ABSTRACT

The present work describes the purification of tumor-associated antigens (TAA) from female and male breast cancer patients, their immunological and physicochemical properties, and relatedness to murine mammary tumor associated antigens.

By DEAE cellulose discontinuous NaCl gradient chromatography of crude extract of human malignant breast tumor from female patients, 3 major protein peaks were obtained. Circulating antibodies against one of the protein peaks, HF₁, was observed in female breast cancer patients. The antibodies were absent in patients with carcinoma of uterine cervix, lung, stomach and liver or benign breast diseases and in healthy women. Absorption of the sera of breast cancer patients with normal human breast tissue pellet did not remove the HF₁-reactive circulating antibodies.

The breast tumor associated antigen (BTAA) was partially purified from HF₁ by subjecting the fraction to SDS-PAGE and eluting the band 3 (HF₁-3). Western blot analysis confirmed the presence of the BTAA in HF₁-3. Using an affinity column of protein A-Sepharose bound IgG, purified from breast cancer patients' sera, the BTAA was also recovered from HF₁. Purification of the BTAA was achieved by subjecting HF₁ to sephadex G-100 gel filtration and size-exclusion high performance liquid chromatography (SE-HPLC). The antigen was characterized as a highly thermostable glycoprotein with a MW of approximately 85 Kd and appeared not to be related with either murine mammary tumor virus (MuMTV) structural antigens or human fetal antigens. But BTAA was found to be cross-reactive with an 83 Kd murine mammary tumor associated antigen (MTAA) purified from MuMTV induced spontaneously arising murine mammary tumor in C₅7/7H/Jax mice. The BTAA reactive circulating antibodies in the female breast cancer patients were of IgG₂ subtype and the level of the antibodies significantly decreased in patients following surgical removal of their breast tumors.

An attempt was made to explore presence of BTAA specific antibodies in male breast cancer patients, as was observed in female breast cancer. But no circulating antibodies were observed against BTAA in
male breast cancer patients' sera. However, circulating antibodies were observed in these patients against the DEAE fraction 3 (HF\textsubscript{3} and MF\textsubscript{3}) of both human malignant breast tumor and murine mammary tumor tissues. A 70-72 Kd antigenic component purified from these two fractions was found to be specifically reactive with the sera of male breast cancer patients. Negligible levels of antibodies were found against these two fractions in the sera of normal healthy male individuals. Both the fractions HF\textsubscript{3} and MF\textsubscript{3} were found to react strongly with anti-MuMTV serum.

These observations strongly indicated possible association of MuMTV with breast cancer of both men and women. However, expression of different molecules as tumor associated antigens by the male and female breast tumors suggested that though MuMTV may be involved in carcinogenesis, the process of malignant transformation of the breast epithelium is different in these two sexes.