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Cellular targets for the transforming proteins of human papillomaviruses

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Human papillomaviruses (HPV) of the high-risk group, e.g. HPV-16, can immortalize and transform mammalian cells, including primary human cells, and thereby contribute to several proliferative disorders in humans, including cancer of the cervix. Apparently, the interaction of viral proteins with cellular growth-regulatory pathways leads to cell transformation. Our studies are focused on better understanding the role of the HPV-16 E7 gene in tumorigenesis.. It was shown that expression of E7 overrides several cell cycle checkpoint controls, mainly at the G1/S boundary. The deregulation of cell cycle control by E7 appears essential for the transforming potential of human papillomaviruses. However, the mechanisms by which viral proteins interfere with cell cycle control in the host cell remain largely elusive. In an attempt to define mechanisms of cell cycle deregulation by E7, we found that E7 stimulates expression of the cyclin E and cyclin A genes. We also found that E7 can antagonize the ability of the cdk2 inhibitor p27KIP1 to block cyclin E-associated kinase, indicating that the ability of E7 to override certain forms of G0/G1 arrest is mediated in part by binding to and subsequent inactivation of cdk inhibitors, e.g. p27KIP1.

In additional experiments, aimed at a better understanding of the immortalizing potential of HPV-16 E7, we screened a human cDNA library for proteins interacting with the C-terminal part of E7 in a yeast two-hybrid system. In that screen, we have isolated cDNA clones corresponding to the products of several human genes. Data on the physical and functional interaction of E7 with these additional cellular targets will be discussed. Since the interaction of viral oncoproteins with cellular target proteins is critical for viral pathogenesis, a careful analysis of these interactions is required for a better understanding of the virus-associated diseases, and for the development of new therapeutic approaches for these diseases

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Abstract not received.

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Is psychology relevant for breast cancer screening?

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The relevance of psychology for breast cancer screening was originally seen in terms of the possible psychological impact of screening: it was suggested in 1989 that 'More psychological research is required in the screening programme (..) to establish the possible harmful effects ..' (MM Roberts, BMJ, 1989).

That impact has been studied extensively by now. Although risk factors for distress have been established, contrary to expectations few or no short term negative effects have been found in most studies, even in women with false positive test results. In the long run, the effects of breast cancer screening on quality of life or QALY's can also be neglected as a) positive as well as negative effects on quality of life have been established; and b) the gain in survival seems to outweigh the magnitude of psychosocial effects.

However, psychology may still be relevant. As the effectiveness of breast cancer screening depends on the level of (re-)attendance, psychology may play a role in secondary prevention: psychological and social factors have turned out to affect attendance and reattendance. Thus, paying attention to a) the attitude of participants; b) the burden of the screening process; and c) information giving, could improve effectiveness.

Even primary prevention might eventually be supported by applying knowledge derived from psychological theory. The screening programme could be used to stimulate or prevent those behaviours that play a role in breast cancer etiology such as a healthy diet, exercise and alcohol use.

In other words, psychology may be relevant to breast cancer screening but in a way different from the one proposed originally.

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Is the appointment of specialist nurses to provide counselling an advantage or disadvantage

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Specialist cancer nurses have been appointed in increasing numbers within the UK and other countries. The aim has been to ensure that patients and relatives are fully informed about treatment procedures and choices and given practical help, emotional support and counselling so that they can adjust psychologically to their predicament. However, there is now evidence that they cannot meet these aims without specific training in key assessment and communication skills.

When they have been so trained other doctors and nurses in the care team tend to leave the burden of psychosocial care to them. There is then a risk of patient overload and personal burnout especially if specialist nurses allow patients to become dependent on them and fail to refer patients on for more expert help. There is also a risk that family members will feel excluded and disempowered by the intensity of the nurse-patient relationship.

The importance of proper training and on-going supervision of specialist s will be argued on the basis of data from a recent randomised controlled trial comparing training in communication skills alone with training plus supervision.

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Psychological adjustment and physical survival in cancer patients: Vision and facts

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It is generally accepted that the diagnose cancer and its treatment have a lot of psychosocial consequences, e.g. negative emotions, social isolation, psychosexual problems, loss of autonomy and control. These psychological problems may be temporarily or endure several years. Cancer as a life threatening disease often implies an existential crisis with long life consequences. An important question in the psycho-oncology is whether variations in the psychological adjustment are related to the progression of cancer. Several studies, however not all, confirm the effects of psychological factors on cancer progression. Relevant factors seems to be social support and non-expression of negative emotions. Conflicting or negative results concern studies on the influence of bereavement, helplessness, active coping and personality. Another approach in studying the relationship between psychological adjustment and physical survival concerns the effects of participation in psychosocial support an counseling to cancer patients. Although several studies show effects of psychological interventions on psychological adjustment, only in few studies attention have been paid to the effects of psychological interventions on recurrence and survival (e.g. studies by Spiegel, Fawzy). The research on psychological adjustment and physical survival in cancer patients is hampered by methodological problems, ignorance of a theoretical psychological models and the lack of attention to biological mechanism connecting psychological factors and disease progression in cancer. Besides these research driven arguments, the question may be raised whether attention to the effects of psychological adjustment on quality of life is more importance than studying the effects of psychological adjustment on life expectancy and survival in cancer.

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Does training in communication skills make a difference to clinical practice and patient outcome?

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Several studies provide evidence that psychological support reduce patients psychological distress. It is also argue that the way doctors communicate with their patients affects not only the adequacy of the clinical interview and the detection of psychological disturbance, but also patients compliance and satisfaction with care. Unfortunately, a substantial proportion of the problems developed by cancer patients remains untreated. This failure to identify many of the patients' problems seems mostly related to insufficient psychosocial knowledge and deficient communication skills among health professionals who care for these patients and their families. Moreover, it is often recognized that caring for cancer patients is highly stressful. Stressors are usually cumulative in oncology: critical decisions, errors yielding

important consequences, communication of bad news, numerous therapeutic failures, administration of treatments with serious side effects, contacts with mutilated/disfigured patients, emotionally loaded relationships, death of patients. A lot of these stressors imply communication with patients, relatives and colleagues. Interventions and strategies have been proposed to help staff to deal with cancer care: staff selection, financial and organisational facilities, staff support groups, and also training opportunities. Psychological training programs are probably the best cost-effective ways of reducing stress in cancer care and of improving satisfaction with care and enhancing quality of care. A research program looking at the effectiveness of training programs aimed at improving health care professionals communication skills has been activated several years ago by our group. The results of two ran studies are showing that training duration is directly related with effectiveness. Moreover these studies are showing the difficulty of trained subjects to transfer their skills into their clinical practice. Results of these studies will be presented and the need to focuse further training programs on the transfer of learned communication skills into clinical practice emphasized.

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Do families benefit from psychological intervention?

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Significant cumulative evidence exists to confirm the beneficial effects of modes of intervention on psychological distress, functional adjustment and treatment-related symptoms of patients and families. Most of the studies found repeatedly that the level of psychological distress and adjustment problems reported by patients were either identical or somewhat higher for the partners. Thus, does the partner constitute a support or distress system? If the partner is distressed, is there a relationship between his/her distress and that of the patient? What impact does the illness have on the lives and relationships of the family members? What impact and influence can the family members have on the life process of the illness? The family in general and the partner in particular, therefore, cannot be looked upon as natural supporters for cancer patients, but rather as a system that is itself in need of psychological help and support.