1.

COLORECTAL TUMORS: EXPERIMENTAL MODELS M.G. Brattain, D.E. Brattain, A.E. Levine, C. Crandall. Bristol-Baylor Laboratory, Baylor College of Medicine, Houston, Texas 77030 U.S.A.

The development of a large bank of human colon carcinoma cell lines was initiated from primary and metastatic specimens obtained from ~30 patients. Cell lines were successfully obtained from ~ 75% of the specimens and the biological properties exhibited by the various lines were reflective of the heterogeneity of the biological properties of the disease encountered in humans, but no single line could be considered to be representative of its corresponding tumor. The lines were classified into 3 broad groups on the basis of tumorigenic potential in athymic mice, xenograft histology and in vitro growth parameters including growth in semi-solid medium and polypeptide growth factor dependence in culture. Group I cell lines were highly tumorigenic, poorly differentiated as xenografts, had high cloning efficiencies in soft agarose and were non-responsive to exogenous growth factors for in vitro growth. Group III cell lines were poorly tumorigenic, well-differentiated as xenografts, had relatively low cloning efficiencies in soft agarose and were responsive to exogenous growth factors for in vitro growth. Group II cell lines had intermediate properties with respect to these parameters. Endogenous inhibitory and stimulatory polypeptide growth factors were isolated from selected cell lines. The characterization of these activities with respect to the groups of colon carcinoma cell lines indicated that a 6kd inhibitory factor was able to induce a reversible differentiation-like response in Group II and III cells but had no effect on Group I cells. This factor referred to as tumor inhibitory factor (TIF) was trypsin and DTT sensitive but stable to acid. The factor was partially purified by chromatography on Bio-Gel P-10 and reverse phase HPLC on μBondapak C_{18}. Supported by NIH grants CA34432 and CA38100.

2.

CONTRIBUTION FROM THE POPULATION-BASED TUMOR REGISTRY. F. Levi et al., for the Vaud Tumor Registry, University Institute of Social and Preventive Medicine, CHUV 1011 Lausanne, Switzerland and the Swiss Tumor Registries Association, Monbijoustrasse 61, 3007 Berne, Switzerland.

The word "registry" actually is used to designate two main kinds of institutions which differ greatly in type and finality whether in organization or in methodology. These are 1) Hospital Registries and 2) Population-based Registries. Their respective peculiarities are reviewed and summarized. In Switzerland, data are available from six population-based cancer registries, three in the German-speaking area (BS-BL, SG-AP, ZH) and three in the French-speaking area (GE, NE, VD). Together they cover 45% of the Swiss population.

Such registries can contribute to "cancer control" at three main levels: descriptive, analytical and experimental, i.e. prevention program evaluations. At the descriptive level, they provide a valid estimate of incidence by e.g. age, sex, subsite, residence and time. Furthermore, survival data (stratified according to age, sex, stage, type of hospital and method of treatment)based on a complete registry area provide important clues both to the clinician and the public health officer regarding cancer therapy and use of various cancer services. At the analytical level, insight into etiology can be gained by studies designed to test hypotheses (case-control either/or prospective) such as e.g. on the role of dietary factors on the occurence, growth and malignant transformation of colorectal polyps. Prerequisite for such studies is a unified methodology and approach provided by the Registries. Finally, at the experimental level, cancer registry may participate either in the evaluation of programs for the detection of cancer and precancerous conditions or even in primary prevention.

3.

EXPRESSION OF CELLULAR ONCOGENES (C-ONC) IN COLONIC TUMORS AND NORMAL COLONIC MUCOSA. M. Monnat*, M. Garcia, G.Mieschen, H. Diggelmann, P. Saraga* and J. Costa*. Institute of Pathology*, University of Lausanne and Swiss Institute for Experimental Cancer Research, Lausanne, Switzerland.

Tumors of the colon are a suitable human material to study malignant progression : some investigators have suggested that dysplasia of different degree of severity may correspond to successive steps in the evolution to carcinoma. Others have found enhanced expression of four c-onc genes, i.e., c-myc, c-fos, c-Ha-ras and c-Ki-ras, in a majority of colonic carcinomas. We have therefore undertaken a prospective study comparing the levels of mRNA expression of these c-onc genes in malignant tumors with the ones expressed in normal mucosa and in the occasional benign polyp found in the same operative specimen. Immediately after operation, samples from tumor and normal mucosa are dissected free of necrotic or adjacent tissues and are then snap frozen. Tissues from the same areas are prepared for histology in an attempt to correlate c-onc-gene expression with morphological alterations. Our preliminary results in 8 cases studied indicate that : 1. no gene amplification or rearrangement can be detected in the tumors with probes for c-myc, c-fos, and c-Ha-ras; 2. increased transcription of these onc c-genes was found in 3 of the cases; 3. cases with increased transcription could not be distinguished histologically from the "negative" group.

4.

IN VITRO GROWTH OF LARGE BOWEL TUMOR CELLS IN SEMI-SOLID MEDIUM

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181 surgically removed colorectal tumor specimens were analyzed for their in vitro colony formation and chemosensitivity by the Human Tumor Colony Assay developed by Hamburger and Salmon. 37 (20%) of these tumors were not evaluable due to contamination (n=30), presence of aggregates (n=5) or insufficient cell yield (n=2). Of the remaining 144 tumors, 96 primary tumors and 48 liver metastases, 46 grew less than 5 col./plate and 24 tumors 5-25 col./plate, and were thus not evaluable for drug sensitivity studies (39%). However, 74 tumors (41%) were successfully assayed for in vitro sensitivity. Sufficient growth for drug testing (>25col.) occurred more frequently in the metastatic lesions (28/48 liver metastases ≙58% versus 46/86 primaries≙48%).

In vitro chemosensitivity of standard anticancer agents reflected the clinical single agent chemotherapy response rates. Of particular interst may become the sensitivity testing in unresectable liver metastases, for these patients are often treated by intraarterial loco-regional chemotherapy. For 8 out of 9 such patients so far evaluable the in vitro assay predicted the clinical response correctly.