ImmunoTools *special* Award 2018

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Long-term efficiency of S1P signaling in low-dose genotoxic stress

The sphingolipid sphingosine 1-phosphate (S1P) is regulating many physiological and pathophysiological processes and therefore plays an important role in the function of the immune system. As part of the inflammatory response, S1P signaling mediates positive effects during genotoxic stress and protects against sepsis. In former studies S1P metabolism and signaling was protective under inflammatory conditions. S1P itself was shown to inhibit histone deacetylases. Therefore an involvement of S1P in long-term cellular reprogramming is assumed.

In previous experiments the role of sphingolipid signaling in low-dose genotoxic stress induced by anthracyclines was investigated, and the inhibitory effect of low doses of the anthracycline epirubicin was shown. The aim of my current studies is the examination of the long-term efficiency of these signaling events due to low-dose genotoxic stress. I investigate the effect of low doses of epirubicin and induced genotoxic stress in cell culture experiments after lipopolysaccharide (LPS) stimulation. After specific time points, ranging from 24 hours up to several days, I analyze the production of pro-inflammatory cytokines. The release of pro-inflammatory cytokines like IL-1β, IL-6, IL-10 and TNFα is measured via ELISA. Further I work with the PE-conjugated antibodies of IL-6, IL-8, TNFα and Annexin V to measure the expression of those cytokines with flow cytometry.

Additionally I want to identify S1P signaling events leading to cellular reprogramming. Therefore I want to test the long-term effect of epirubicin on S1P metabolism and signaling. The influence of S1P and its signaling pathways on long-term adaptation mechanisms of cells and the following epigenetic regulation will be analyzed. The main focus will be on histone modifications and the connection between S1P signaling and histone deacetylation. To identify the differences of histone acetylation following S1P stimulation, mass spectrometry, ChIP-assay and qPCR will be used. Furthermore flow cytometry is used to check the production of cytokines (IL-6, IL-8, TNFα) of cells with different histone acetylation status. And with the help of recombinant cytokines (rh IL-1β, rh IL-6, rh IL-8, rh IL-10, rh TNFα) I want to stimulate cells and analyze the gene expression pattern depending on their histone acetylation status.

Carrying out these analyses, the role of S1P signaling in low-dose genotoxic stress-induced situations will be characterized to reveal pathways resulting in long-term protection from sepsis.

ImmunoTools *special* AWARD for **Anke Ziegler**

includes 25 reagents

PE - conjugated anti-human antibodies: IL-6, IL-8, TNFα and Annexin V

recombinant human cytokines: rh IL-1β, rh IL-6, rh IL-8, rh IL-10, rh TNFα

human ELISA-set (for one 96 plate): IL-1β, IL-6, IL-10 and TNFα

DETAILS more AWARDS