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—SPECIAL ADDRESS I—

ANTIGENIC PROFILES OF CARCINOMA CELLS OF HUMAN GASTROINTESTINAL TRACT, AS DETECTED BY IMMUNOFLOUORESCENCE TECHNIQUES

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The immunochemical profiles of the malignant state of a variety of cells and tissues were first reviewed by E. D. Day in 1965: *Antigenic deletion*, where any isoantigens or organ-specific antigens of a normal tissue are lost during malignant transformation. Uncontrolled growth of malignant cells may be due to the loss of certain cellular constituents that enable normal cells to respond to regulative stimuli. *Antigenic diversion*, where the profile of the normal tissue of origin is replaced by that of other normal tissue, as is well-known from cases of enzyme excursion. *Antigenic reversion*, where the profile of the embryonal state is recapitulated in the malignant state. The embryonal alpha-globulin reported by Avelev et al. is an excellent example of this. In this review, however, only a few references to the gastrointestinal tumors were cited.

According to Day's indications and suggestion, we carried out analyses on some antigenic profiles of carcinoma cells in the gastrointestinal system, on the basis of examination of the distribution of mucosal glycoprotein.

Because of the complex nature of tissue antigens, the studies concentrated primarily on purification of specific antigenic components of carcinoma cells, as well as chemical and immunochemical characterization of these components.

The direct immunofluorescence technique, using the fluorescein isothiocyanate-labeled antibodies against isolated individual antigens, was employed to investigate their immunohistological localization.

The present address involved five questions selected from our studies, and a summary was made as follows.

I. Gastric mucosal glycoprotein, a product of mucous cells in normal gastric mucosa and Brunner's cells in the duodenum, was the fucomucan-type in chemical nature and present in less- or un-differentiated carcinoma cells of the gastrointestinal tract. However, it was not found in well-differentiated ones having an ordered glandular structure. Though it runs contrary to the thesis of antigenic

deletion, this result might suggest that such a mucous material could be an essential product for the maintenance of the viability of these incompletely differentiated cells.

II. Intestinal mucosa-specific mucosal glycoprotein, a product of goblet cells in normal intestinal mucosa, was the sialomucan-type one and was present only in gastrointestinal carcinomas with less orderly arranged glandular structures which were similar to the gastric mucosal glycoprotein. It was also present in the intestinalized gastric glands.

The sharp disappearance of the mucosal glycoprotein detected in the intestinalized gastric carcinoma cells and the co-existence of gastric and intestinal mucosal glycoprotein found in the low-differentiated carcinoma cells were accounted for in the former as a profile of antigenic deletion from the metaplastically differentiated cells and in the latter as one of antigenic diversion.

III. Placental alkaline phosphatase isoenzyme was present in carcinoma cells of both the differentiated and undifferentiated type in the gastrointestinal tract, but found in neither the intestinalized cells nor in the connective tissue components.

The present immunohistological techniques could distinguish the alkaline phosphatase isoenzymes in carcinoma cells and other types, including intestinalized epithelial cells. This seemed to indicate the difference in the mode of proliferation between carcinoma and intestinal metaplasia or the normal gene expression in cancer.

IV. Serum glycoprotein was found to attach firmly to carcinoma cells as 'Symbodies', resulting in immunological unresponsiveness.

The unequivocal mechanism for explaining why it attaches exclusively to malignant cells and how firmly it attaches is, however, still unknown.

V. Crossreacting antigen between gastric tumor and some normal proliferating cells (some lymphocytes of the spleen and bone marrow, alveolar epithelial cells of the lung) was demonstrated on immunofluorescent tissue preparations. Its amino acid composition was similar to CEA and NCA (non-specific crossreacting antigen, P. Burtin), but not to the gastrointestinal glycoprotein. The antisera against those antigens proved to be different from each other in terms of antibody activity.

Regardless of the presence of this antigen in the normal tissue cells mentioned above, it was always absent in any cells of normal gastrointestinal mucosa which were highly proliferative but arranged in ordered glandular structure.

Occurrence of such an antigen in malignancy might refer to an ectopic antigen production (antigenic diversion), shared commonly with some genetically-active cells in their certain differentiating stage.

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—SPECIAL ADDRESS II—

**TUMOR CELL SURFACES: SOME CHARACTERISTICS
OF NEOPLASTIC CELLS THAT DETERMINE STATES
OF TRANSFORMATION AND MALIGNANCY**

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Both normal and neoplastic cells are surrounded by fluid, dynamic plasma membranes which are involved in a variety of important physiological processes. Although several modifications in composition, organization, dynamics, enzymology and immunology have been found in transformed and tumor cell membranes when compared to their untransformed and normal cell counterparts, few of these changes may be important in the actual survival, growth and spread of tumor cells *in vivo*. One of the most important characteristics of malignant cells *in vivo*—the ability to metastasize to distant host sites—provides an important approach for studying *in vivo*