METABOLISM OF BENZO(a)PYRENE IN HUMAN EMBRYONIC FIBROBLASTS (ICP-23). N.Voiculetz, M.Vasilache, M.Sbenghe, N.Gaicu[1], D.Petrasincu[1] and D.Galdean. Institute of Oncology, [1]Institute Dr. I. Cantacuzino, Bucharest, Romania.

Recent data has indicated that human dermal fibroblasts do not activate benzo(a) pyrene (BP) (Kuroki et al., Cancer Res., 42, 1859, 1982). We have investigated whether human embryonic lung fibroblasts (ICP-23 cells) have the ability to metabolize BP. The methods used were: measurement of unscheduled DNA synthesis (UDS) using the incorporation of ^{3}H-TdR in the presence of hydroxyurea, and the mutagenicity of BP activated by S-9 fraction of ICP-23 cells on S.typhimurium, TA 100 strain under specific conditions, BP induced levels of UDS in a dose-related fashion, with a peak at 10^{-5}M (50%). A marked increase in UDS (30-40%) was noted when benzo(a)anthracene (13µmols/ plate) was used (20 hr before) as an inducer of BP metabolizing enzymes.

The preincubation of BP with the S-9 fraction of ICP-23 cells (15 min, at 37°C in the presence of NADPH) led to a significant number of his^{+} revertants.

The data thus obtained suggest that in contrast to human dermal fibroblasts, the human embryonic lung fibroblasts are able to metabolize BP and to induce their own drug metabolizing enzymes.

THE ROLE OF MINOR FAECAL BILE ACIDS IN THE AETIOLOGY OF COLON CANCER.
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Bile acid metabolites having a 4 ene-3-one or a 4,6 Diene 3-one configuration have been implicated in the aetiology of colon cancer. The production of these metabolites by intestinal organisms has been demonstrated in vitro, but they have not yet been isolated from human faeces. It is likely that in the anaerobic environment of the gut such metabolites have only a transitory existence, being reduced to saturated metabolites with the possibility of inversion of the geometry of the A/B ring junction to produce 5α bile acids. In the present study faecal samples were solvent extracted and subjected to chromotography on DEAP sephadex, followed by passage through a column of alkoxpropyl sephadex. Fractions were characterised by capillary g.c., and g.c.m.s. A large range of 5β bile acids have already been identified, including 3α, 3β, 3 oxo, 12 oxo, 3α OH 5 ene, among the monosubstituted acids, all of the theoretically possible 3, 12 isomers, and various epimers of 3,6,3,7 and 7,12 disubstituted acids, and several 3,7,12 trisubstituted isomers. Hydroxylated compounds containing 3 or 12 keto groups are also abundant. The 5α bile acids identified most commonly were substituted in positions 3 and 12 and include 3α, 12α 3α 12β and 3α 12 keto. Unsaturated compounds of either ring geometry were found only in trace amounts; however the identification of 5α bile acids provides indirect evidence for the transitory presence of 4 ene intermediates in vivo.

LAMININ, A NON-COLLAGENOUS BASEMENT MEMBRANE COMPONENT IN HUMAN CARCINOMAS.
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Extracellular matrices and basement membranes interact with cells and influence their adhesion, growth and differentiation. Laminin (MW. 800,000 Daltons) has been identified and characterized as a major non-collagenous basement membrane protein. We have recently produced monoclonal antibodies against human laminin. In the present study we have investigated the presence of laminin in various human carcinomas using an immunohistochemical staining technique. We found a significant correlation of disintegration of the laminin-containing basement membrane of tumours with increasingly anaplastic appearance. This finding supports the notion that basement membranes may play a role in tumour invasion.