I. INTRODUCTION

Immunodiagnosis of cancer may provide an early and objective diagnosis, and aid in staging, monitoring treatment and clinical follow-up of cancer patients. It also may lead to a new classification of human neoplasia based on immunohistogenesis.

Two different approaches have been used to detect tumor-associated antigens of relevance in immunodiagnosis: 1) Immunohistochemistry (using tissue sections) (1,2); and 2) Immunochemistry of body fluids (especially blood plasma or serum and urine) (3,4). Unfortunately, serum and urine are not stored frequently at the initial diagnosis, whereas fixed and/or frozen tissues are usually available for most cancers.

Conventional histochemistry was used in an attempt to produce specific tissue and/or tumor markers, and it has been of some value in the classification of certain tumors. Unfortunately, these markers lack specificity and they have not been found to discriminate between normal and tumor cells.

In contrast, the introduction of immunohistochemical methods has permitted many applications where high resolution and sensitivity are required, using antibodies (Ab) as powerful probes for localization of tissue antigens (Ag).

Heterologous and autologous antisera raised against carcinoma and sarcoma lesions were used to distinguish tumor-associated Ags from other nonrelated Ags (5,6). With the advent of the hybridization technique and the production of monoclonal antibodies (mAb), described by Kohler and Milstein (7), immunohistochemical methods have become very powerful. Highly specific markers have been produced that offer promise in fundamental as well as applied aspects of human tumor biology and immunopathology (8-10).

It is becoming increasingly evident that differentiation Ags and tumor-associated Ags, as well as protein products encoded by oncogenes, play some
role in the development of human cancer (11). Because they reflect the origin and function of the tumor, mAbs to these Ags are potentially of value to the pathologist to characterize and subclassify undifferentiated and like-appearing tumors of different origins or different clinical behavior. While it is possible that a single highly specific Ab will recognize a particular tumor, most cancer probably will require a battery or panel of several antibodies for their identification and subclassification.

Ultimately, we anticipate a new subclassification of human tumors based on their immunohistogenesis. The value of this subclassification will be determined by correlation with clinical and conventional pathologic features, rate of tumor progression and metastases, response to therapy and prognosis. If highly restricted Ags detected by these mAbs are identified it is conceivable that they may also be of value for clinical imaging (12) and/or immunotherapy (13,14).

2. GENERATION AND ANALYSIS OF MONOCLONAL ANTIBODIES

The strategy followed at Memorial Sloan-Kettering Cancer Center to analyze Abs which will be used in future research and clinical projects is as follows:

a) Antibody specificity is determined by serology on panels of over 100 established human cell lines. They include short term cultures of normal cells, as well as panels of carcinomas, sarcomas, melanomas and lymphomas.

b) Antigen characterization is studied by immunoprecipitation and/or immunoblotting tests.

c) Antigen distribution is analyzed using frozen and paraffin-embedded tissue sections on panels of normal human fetal and adult tissues.

d) Antigen expression and/or modulation is studied using frozen and paraffin-embedded tissue sections on panels of human tumors, including carcinomas and sarcomas.

The diversity of Ags and other molecules difficulty (if not impossible) to be identified using conventional histology and subjective interpretation, has been the main reason for the approach presented above. Detailed description of the methods used has been previously reported (15-17).