of T2D4 cells exposed to the 3T3-F were capable of transmitting the proliferative signal to naive T2D4 cells, within 15 min. The possibility of a relationship between the fast acting mitogen (FAM) in the T2D4 supernatants and immunoglobulin binding factor (IBF) was tested. IBF is a soluble form of FcR, released by T2D4 cells, with culture conditions similar to those allowing the release of FAM. Indeed, the exposure of T2D4 cells to the 3T3-F enhanced the release of IBF, shown to be acting as a self mitogen.

DEVELOPMENT OF NON-TUMOURIGENIC HUMAN MESOTHELIAL CELL LINES WITH TRANSFECTED SV40 LARGE T ANTIGEN GENE

R.Reddel, Y.Ke, M.McMenamin, B.Gerwin, J.Lechner and C.C.Harris

Laboratory of Human Carcinogenesis, NCI, NIH, Bethesda, MD 20892, U.S.A.

Human mesothelial cells were obtained from pleural effusions or ascites fluids of patients with non-malignant conditions, and transfected with a plasmid, pRSV-T, containing the SV40 large T antigen gene and the Rous sarcoma virus long terminal repeat. Colonies of morhologically transformed cells occurred with a frequency of 1 to 2 x 10^{-4} transfected cells; transformed cells were not seen in control cultures. Individual colonies were isolated and cultured. These cells retained electron microscopic features of mesothelial cells, and all expressed keratin, vimentin and SV40 T antigen as detected by indirect immunofluorescence. The cells were aneuploid but most had near-diploid chromosome counts. For all cultures studied, the time to senescence was extended (60 to 70 population doublings (PD), 140 days) compared to normal mesothelial cells (15 PD, 30 days). For at least one culture, cells have escaped senescence and appear to be immortalized. Injection of 5 x 10^6 cells per site into nude mice has yielded no tumours after 6 to 12 months. Experiments are in progress to determine the response of these cells to asbestos and to transfection by other oncogenes and growth factor genes.

PHOSPHORYLATION OF L-TYPE PHOSPHOFRUCTO-KINASE IN HUMAN GLIOMAS

G.Rijksen, A.Kalff, E.C.Heesbeen, C.W.M.van Veelen and G.E.J.Staal

University Hospital, Utrecht, The Netherlands

The activity of the enzyme phosphofructokinase was decreased in human gliomas in comparison to normal brain. This decrease was accompanied by a relative increase in the expression of the L-type subunit of the enzyme. In addition, this particular subunit could be phosphorylated, most probably by a cAMP-independent protein kinase. This phosphorylation could not be detected in normal brain. The tumour enzyme appeared to be less sensitive to citrate inhibition and, more importantly, more sensitive to the activation by fructose--2,6-bisphosphate. The enzymes from tumour and normal brain showed no significant differences in their affinity towards the substrate fructose-6-phosphate. The results suggest an altered regulation of glycolysis in human gliomas by a reversible, cAMP-independent phosphorylation of phosphofructokinase.

DNA ADDUCTS IN MOUSE AND RAT EPIDERMIS VERSUS DERMIS AFTER TOPICAL APPLICATION OF (±)-TRANS7β,8α,-DIHYDROXY-9α,10α,-EPOXY-7, 8,9,10- TETRAHYDROBENZO(a)PYRENE AND (±) BENZO(a)PYRENE- 4.5-OXIDE

M.Rojas and K.Alexandrov

Institute de Recherche sur le Cancer, BP No. 8. F-94802, Villejuif, France

Mice and rats were treated topically with the BP metabolites, (±)-7β,8α,-dihydroxy-9α,10α,-epoxy-7,8,9,10-tetrahydrobenzo(a)pyrene (anti-BPDE) and (±) benzo(a)pyrene-4,5-oxide (BPO). Rat epidermal DNA was extensively modified by BPO, while mouse epidermal DNA was preferentially modified by anti-BPDE. Anti-dGuo adducts were observed only in mouse dermal DNA. DNA adducts were absent from the rat dermis. This adduct formation could produce the significantly different biological effects observed in vivo in the two species.

BREAST CANCER RISK FACTORS IN FINLAND AND THE UNITED STATES

D.P.Rose, K.Laakso, E.L.Wynder(1) and K.Kettunen(2)

(1)American Health Foundation, Valhalla, New York, U.S.A.; and (2)University Centre Hospital of Kuopio, Kuopio, Finland

Breast cancer (BC) incidence is lower in Finland than in the United States, yet both popoulations have the same high dietary fat intake, a suspected risk factor for this tumour. To explore this discrepancy, other potential risk modifiers were compared in 286 healthy women and 124 BC patients in New York (NY) , and 163 healthy controls and 106

cases in rural Kuopio. Menarche occurred earlier in both the NY cases and controls, but menarcheal age of the cases in the 2 locations did not differ from that of the corresponding control groups. Menopausal age was similar in all 4 groups. More NY women were nulliparous, with no difference between cases and controls; in Kuopio more BC patients were nulliparous ($p<0.05$). Age at first pregnancy occurred later in the cases than controls in both locations. Breast feeding was practiced more frequently and for longer in Kuopio, but fewer cases than controls had breast fed ($p<0.001$). There were no differences in body weight between the 4 groups. The small differences in reproductive risk factors appear insufficient to explain the higher BC risk in the United States, which may be due to modifying dietary factors such as fiber intake.

ANALGESIC ACTIVITY OF CALCITONIN IN PATIENTS WITH PAINFUL OSTEOLYTIC METASTASES OF BREAST CANCER

Anton Roth and Krsto Kolarić

Central Institue for Tumours and Allied Diseases, Zagreb, Yugoslavia

The analgesic effect of salmon calcitonin was tested over 28 days in a double-blind clinical randomized controlled trial in 40 female patients with painful osteolytic metastases. The effect of calcitonin was monitored with respect to daily analgesic consumption, duration of pain, patients' functional capacity, patients' own assessment of pain, and assessment of efficacy by the investigator. Statistically significant differences were established in terms of reduced analgesic consumption, shorter duration of pain and the patients' subjective assessment of pain duration and intensity. The objective assessment of the analgesic effect of calcitonin by the investigator showed the drug to be extremely useful in 3 patients and moderately useful in 11 patients. No changes were observed in serum calcium levels; there were likewise no skeleton changes as established by X-rays and bone scintiscans before and at the end of treatment. The trial has shown calcitonin to produce a pronounced analgesic effect in breast cancer patients with painful osteolytic metastases.

TWO SUB-SETS OF SIGNET RING CELL CARCINOMA IN RAT COLON

C.Rowlatt and J.P.Cruse

Imperial Cancer Reserch Fund and Royal Free Hospital Medical School, London, U.K.

A dimethylhydrazine-induced colon carcinoma in rat, composed entirely of dissociated locally invasive signet ring cells (SRC) or their precursor cells, has been investigated. The single ultrastructural difference from the normal epithelium is absence of junctional complexes, apparently allowing both cellular mobility from the epithelial sheet and loss of polarity with failure to secrete. Such a uniform tumour demonstrates an effective neoplastic process, with mobile precursor cells maturing to SRC.

In contrast a typical invasive mixed adenocarcinoma with SRC has tight junctions preserved in the loose glandular structure, loss of polarity, and retained secretion in SRC.

This comparison illustrates two sub-sets of SRC carcinoma, and intra-cytoplasmic lumens may provide a third. Their differential prognosis awaits a properly targetted survey. The absent junction in SRC may confer the extra invasiveness.

SMALL CELL LUNG CARCINOMA (SCLC): A SYSTEMIC DISEASE

J.-C.Salomon

C.N.R.S., P.B. 8, 94802 Villejuif, France

As a complement to the cellular hypothesis of SCLC, we propose a neuroendocrine or systemic hypothesis.

ASSUMPTION: The toxins which play a role in lung carcinomas induce central neuroendocrine lesions leading to a deficit in peptide hormone production that result in bronchial hyperplasias and dysoplasias.

HYPOTHESIS: As a consequence of this deficit, the stimuli which normally control the production of peptide hormones are increased. The next target cell for these stimulating factors are bronchial cells at the level of toxin induced structural derangements. Those bronchial cells which are programmed to respond to neuroendocrine signals, regardless of their embryological origins (Kulchitsky cells) multiply and produce compensatory peptide hormones. However, since these cells in adult hyperplastic or dysplastic bronchi are not equipped to manufacture perfectly active hormones, they are not able to provide the feedback control of stimulating factor production. The neuroendocrine systemic hypothesis has therapeutic corollaries which probably provide the most accessible framework in which to devise experiments for testing the hypothesis.