Abstract

IFNγ is an important cytosine mediating imune responses, including antitumor immunity. It can affect expression of a lot of genes, which regulate different cellular processes. In tumor cells defects in signal cascade of IFNγ and mistakes in expression of genes regulated by IFNγ, for example genes for antigen adjustment and presentation (APM) or genes for major histocompatibility complex (MHC), were observed. Epigenetic mechanisms, can play a role in regulation of expression of genes for IFNγ, as well as in regulation of expression of genes regulated by IFNγ, including the components of the IFNγ signalling pathway. In lymphocytes from tumors the ability to produce IFNγ was limited by epigenetic silencing of genes for IFNγ. In tumor cells, epigenetic silencing of genes regulated by IFNγ, of genes of the IFNγ signaling cascade, for example IRF transcription factors, and other genes regulated by IFNγ, such as genes for APM, MHC or indoldioxygenase coding genes (IDO), was demonstrated. In case of their activation by IFNγ, epigenetic changes in regulation sequences of appropriate genes, were observed. IFNγ thus can be considered as an epigenetic agent. Epigenetic modulators are able to activate expression of genes regulated by IFNγ. By this way it´s possible to explain some of immunomudullatory effects of these agents. Epigenetic regulations of genes regulated by IFNγ are important for immune escape of tumor cells from antitumor immunity.

Key words:

Interferon γ, epigenetics, DNA methylation, antigen presentation, JAK-STAT signalling pathway