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## ISOLATION AND CHARACTERIZATION OF CELL CLONES PRODUCING VARIOUS AMOUNTS OF BOVINE LEUKOSIS VIRUS

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Several single-cell clones were isolated from a lamb kidney cell line (FLK) persistently infected with bovine leukosis virus (BLV). The clones differed in the amount of virus produced, some were highly virus productive, others produced less virus. Restriction analysis of cell DNA from clones revealed the existence of several numbers of integrated BLV-DNA proviruses in various cell clones. In some cell clones the unintegrated proviral DNA was observed. The proviral BLV sequences were found integrated in reiterated DNA in a part of cell clones. There was no apparent relationship between the number of integrated BLV proviruses and the extent of the virus production. The origin of the different number of the integrated BLV proviruses in various cell clones has been evaluated.

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## RAS ONCOGENES AND CHEMICAL CARCINOGENESIS

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Transforming alleles of the ras gene family have been identified in a significant fraction (15%) of human tumours including the most common forms of human neoplasia. Understanding the role of these oncogenes in human tumour development is hampered by the impossibility of experimental manipulations and the unknown etiology of most human cancers. Thus, we have investigated the presence of ras oncogenes in animal tumour systems. Studies from ours, as well as other laboratories, have demonstrated the reproducible activation of specific ras loci in a variety of carcinogen-induced animal tumours and chemically transformed cells. For instance, induction of mammary carcinomas in rats by nitroso-methyl-urea (NMU) invokes the activation of the H-ras oncogenes in 83% (48 out of 58) of the tumours. More importantly, each H-ras oncogene became activated by a G→A transition, the type of mutation most commonly induced by NMU. Considering the short half life of NMU and the fact that these mammary carcinomas were induced by a single injection of the carcinogen, our results imply that H-ras oncogene activation occurs during the onset of carcinogenesis in this animal model system. Research supported by the National Cancer Institute, DHHS, under contract no. N01-CO-23909 with Litton Bionetics, Inc.

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## MONOCLONAL ANTIKERATIN ANTIBODIES IN THE STUDY OF DIFFERENTIATION AND MALIGNANCY IN THE HUMAN BREAST

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Two IgG1 monoclonal antibodies, BA16 and BA17 have been developed which recognize different epitopes on the 40kd cytokeratin (keratin 19) as judged from the filamentous staining pattern of cultured epithelia, immunoblot analysis as well as from the immunohistochemically defined tissue distribution. In the human mammary gland both antibodies stain only luminal cells (not myoepithelium) but while in the large ducts and most alveoli all the luminal cells stained, in smaller ducts and ductules a subpopulation of non-staining luminal cells was found. Staining of cells cultured from human milk on plastic and of structures developing from reduction mammaplasty organoids in collagen gels showed that the heterogeneity of expression of the 40kd keratin was maintained in vitro. Among more than 150 breast tumours examined, benign lesions and some in situ carcinomas were heterogeneously stained while most in situ carcinomas and all infiltrating carcinomas and metastases were homogeneously positive for keratin 19 expression. On the basis of their topographic distribution, proliferative potential and expression in tumours, the keratin 19 -ve luminal cells are considered as potential stem cells in normal growth and target cells in breast tumours.