PROGRESS IN NUCLEOMEDICAL UTILIZATION OF MONOCLONAL ANTIBODY (MoAb)

The purpose of this study was to study the molecular structure of human thyroglobulin (Tg) and to develop a MoAb against Tg.

Six MoAb were prepared using hybridoma cells of mouse myeloma cells and spleen cells and the binding sites of these MoAb on the surface of Tg molecule were investigated using radioimmune blocking assay. Normal Tg coated wells were incubated with MoAb and a inhibitor, such as various iodine content Tg, rat Tg and Tg and inhibitors of binding of MoAb to Tg by these inhibitors were examined. The results of this inhibition study showed that Tg presents on the surface of Tg molecule and that iodine related portions of human Tg share antigenicity with rat Tg and that iodine related portions do not.

In order to develop MoAb able to measure Tg in the presence of Auto Ab, only one MoAb which does not cross react with Auto Ab and has high binding affinity for and specificity for human Tg could be obtained after making hybridom 

c times and screening approximately 20,000 wells. Using this MoAb, a RIA for Tg has been developed employing sandwich method. The 96 well plates were coated with MoAb and serum or standard samples were added after blocking these wells with bovine albumin solution and 125I MoAb was added after washing the wells. The sensitivity of this method to detect serum Tg was as low as 4ng and Auto Ab did not interfere with standard curves. Dilution curves of serum Tg with Auto Ab showed a straight line and the recovery rate of added Tg into Auto Ab positive serum was about 90%. The concentrations of serum Tg measured by a conventional RIA were compared with those by this method. A good correlation was observed in Auto Ab negative samples, but the serum Tg concentrations by the conventional RIA were clearly lower than those by this method in Auto Ab positive samples. The results suggest that the measurement of Tg in the presence of Auto Ab can be possible in this method. In summary, MoAb is very useful clinically and laboratorily.

CURRENT STATUS OF RADIOIMMUNODIAGNOSIS IN THE UNITED STATES.

The number of presentations concerned with monoclonal antibodies increased and reached 65 in number, or about 10% of the total presentations, at the recent meeting of the Society of Nuclear Medicine of Houston, 1985. Anti melanoma, cancer, ovarian cancer, prostatic cancer, B-cell lymphoma, cutaneous T-cell lymphoma, and soft tissue sarcoma antibodies were reported for clinical application.

The detection ratio with these antibodies varied from 40-90%. An interesting approach, immunolymphoscintigraphy, was described and showed promising results. While no severe side-effects have been reported to date regardless of the route of administration, a significant number (22of 47, 47%) of patients that received intact murine IgG developed a positive antinouse antibody test. Two groups reported regression of T-cell lymphoma or renal cell carcinoma when treated with I-131 labeled specific monoclonal antibody (MoAb). Techniques of radio-labeling were extensively discussed at this meeting. Antibodies were found to have better in vitro and in vivo behavior when iodinated at less than 1 to 10 ug and conjugated with DTPA at less than 5 to 1. Newer chelating agents such as BrEDTA, heterobifunctional reagents and so forth were described.

Pharmacokinetic studies revealed that the biodistribution of some MoAbs is dose-dependent, that is, larger doses of intact antibody delay the blood disappearance.

Differences in the biodistribution of In-111 labeled and iodide labeled antibodies were described. The uptake in the liver and tumor were higher with In-111 labeled MoAb. Multicompartmental modeling was applied to analyze the pharmacokinetics of these different circunstances. A nonlinear, saturable antibody processor was demonstrated. Simulation curves of blood disappearance for different amounts of administered antibody clearly showed dose dependency. Recently several MoAbs labeled with In-111 have become available in kit from (Hybech Inc.) and have been used in clinical trials. Anti melanoma or prostatic cancer MoAbs have shown very promising results in the imaging of patients.