SOMATIC CODE AND CANCER

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More and more informational molecules (IM) are known, but most of them are apparently plurifunctional (hormones, factors, mediators, receptors ...). Interactions are complex beyond description.

We propose the following hypothesis:

(1) a language of functions does exist, of which the IM are only the words. In order to get a synthetic view it is necessary to decipher specific functional messages, not at the level of IM, but at the level of their associations in meaningful sentences;

(2) between the genome and IM, interactions are not hierarchical: genes and their products are closely linked, since many gene products are IM which activate or repress other genes. The linear structure of the genome is completely functional because it is integrated into a network.

In cancers, the association of a tumour and of pareneoplastic phenomena could be a "Rosetta Stone" giving an insight into the somatic code.

LOCAL PROTEOLYSIS IN MALIGNANT TRANSFORMATION AND TISSUE DESTRUCTION

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We have shown previously that components of the proteolytic machinary, pro-PA and (Lys)-plasminogen, bind to immobilized fibronectin and laminin. This led us to introduce the concept "directional proteolysis" which implies that both normal and malignant cells direct pericellular proteolysis to specific sites. In actively growing HT-1080 sarcoma cells, we found using immunofluorescence and immunoelectromicroscopy, that u-PA was confined to cell-cell and focal contacts, colocalized with vinculin. PA-inhibitor (PAI-1) was deposited in cultures of both HT-1080 cells and normal human fibroblasts on the substratum except at focal contact sites. The different distributions of PA and PAI-1 may permit PA-mediated focal (directional) proteolysis in the presence of large amounts of PAI in the cell periphery.

The same mechanisms of proteolytic activation that operate in cancer also appear to act in other tissue destructive processes. We have identified plasmin in the tear fluid of patients with therapy-resistant corneal ulcers. Aprotinin inhibited this activity and was successfully used in patient treatment.

DETERMINATION OF ADDUCTS BETWEEN STYRENE OXIDE AND N-7 GUANINE WITH ACETYLATION METHOD IN VITRO

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Styrene is an important monomer in the plastics and rubber industry. The natural metabolite of styrene oxide is styrene 7,8-oxide. The products of deoxynucleosides and DNA with styrene oxide are well characterized in vitro. Styrene oxide reacts through the $\alpha$ and $\beta$ carbon and four isomeric products are formed.

We have been developing a more sensitive method to detect the products of styrene oxide with N-7 guanine. The formation of two acetyl derivatives of N-7 alkylguanine were observed and isolated by HPLC analysis. The mass spectral and chemical investigations suggested the binding of acetyl group into N2-position of N-7 alkylguanine and into hydroxyl group of styrene oxide.

Furthermore we have incubated in small reaction vessels nanomolar amounts of tritiated acetic anhydride with N-7 alkylguanine. The bound [3]H-acetic anhydride can be estimated by using the internal standard.

ANTIGENOTOXIC EFFECT OF PHENOLIC ANTIOXIDANTS OF BENZO(a)PYRENE IN SOS CHROMOTEST IN THE PRESENCE OF S9 FRACTIONS OF MOUSE LIVER UNDER VARIOUS INDUCTIONS

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The new bacterial test SOS Chromotest was used to study the in vitro effect of the antioxidants, butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) on the genotoxicity of benzo(a)pyrene (BP). BP was activated by the S9 liver fraction of mice in the basal state and induced with 3-methylcholanthrene (MC) or Aroclor 1254. Results from our experiments demonstrated that genotoxicity of BP was decresed by BHA and BHT and this inhibitory effect depends on S9 fraction. The highest and lowest inhibition was observed when BP was