and drug administrations. It was concluded that (1) metabolic imbalnce of ornithine was markedly changed by polyamine depletion to leukaemia cells and (2) combined therapy enhanced the cytotoxicity of cyclophosphamide and increased the life span of tumour bearing animals by 200 to 300 per cent.

MITOCHONDRIA AS INTRACELLULAR TARGETS FOR ANTICANCER THERAPY

A.M.Kroon and C.van den Bogert

Laboratory of Physiological Chemistry, State Universty, Medical School, Bloemsingel 10, 9712 KZ Groningen, The Netherlands

The presence and expression of DNA within mitochondria is now well established. In a series of studies with various tumour model systems, it has been shown that inhibition of mitochondrial gene expression leads to cell proliferation arrest and in some cases even to tumour eradication. Tetracyclines, which specifically inhibit mitochondrial protein synthesis exert these effects. We consider depleted energy generation capacity to be the most likely explanation. Also MGBG, an inhibitor of polyamine biosynthesis, preferentially impairs mitochondrial biosynthetic processes. The presence of two genetic systems in all tumour cells raises the question whether or not the mitochondrial system is also a target in other treatments primarily designed to interfere with the nucleocytoplasmic system. For doxorubicin and cytosine-arabinoside, effects on mitochondrial biogenesis and function have been observed and the findings are under further investigation.

HERPES VIRUS SPECIFIED EARLY PROTEINS INDUCE CELLULAR DNA SYNTHESIS IN VIRUS INFECTED CERVICAL CANCER CELLS

P.Kulmala(1), M.Lehtinen(1), O.-P.Kallioniemi(2) and J.Paavonen(3)

(1)Department of Biomedical Sciences, (2)Department of Clinical Chemistry, University of Tampere; and (3)Finnish Academy, Finland

The mode of DNA synthesis in virus infected HSV-2 permissive and non-permissive cervical cancer cells was studied. The flow cytometric detection of BrdU in newly synthesized DNA was achieved using a monoclonal antibody. PFA was used to differentiate between cellular and viral DNA synthesis. In the permissive CaSki cells an exponential increase of both DNA-synthesis and amounts of infectious virus was seen. In the non-permissive C-33A cells, a comparable increase of DNA synthesis was seen 6 hr after infection, but not later. The inhibition of viral DNA synthesis by PFA was able to inhibit the virus induced DNA synthesis in the CaSki but not in the C-33A cells. In the CaSki cells the exponentially increasing DNA synthesis corresponded to the virus replication. In the C-33A cells a transient induction of DNA synthesis was noted. This is likely to represent virus induced cellular DNA synthesis. In the CaSki cells, HSV-specified major DNA-binding protein (ICSP 11/12) was seen in the nucleus, whereas in the C-33A cells the protein was located both in the cytoplasm and the nucleus. Early viral proteins are expressed also in the PFA treated cells and show (ICSP 11/12) affinity to DNA. Whether the early viral proteins mediate the virus induced increase in cellular DNA synthesis in the non-permissive cancer cells has been evaluated.

THE E3/19K PROTEIN OF ADENOVIRUS TYPE 2 BLOCKS CELL SURFACE EXPRESSION OF HLA CLASS ANTIGENS AND INTERFERES WITH THE IMMUNE RESPONSE

S.Kvist(1) and H.-G.Burgert

Swiss Institute for Experimental Cancer Research, 1066 Epalinges/Lausanne, Switzerland, and (1)Present address: Ludwig Institute for Cancer Research, Stockholm, Sweden

The adenovirus type 2 encoded protein E3/19K binds to human HLA class I antigens. The formation of the HLA-E3/19K complex prevents the HLA antigens from being correctly processed by inhibiting their terminal glycosylation and cell surface expression. This reduced level of antigens influence the cytotoxic T cell response. Also the murine H-2 K^d antigen binds to the viral protein whereas the allelic K^k antigen does not. Hybrid genes between the K^d and K^k alleles were constructed and have allowed us to map the 1 and 2 domains of the class I antigen to be the essential structures involved in the complex formation. Interestingly, these domains are also crucial for T cell recognition.

ALKYLATING AGENT-INDUCED MUTAGENESIS AND ACTIVATION OF THE Ha-ras ONCOGENE

S.A.Kyrtopoulos and V.Pletsa

National Hellenic Research Foundation, Biological Research Center, Athens, Greece