COMMON THEMES IN CANCER AND VIRUS-INFECTED CELLS

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Cellular homeostasis and metabolism are key determinants of different aspects of the life of the cell, its survival, death or division. These processes are regulated at various levels, depending on both extracellular and intracellular stimuli, with energy supplies strongly affecting or limiting the course and outcome of individual processes. The energy supplies in form of ATP are generated very efficiently by mitochondrial oxidative phosphorylation or less efficiently by glycolysis. A major by-product of oxidative phosphorylation is generation of reactive oxygen species while glycolysis can promote cellular antioxidant defenses. Different cells and tissues are more or less resistant to the oxidative damage and/or lack of energy supplies. However, usually only high levels of free radicals are harmful, while their low levels stimulate redox-sensitive transcription factors, promoting cellular metabolism and growth as well as angiogenesis. Blood supply then determines delivery of oxygen, glucose and other nutrients, and/or removal of toxic products of metabolism. Cellular metabolism also affects inactivation or exclusion of xenobiotics as well as growth of intracellular parasites.

We have focused on the interactions of viruses with the host, especially on the role of energy metabolism, redox stress, and the type of virus-induced cell death with implications for the cellular and immune responses. Namely, we have found that the type of energy metabolism determines the typical anti-apoptotic and a paradoxical pro-apoptotic effect of Bcl-2 protooncogene expressed by a recombinant vaccinia virus. Further, we have described inhibitory effects of high levels of nitric oxide on the growth of vaccinia virus and HIV-1, as well as stimulatory effects of low levels of nitric oxide on the growth of these two viruses. Finally, we have employed heme- and iron-induced redox stress to reactivate latent HIV-1 with the aim to eliminate this deadly virus from the organism.

There are many themes and aspects common to both cancer and virus-infected cells. Moreover, many viruses are suspected or proved to induce tumorigenesis while they can be useful for the oncolytic therapy or anti-tumor vaccination. Thus, the investigation of both cancer and virus-infected cells with respect to the underlying cellular metabolism can be fruitful.