Abstract

Veronika Vlková: Epigenetic mechanisms in the regulation of antigen presentation and anti-tumour immunity.
Charles University in Prague, Faculty of Science, Molecular and Cellular Biology, Genetics and Virology
Dissertation, 2014

Reversible downregulation of MHC class I expression on tumour cells, a common mechanism by which tumour cells can escape from specific immune responses, is frequently associated with coordinated silencing of antigen-presenting machinery genes. The expression of these genes can be restored by IFN-γ. Here we describe association of DNA demethylation of selected antigen-presenting machinery gene regulatory regions upon IFN-γ treatment with MHC class I upregulation on tumour cells thus demonstrating that IFN-γ acts as an epigenetic modifier. Our results cast more light on the role of DNA methylation in tumour cell escape from specific immunity. Treatment of MHC class I deficient tumour by epigenetic modifiers sensitized neoplasia to the immunotherapy. Our data also provide knowledge about differentiation cancer chemotherapies, especially for use in combination with other drugs to achieve lower immunosuppressive function of tumour microenvironment. In addition, our data provide evidence that besides the known targets of epigenetic agents or immunoregulatory antibodies other unspecific or indirect activities should be considered during the therapy. The aim of whole work was to describe in detail reversible mechanisms in the tumour cell escape from specific immunity.