tolerance to treatment vary with age and affect prognosis. Extrinsic factors such as patient (or parental) choice also vary with age and thus need to be taken into account when assessing crude survival rates with a particular treatment regimen.

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Computer-aided oncology: From basic research to clinical practice

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Since the announcement of the Human Genome Project in 1990, the advances in genome mapping and sequencing methods have led to an unprecedented increase in the amount of genomic information available. Indeed, as of today we have accessto more than 20 completely sequenced genomes from several species, including major pathogens and important model organisms. In addition, the new high-resolution map of the human genome contains more than 30,000 genes and the first working version of the human genome sequence is expected to be available in the spring of 2000. Furthermore, ongoing large-scale efforts are aimed at analysing the gene expression profiles of a variety of tumours at different stages. Besides generating new hypotheses about biochemical pathways that lead to malignancy and providing new potential targets for therapeutic intervention, such information can also form the basis for a detailed classification of tumours based on their molecular rather than morphological profiles.

The rapid advances in these areas are already changing the way we view and understand the cancer cell. The impact on diagnosis and therapy is already tangible and will be more dramatic in the near future. The genomic databases andassociated computational analysis tools on the Internet, initially aimed solely at the bench researcher, are already emerging as valuable resources for clinicians and counselling specialists. The lecture will provide an overview of these resources and their use, including case examples of applications to clinical oncology.

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Knock-out mice in cancer research

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Gene inactivation studies are invaluable in assessing the function of oncogenes and tumor suppressor genes in development and malignant growth. However, detailed analysis of the role of tumor suppressor genes in these processes using the conventional knockout mouse models is often hampered by embryonic lethality or developmental aberrations. To circumvent these complicating factors associated with loss-of-tumor suppressor gene function we have generated a series of conditional tumor suppressor gene knockout mice. We have explored methods to switch the genes in a time-controlled and tissue specific fashion. Both transgenesis and somatic gene transfer was used to express Cre recombinase in the desired tissues. This technology permits us to induce specific tumors, to correlate specific genetic lesions with phenotypic characteristics, and hopefully to generate better models for testing intervention protocols. In addition, these mice are valuable source of cell lines that can be tested with respect to parameters that can be better studied in vitro such as growth, cell cycle regulation, response to irradiation, resistance to apoptosis, and genomic instability.

Some of the general points mentioned will be illustrated on the basis of studies performed with compound conditional mutants. Genes studied in various combinations include pRb, p53, Nf2, and p107. Inactivation was directed to specific tissues such as photoreceptor cells (IRBP-specific expression), Schwann cells, the intermediate lobe of the pituitary gland and the mesothelial lining of the thoracic cavity giving rise to an array of tumors such as primitive neuroectodermal tumors, pituitary tumors, choroid plexus tumors, and mesotheliomas.