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Effector Cells against Cancer

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PS 1.1

VARIABILITY OF T CELL RECEPTORS IN TUMOR INFILTRATING LYMPHOCYTES

Thierry HERCEND

One way to progress in the understanding of immune response against cancers is to better characterize T lymphocytes infiltrating the tumor sites (TIL). This is often attempted through the generation of IL2 dependent cell lines or clones derived from biopsies. A weakness of this approach relates to the potential selection in culture of minor cell populations which do not reflect the actual in vivo situation. To circumvent this problem, we have attempted to study directly, through molecular biology procedures, the repertoire of T cell receptors expressed by TIL in two model situations, melanoma and naso-pharyngeal carcinoma. A modified anchored polymerase reaction and conventional PCR with a library of relevant V specific oligonucleotides have been employed. The advantages and limitations of these methods will be discussed.

PS 1.2

ACTIVATION OF THE CYTOTOXIC EFFECTORS BY AUTOLOGOUS EX-VIVO SOLID HUMAN TUMORS. Vánky F., Wang P., Végh Zs. and Klein E.
Department of Tumor Biology, Karolinska Institute, Stockhlm, Sweden.

Ex-vivo carcinomas and sarcomas induced proliferation of autologous blood lymphocytes and activated their cytotoxicity. Activation required both the expression of MHC class I antigens and the presence of ICAM-1 on the tumor cells. Quantitative and qualitative alterations of the class I gene products was demonstrated on the ex-vivo tumor cells by isoelectric focusing (IEF). IFNγ induced biphasic elevation of the class I antigens, i.e. the early peak was followed by a transient decrease. Influenza virus haemagglutinin nucleoprotein peptides specific for A2 or B8 gene products induced assembly and membrane expression of the relevant gene products on a monophasic manner and stabilized the IFN-γ induced early expressed molecules.

Tumor cells induced for MHC class I antigen expression, generated cytotoxicity in the MLTC also against the original, untreated, class I antigen negative tumor cell aliquot which was not recognized by the ex-vivo blood lymphocytes.

PS 1.3

A new family of NK-specific surface molecules involved in human NK cell function.
Alessandro Moretta. Ist. Istologia ed Embriologia - University of Genova.

We recently described two monoclonal antibodies (mAb) termed GL183 and EB6. These mAbs stain 10-40% of peripheral blood CD3- CD16+ NK cells and react with distinct 55-58 kd surface molecules belonging to the same molecular family. Interestingly, GL183 and EB6 mAbs recognize different members of this family thus allowing to identify distinct subsets of human NK cells. Indeed, on the basis of GL 183 and EB6 expression, it has been possible to distinguish four phenotipically stable subpopulations: GL183+ EB6+ (double positive), GL183- EB6- (double negative) GL183+ EB6- and GL183- EB6+. The proportions of each NK subset was found to be different in different donors. Importantly, both mAbs selectively triggered the NK subset expressing the corresponding surface antigen to release lymphokines and to lyse tumor cells of different histotypes. In addition, a strict correlation has been found between the subset assignment and the ability of NK clones to specifically recognize and kill normal allogeneic cells. More recently, we selected a third mAb, termed 7A6, which appears to react with all the members of the GL183/ EB6 molecular family. It is of note that the analysis of the cellular distribution of the 7A6 determinant demonstrated the existence of the 55 - 58 kd molecules on the surface of all CD3- CD16+ cells, (including the "double negative" subset), thus indicating that all NK cells express members of the GL183/EB6 family of triggering surface molecules.

PS 1.4

ORIGIN AND REGULATION OF TUMOR-ASSOCIATED MACROPHAGES (TAM). Alberto Mantovani, Barbara Bottazzi, Francesco Colotta. Istituto di Ricerche Farmacologiche "Mario Negri", via Eritrea 62, 20157 Milan, Italy.

Macrophages are a major constituent of the lymphoreticular infiltrate of tumors. TAM are recruited from the blood in response to chemoattractant released by tumor cells. A tumor-derived chemotactic factor has been molecularly identified and belongs to the Cys-Cys family. Its molecular properties, producing cells and transduction pathways will be discussed. Gene transfer experiments have formally demonstrated that this cytokine can regulate the infiltration of macrophages.