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IL12 increases sensitivity to apoptotic stress of cancer stem cells

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Polorectal cancer is one of most common cancers in the World. Many studies have shown that only small number of tumor cells able to initiate cancer in immunodeficient mice. This small fraction of cells has stem cells like properties and is named cancer stem cells. Previous studies revealed that colon, prostate, breast cancers have up regulation in several cytokines: interleukin (IL)-6, IL-4, IL-8. In other hand expression level of IL-12 is not detected in the sera of patients with colorectal cancer. Recent studies showed that IL-4 mediates protection from apoptosis through activation of an anti-apoptotic mediator survival by Stat6 pathway. Stat6 positively regulate molecules such as IL-4Ra, CD23, MHC class II, negatively regulate proinflammatory cytokines, including IL-12. According to B.H. Li investigation HT-29 cells having active Stat6 pathway with increased mRNA levels of IL-4 using RT-PCR. IL-12 inhibits the production of IL-4 in human CD4+T lymphocytes but its effects on IL-4 secretion of cancer stem cells are unclear. Here we have investigated different concentration of IL-12 on sensibility of cancer stem cells to staurosporine. HT-29 cells were cultured in DMEM media with different concentration of glucose: 4.5 and 1 g/l, because glucose is one of the main activator of tumor growth. Experiments with low glucose concentration did not give significant difference with control samples. We have checked IL-12 in 10, 5, 2.5, 1.25, 0.625, 0.312, 0.156 ng/ml concentrations. In DMEM with 4.5 g/l glucose IL-12 did not significantly regulate proliferation rate of HT-29 cells only 10 ng/ml of IL-12 1.4 times decreases proliferation and two times increases sensitivity to staurosporine (8 µM). These data have confirmed that IL-12 effects direct to cancer stem cells and also cancer microenvironment. Implication of IL-12 is very important during carcinogenesis because it may modulate adaptive immune response thought stimulation of natural killer cells and maturation of cytotoxic lymphocytes.

Biography

Issabekova A S has completed her PhD from Al-Farabi Kazakh National University, Almaty, Kazakhstan. She is the senior researcher of Stem cells Laboratory at National Center For Biotechnology, project leader about cancer stem cells supported by Education and Science Ministry Republic of Kazakhstan. She has published more than 18 papers in journals.

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