12.007

THE E5 PROTEIN OF HPV-16 CAN TRANSFORM MURINE CELLS AND CO-OPERATE WITH HUMAN EGF RECEPTORS.

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Human papillomavirus (HPV) type 16 is a small DNA tumour virus, strongly associated with malignant ano-genital lesions particularly carcinoma of the cervix. Two HPV-16 early genes, E6 and E7 are known to have transforming activity.

Presented in this work is evidence of the transforming activity of another HPV-16 early gene, E5, in murine 3T3 and C127 cells. HPV-16 E5 expressed from a strong heterologous promoter results in a loss of contact inhibition and the anchorage independent growth of colonies in suspension. Furthermore, the biological activity of HPV-16 E5 is stimulated by epidermal growth factor (EGF) by co-operation with the EGF receptors.

12.009

HIGH PREVALENCE OF HPV INFECTION IN A POPULATION WITH A LOW CERVICAL CANCER INCIDENCE.:ANALYSIS BY .DNA HYBRIDISATION AND POLYMERASE CHAIN REACTION.

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The regular presence of specific types of papillomavirus in CIN and cervical cancer tissue has led to the concept that HPV plays a crucial role in the process of malignant transformation of the cervical epithelium. However,avalaible data supporting the HPV/cervical cancer association has been obtained from populations at a high risk of cervical cancer.It is of interest, therefore, to investigate the prevalence of HPV infection in populations at low cervical cancer risk since this information would help to clarify the role of the virus. The incidence of cervical cancer in the Basque Country (BC) is among the lowest in the world . The present study was undertaken to determine the age-related prevalence rates of infection with especific HPV types in the BC population. Cervical smears from 1178 women with citologically normal cervices and 67 women with CIN or cervical carcinoma were analysed for the presence of HPV 6/11/16 and 18 DNA by slot-blot hybridization. A subset of the samples were also investigated by PCR. We have found that HPV is present in our area at the same frequency as in others parts of the world. The high prevalence of HPV infection demonstrated further supports the role of cofactors as determinants of the different geographic rates of cervical cancer incidence.

12.011

IDENTIFICATION OF CANINE ORAL PAPILLOMAVIRUS IN THE SKIN OF AN IMMUNOSUPPRESSED DOG

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An eight month old female Chinese Shar Pei was noted to have generalized exophytic papillomatosis of the oral mucosa as well as the perioral, truncal and appendicular skin. The dog had been maintained on corticosteroids for an unrelated skin condition for a prolonged period of time. Microscopically, the tumors had features consistent with that of viral induced papillomas. This was confirmed by immunohistochemical screening for papillomavirus group-specific antigens. Stringent southern blot hybridisation and restriction enzyme analysis revealed that the virus in the cutaneous lesions was identical to the previously described canine oral papillomavirus (COPV). This report provides evidence that immunosuppression can expand the tissue tropism of the virus. This raises the possibility that the tissue specificity of papillomaviruses is influenced by the immune system.

12.008

NEW HUMAN CERVICAL CARCINOMA CELL LINES WITH INTEGRATED HPV16

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We have derived a number of cell lines from human squamous and adenosquamous cervical carcinomas. Five of these - XH1, EH2, DE3, EL4 and JE6 - have been cloned by single cell selection. The single locus hypervariable minisatellite probe MS31 was digoxigenin labelled and used to probe a *Hin*f I digest of genomic DNA from each of the cell lines. The bands obtained were different from each other and from the A431, Caski, Bowes melanoma and 3T3 cell lines also maintained in this laboratory. PCR was performed, using the degenerate primers MY09 and MY11 to amplify a region of approximately 450 bp located in the L1 open reading frame of all sequenced papillomaviruses. The results suggested that all five had HPV integrated into the genome. The PCR products were further analysed and were seen to exhibit the single *Eco*R I and *Pst* I sites characteristic of HPV16. Subcutaneous xenografts have been produced in nude mice using three of the cell lines - XH1, EH2 and DE3. These cell lines hold promise for the investigation of mechanisms for the involvement of HPV16 in human epithelial cell carcinogenesis.

12.010

PHYLOGENETIC ANALYSIS ALLOWS CLASSIFICATION OF NEW HPV TYPES BASED ON LIMITED SEQUENCE ANALYSIS

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The recent use of general primer mediated PCR leads to the detection of a wide variety of HPV genotypes, often including unsequenced and new types. To classify such HPVs and to predict their biologic behaviour, minimum-length phylogenetic trees were generated using parsimony algorithms. This resulted in classification of the HPVs into three major groups which correspond to their known tissue tropism and oncogenic potential. The first group consists of viruses that infect the skin, including the epidermodysplasia verruciformis types. The second group comprises the HPVs associated with benign genital lesions. The third group consists of HPVs associated with malignant genital lesions. The branching pattern was essentially independent of the region of the genome .used and was stable when as few as 300 basepairs were used for the alignment. These data indicate that phylogenetic analysis accurately classifies distinct types into clinically relevant families. We suggest that this approach can be used to rapidly classify novel HPV genomes when limited sequence data is available.