не происходит, и клетки вступают в апоптоз без участия митохондрий. Поскольку СВЕ, как правило, в первую очередь направленно действует на митохондрии (Савицкая и др., 2016), можно предположить, что митохондриальный путь апоптоза в клетках А431 является основным и дополнительно усиливается стрессом ЭПР. Возможно, такое различие лежит в основе разной чувствительности клеток А431 и HaCaT к воздействию СВЕ.

Исследование воздействия СВЕ на нормальные и опухолевые клетки актуально как с теоретической, так и практической точки зрения. Изучение эффектов СВЕ по отношению к клеткам опухолей поможет лучше понять механизмы лежащих в их основе процессов, а в перспективе – разработать противоопухолевый препарат с селективным действием и минимальным количеством побочных эффектов.

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СОБЛЮДЕНИЕ ЭТИЧЕСКИХ СТАНДАРТОВ

В работе отсутствуют исследования человека или животных.

КОНФЛИКТ ИНТЕРЕСОВ

Авторы работы заявляют, что у них нет конфликта интересов.

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ALPHA-TOCOPHERYL SUCCINATE INDUCES ER STRESS, DISREGULATES LIPID METABOLISM AND LEADS TO APOPTOSIS IN NORMAL AND TUMOROUS CELL LINES OF EPIDERMAL ORIGIN

M. A. Savitskaya[a], I. I. Zakharov[a], A. A. Saidova[a], E. A. Smirnova[a], G. E. Onishchenko[a, *]

*[a] Lomonosov Moscow State University, Department of Cell Biology and Histology, Moscow, 119234, Russia *e-mail: galina22@mail.ru*

Vitamin E succinate (VES, α-tocopheryl succinate), is a potential antitumor agent known to selectively affect the mitochondria of tumor cells. However, the data on the proapoptotic mechanism of action of VES are unclear, and the effect of VES on normal, non-tumorigenic cells has not been fully investigated. Previously, we showed that VES induces apoptosis via the mitochondrial pathway in A431 human epidermoid carcinoma cells. The goal of this work is to investigate the effect of VES on non-tumorigenic cells and to reveal commonalities and differences in pathways activated in normal and tumorous cells. To achieve this, we studied how VES affects such organelles as the ER and the Golgi apparatus, analyzed the expression of ER stress-associated genes, and also assessed the ROS content and the accumulation of lipid droplets in A431 human epidermoid carcinoma cells and HaCaT immortalized human keratinocytes. We show that in both cell lines there are signs of ER stress, the amount of ROS and lipid droplets increases, as does the number of apoptotic cells. At the same time, the key difference in the mechanisms apoptotic cell death induction in A431 and HaCaT cells treated with VES lies in the reaction of mitochondria: in A431 cells, apoptotic cell death is triggered via the mitochondrial pathway, while HaCaT cells initiate apoptosis without involving mitochondria. Thus, the targets of VES in normal and tumor cells may differ and can possibly complement each other during apoptosis induction.

Keywords: α-tocopheryl succinate, ER stress, apoptosis, lipid inclusions, ROS