SIALIDASE ATTENUATES ERLOTINIB RESPONSE IN HUMAN ALVEOLAR EPITHELIAL CELLS (A549 CELL LINE) STIMULATED BY EGF.

A. Rybak, M. Zarzecki, E. Golabiewska, A. Niechoda and A. Holownia.

Department of Pharmacology, Medical University, Mickiewicza 2C St, 15-222 Bialystok, Poland, Holow_sinai@hotmail.com

Erlotinib (ERL) is a widely used, reversible tyrosine kinase inhibitor targeting epidermal growth factor receptor (EGFR)-related signalling. The drug was approved for the first-line treatment of patients with metastatic non-small cell lung cancer with EGFR mutations. It was shown that extracellular glycans can affect the expression, dimerization, phosphorylation and EGF binding to EGFR. In this study we investigated the effects of EGF and ERL on the cell cycle of naive and sialidase (alpha-neuraminidase)-pretreated (24 hours) human alveolar epithelial cells (A549 cell line). The cells were labelled with propidium iodide and cell cycle distribution was quantified by flow cytometry. Neither desialilation nor EGF or ERL treatment increased damaged cell numbers („early” G0/G1 cell fraction) while ERL increased G0/G1 cell numbers and significantly decreased S+G2/M cell fractions. In naive cells, EGF increased proliferating cell numbers and proliferation index by more than 40% and this effect was blocked by ERL. In desialylated cells the proliferation was significantly lower (decreased by about 29%), while EGF and ERL were without major effects. Our results indicate that changes in cell membrane glycosylation of A549 cells may affect not only EGF effects and EGFR-related signalling but also ERL efficacy.