Symposium no. 1: Effector Cells against Cancer

1.025

CELL MEDIATED IMMUNITY (CMI) IN NON RELAPSED BREAST CANCER PATIENTS

A. Nicolini, A. Pieraccini, C. Tibaldi, *G. Meucci, C. Colombini, *L. Giuliani, **F. Ambrogi.

Istituto di Clinica Medica II, *Istituto di Clinica Chirurgica e **Istituto di Clinica Medica I dell'Università di Pisa.

In 101 N_0, 28 N_{1b}, 5 N_{2-3} breast cancer patients (pts) serum serial determinations of T_4, T_8, T_3, B, NK lymphocytic subpopulations and the T4/T8 ratio were post-operatively measured. The same parameters were determined in 15 others before mastectomy and in a control group. In most breast cancer pts T-lymphocytic function as well was serially investigated by IMC Multitest and compared to that of a control group. In all breast cancer subsets T_4, B and NK subpopulations were similar to those in the control group, while a significant T_3 decrease (65.6 ± 8, 65.3 ± 6, 64.4 ± 11, 62.3 ± 10 vs 71 ± 6 (M $\pm$ SD) respectively), T_8 decrease (22.4 ± 6, 25.5 ± 8, 25.3 ± 8, 22.5 ± 9 vs 28 ± 4) and T_4/T_8 ratio increase (2.2 ± 1, 2 ± 1, 2 ± 1, 2.3 ± 1.7 vs 1.5 ± 0.3) were found. In N_0 breast cancer subset T lymphocytic function was similar to that of the controls, while it progressively decreased in N_1, N_{2-3} and basal ones (score = 6.7 ± 2, 4.6 ± 1.8, 2.8 ± 1 vs 7 ± 3 (M $\pm$ SD) respectively). These data suggest: a) in non relapsed breast cancer pts T_3 lymphocytic subpopulation has decreased; b) the T_3 decrease mainly affects T_8 subpopulation with a tendency to T4/T8 ratio increase; c) in these pts CMI is preoperatively depressed and post-operatively it decreases if the risk of relapse is greater.

1.026

IMMUNODEFICIENCY AND SOLID TUMORS IN CHILDHOOD: POSSIBLE PATHOGENIC ROLE OF CYTOMEGALOVIRUS

G.Nigro, E.Properzi, S..Mattia, C.A.Cappelli, T.Perrone, A.Schiavetti, M.Artini°, A.Petruccelli, A.Clerico, R.Lubrano, C.Mondaini, M.A.Castello.
Pediatric Inst.,°I Clinica Medica,"La Sapienza" Univ.,Rome. Italy.

From January 1987 to March 1991, viral cultures and detection of CMV-DNA by PCR and CMV-specific antibodies by EIA in 32 children with solid tumors showed 28 CMV-infected patients (87.5%), of which 11 (34.4%) had productive infection, and in 16/35 control subjects (46%). Three infants, aged 1 to 3 years, showed concomitant CMV infection and tumor, and an 11-year old girl had CMV-associated persistent lymphadenitis for two years prior to the development of Hodgkin's lymphoma. All CMV patients showed relevant decrease of CD4+ cells and NK activity. Ganciclovir therapy was followed by clinical, immunologic and virologic findings, without significant adverse effects. CMV, being controlled by the immune system and yet capable of inducing immunosuppression, appeared to play a pathogenic role in our patients.

1.027

Three aspecific CTL clones lyse melanoma cells in presence of bispecific monoclonal antibody (bsmAb) CBT3xEp2.

P Nisticò, PG De Berardinis, LB De Monte, R Tecce, M Londei, I Malavasi, PG Natali.

BsmAb recognizing tumor associated antigen and CD3 structure offer a potent laboratory tool to analyze the cytotoxic potential of different subpopulation of effector cells to human tumors and may offer a new approach in cancer immunotherapy. To investigate whether the effector clones phenotype could affect the CBT3xEp2 mediated lysis of melanoma cells,three aspecific CTL clones isolated from the same healthy donor were tested against different melanoma target cells.In the presence of CBT3xEp2 all CTL clones were capable of inducing a specific lysis of all the melanoma cell lines tested,indicating that CBT3xEp2 can focus different effector cells on tumor target.Supported by A.I.R.C.

1.028

Isolation and characterization of cytotoxic T lymphocytes (CTL) clones derived from a patient with breast carcinoma.

P Nisticò, PG De Berardinis, C Full, S Morrone, T Alonzi, I Venturo, PG Natali.

The isolation and propagation in vitro of autologous CTL clones have been obtained in a number of malignancies. To obtain the same effectors in breast carcinoma bearing patient we co-coltivated the patients' PBL with autologous tumor cell (+PHA + 10U/ml IL2). In this way two stable CTL clones ($CD3^+$ $CD8^+$,and $CD3^+$ $CD4^+$) were isolated and expanded. They preferentially lyse the autologous target while unable to kill allogeneic tumors and NK-sensitive cells (K562). These findings provide experimental evidence that CTL to breast tumor can also be developed and analyzed in their mechanisms of target killing. Supported by A.I.R.C.

1.029

CELLULAR INTERACTIONS IN BREAST CARCINOMAS: STUDIES ON PRIMARY CULTURES. Ögmundsdóttir HM[1], Pétursdóttir I[1], Guðmundsdóttir I[1], Ámundadóttir L[1], & Petersen OW[2]. 1: Molecular and Cell Biology Research Laboratory, Icelandic Cancer Society, Reykjavík; 2: Dept. of Anatomy, Panum Institute, Copenhagen.

Breast carcinomas contain several different cell types including cancerous as well as normal epithelial cells, fibroblasts and cells of the immune system. Dickson and Lippmann (1987) have proposed a model of growth regulation in breast cancer involving hormones, peptide growth factors and "cross-talk" between stroma and malignant epithelium. This model extrapolates from analyses made *in vitro* on isolated breast cancer cell lines to the situation *in vivo*. In an effort to bring experimentation closer to human breast cancer we have used primary cultures of breast cancer epithelium directly in co-culture experiments with lymhpocytes and fibroblasts. Primary cultures were obtained from 30 out of 37 samples of breast carcinoma and 23 out of 28 samples of non-cancerous tissue from the same breast. Of 20 experiments with carcinoma samples maximal growth occurred once in the control, 11 times with lymphocytes, 6 times with fibroblasts and in 2 experiments no differences were seen. In 6 of these 20 phenotypically malignant cells were identified. In contrast out of 17 experiments with non-cancerous epithelium 8 showed no differences, 2 yielded most growth in the control, 5 with lymphocytes and 2 with fibroblasts. It is feasable to use primary cultures from breast carcinomas for experimentation. Initial results of co-culture experiments indicate that lymphocytes may stimulate the growth of breast cancer epithelium.

1.030

MINOR EPITOPES TO ELICITE SELF REACTIVE T CELLS: A TOOL FOR CANCER IMMUNE THERAPY?

Giovanni Pani, Marco Piastra*, Francesco Ria.
Inst. General Pathology and *Paediatrics, Catholic Univ., L.go F. Vito 1, 00168 Rome, Italy.

It has been shown that T cell tolerance induced by non self protein is restricted to few epitopes, namely the ones that are responsible for T cell response in immunization. These epitopes are called "major epitopes". However, other epitopes, that survive antigen processing, can still elicite an immune response in mice made tolerant to a given protein (F. Ria et al.: NATURE, 343 (1990), p. 381; G. Gammon and E. Sercarz: NATURE, 342 (1989), p. 183). Here we analyze the possibility of using such "minor epitopes" in order to induce immune response toward one self protein. Furthermore, we examine the capability of eliciting a cytotoxic response directed against a tumoral cell line that produces the protein.