HEPATOCELLULAR MARKERS OF CARCINOGENESIS DETECTED SIMULTANEOUSLY BY BIOCHEMICAL AND HISTOCHEMICAL TECHNIQUES. H.Taper, J.de Gerlache, M.Lans and M.Roberfroid. Unité de Biochimie Toxicologique et Cancérologique, U.C.L. B-1200 Bruxelles, Belgium.

Simultaneous detection of hepatocellular markers of carcinogenesis by biochemical and histochemical techniques in the same cellular populations enables mutual control of both techniques as well as taking advantage of the specific values of each of them (quantification and localization). A technique has been elaborated for separate isolation of hepatocytes from neoplastic nodules and from the surrounding parenchyma of the same precancerous rat liver. Amongst various neoplastic markers the decrease of acid DNAse activity and increase of γ-GT in the nodular fraction versus surrounding demonstrated the best correlation for biochemical and histochemical techniques. Some discrepancies in the results of ATPase and glucose-6-phosphatase might be explained by phenotypical heterogeneity inside nodules and by contamination of surrounding fraction by hepatocytes deriving from altered foci.

IATROGENIC FACTORS IN HUMAN CARCINOGENESIS. B.Terracini
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A recent review by the International Agency for Research on Cancer lists 13 therapeutic drugs or groups of drugs with "sufficient evidence" for carcinogenicity in humans and 7 with "limited" evidence. Most evaluations relied upon analytical epidemiological studies. The present paper describes: 1. the patterns through which scientific evidence of carcinogenicity in humans of these substances has accumulated in time; 2. where possible, a comparison of carcinogenic doses and target organs between man and laboratory animals; 3. available knowledge on long-term effects on humans of other therapeutic drugs convincingly shown to be carcinogenic in laboratory animals. In considering epidemiological studies, a distinction is made between hypothesis-seeking and hypothesis-testing studies.

PHYSIOLOGICAL MODULATORS OF DIAMINE OXIDASE (DAO) ACTIVITY IN HUMAN MELANOMA CELL LINES: RELATIONSHIP WITH TUMOURIGENICITY IN NUDE MICE. N.Thomasset[1], G.A.Quash[2] and J.F.Doré[1]. [1]INSERM U.218, Centre Léon Bérard, 28 rue Laënnec, 69800 Lyon, France; [2]INSERM U.51, 1 place J. Renaut, 69008 Lyon, France.

Previous kinetic studies from this laboratory showed that the activity of DAO which converts putrescine into γ-aminobutyraldehyde in the degradative pathway of the polyamines, is increased in the highly tumourigenic lines (M_4Dau, M_3Beu) and that the Km value of DAO for putrescine is about 3 times greater in the highly tumourigenic cell lines (14 μM) than in the poorly tumourigenic cell lines (4.5 μM) (M_2GeB, M_3Dor). To determine whether physiological metabolites contributed to these altered kinetic findings the transamidinase pathway leading to guanidinoacetate and methyl guanidine, an inhibitor of DAO was examined. In the poorly tumourigenic cell line M_1Dor, methyl guanidine accounted for 93% of the metabolites formed from guanidinoacetate while in a highly tumourigenic cell line (M_3Dau), methyl guanidine accounted for 44%.

The contribution of these physiological metabolites to the modification of the kinetic properties of DAO and their involvement in the malignant growth of melanoma cells has been evaluated.