка Mre11 еще нуждается в дополнительном обосновании в исследованиях с применением более специфических ингибиторов фосфатазы и методов генетической инактивации *wip1*. Однако полученные результаты позволяют сделать предположение об участии p38/Wip1-пути в ИГД-индуцированном накоплении γH2AX и ингибировании репарации ДНК в трансформированных клетках.

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В экспериментах представленной работы животные и люди не участвовали.

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The Role of MAP Kinases in the Induced Histone H2AX Phosphorylation in Transformed Cells

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Previously, we have shown that inhibitors of histone deacetylases (HDIs) do not induce DNA double strand breaks (DNA DSBs). However, like genotoxic agents, HDIs initiate the accumulation of phosphorylated histone H2AX (γH2AX), which is a DNA DSB marker. HDIs can also reduce the efficiency of repair of DNA damaged by genotoxic effects in transformed cells. The aim of this work was to identify the signaling pathways leading to the accumulation of γH2AX under the HDIs treatment in transformed cells. There was considered the role of the MAPK family kinases in phosphorylation of histone H2AX as well as inhibition of DNA repair induced with HDI sodium butyrate (NaBut). It was shown that the accumulation of γH2AX under the NaBut treatment is accompanied by a decrease of the ERK and PKB/Akt kinases phosphorylation level in transformed cells. The activating phosphorylation of p38 kinase increases under the NaBut treatment, causing Wip1 phosphatase accumulation, which may be one of the reasons for the DNA repair inhibition. Suppression of p38 kinase activity abolishes the NaBut-induced inhibition of repair efficiency. The data obtained suggest the role of the p38/Wip1 pathway in the HDIs-induced decrease in repair efficiency in transformed cells.

Keywords: HDAC inhibitor, sodium butyrate, histone H2AX phosphorylation, MAP kinase, DNA repair, Wip1 phosphatase