Abstracts

Immunotherapy using T cell-engaging bispecific monoclonal antibodies (BiMAb) is a promising cancer therapy. Such BiMAbs bind simultaneously to immune effector cells and to a cancer-specific antigen on tumor cells, resulting in killing of the latter. Placental alkaline phosphatase (PLAP), a plasma membrane-bound glycoprotein, is one of the four members of alkaline phosphatase isozyme family. PLAP is encoded by the ALPP gene. PLAP is expressed in placenta and has not been detected in other normal tissues. It has been shown that PLAP is released into the serum of patients with PLAP expressing colorectal cancer cells. However, we have identified CD45 and CD43 cell surface glycoproteins as main binding targets on the cell surface of Jurkat cells. How- ever, recombinant CNL treated Jurkat T cells exhibited archetypal features of early apoptosis, homotypic adhesion, and induced caspases since none of the features of CNL-induced cell death was effectively blocked with the pan-caspase inhibitor or other peptidase inhibitors. In addition, CNL binding to PC3 cells has been shown to induce cell death in PC3-positive ones, indicating a bystander effect. The bystander effect on PLAP-negative cells is only visible after 48 hours of treatment, suggesting an indirect killing mechanism. The important to study bystander killing to target cancer cells immune killing escape. To investigate further the mechanism of bystander killing, our early findings suggest CD3 x PLAP BiMAb activated T cells induce killing on bystander killing. We are studying the effect of the T cells subtypes and of the soluble factors secreted by the activated T cells.

Disclosure Information N.S. Alrishedan: None. W. Bodmer: F. Consultant/Advisory Board; Moderate; ProMaB Biotechnologies. V. Liebe lastun: B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Moderate; Roche Glycart AG, Switzerland. V. Golubovskaya: A. Employment (full or part-time); Moderate; ProMaB Biotechnologies. J. Wu: A. Employment (full or part-time); Moderate; ProMaB Biotechnologies. A. Bransi: A. Employment (full or part-time); Moderate; Roche Glycart AG, Switzerland. P. Umana: A. Employment (full or part-time); Moderate; Roche Glycart AG, Switzerland. C. Klein: A. Employment (full or part-time); Moderate; Roche Glycart AG, Switzerland. R. Mateus Seidl: A. Employment (full or part-time); Moderate; Roche Glycart AG, Switzerland.

Poster Presentations

P01 Emerging concepts/new agents

P01.01 PLAP AS TARGET FOR CANCER IMMUNOTHERAPY – DEVELOPMENT AND PRECLINICAL CHARACTERIZATION OF BISPECIFIC MONOCLONAL ANTIBODY IN COLORECTAL CANCER IMMUNOTHERAPY

1NS Alrishedan*, 1W Bodmer, 1V Liebe lastun, 1V Golubovskaya, 1J Wu, 1A Bransi, 1P Umana, 1C Klein, 1R Mateus Seidl. 1Weatherall Institute of Molecular Medicine, Oxford University, Oxford, UK; 2ProMaB Biotechnologies, California USA, CA, USA; 2Roche Glycart AG, Switzerland, Switzerland

Immunotherapy using T cell-engaging bispecific monoclonal antibodies (BiMAb) is a promising cancer therapy. Such BiMAbs bind simultaneously to immune effector cells and to a cancer-specific antigen on tumor cells, resulting in killing of the latter. Placental alkaline phosphatase (PLAP), a plasma membrane-bound glycoprotein, is one of the four members of alkaline phosphatase isozyme family. PLAP is encoded by the ALPP gene. PLAP is expressed in placenta and has not been detected in other normal tissues. It has been shown that PLAP is released into the serum of patients with PLAP expressing colorectal cancer cells. However, we have identified CD45 and CD43 cell surface glycoproteins as main binding targets on the cell surface of Jurkat cells. How- ever, recombinant CNL treated Jurkat T cells exhibited archetypal features of early apoptosis, homotypic adhesion, and induced caspases since none of the features of CNL-induced cell death was effectively blocked with the pan-caspase inhibitor or other peptidase inhibitors. In addition, CNL binding to PC3 cells has been shown to induce cell death in PC3-positive ones, indicating a bystander effect. The bystander effect on PLAP-negative cells is only visible after 48 hours of treatment, suggesting an indirect killing mechanism. The important to study bystander killing to target cancer cells immune killing escape. To investigate further the mechanism of bystander killing, our early findings suggest CD3 x PLAP BiMAb activated T cells induce killing on bystander killing. We are studying the effect of the T cells subtypes and of the soluble factors secreted by the activated T cells.

Disclosure Information N.S. Alrishedan: None. W. Bodmer: F. Consultant/Advisory Board; Moderate; ProMaB Biotechnologies. V. Liebe lastun: B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Moderate; Roche Glycart AG, Switzerland. V. Golubovskaya: A. Employment (full or part-time); Moderate; ProMaB Biotechnologies. J. Wu: A. Employment (full or part-time); Moderate; ProMaB Biotechnologies. A. Bransi: A. Employment (full or part-time); Moderate; Roche Glycart AG, Switzerland. P. Umana: A. Employment (full or part-time); Moderate; Roche Glycart AG, Switzerland. C. Klein: A. Employment (full or part-time); Moderate; Roche Glycart AG, Switzerland. R. Mateus Seidl: A. Employment (full or part-time); Moderate; Roche Glycart AG, Switzerland.

P01.02 SELECTIVE INDUCTION OF CELL DEATH IN JURKAT CELLS WITH RECOMBINANT FUNGAL LECTIN CNL

1MM Perišič Nanut*, 1Ž Žurga, 1Š Konjar, 1M Prunk, 1J Kos, 1J Sabotić. 1Institute Jozef Stefan, Ljubljana, Slovenia; 2Faculty of Pharmacy, University of Ljubljana, Ljubljana, Slovenia


Background Due to their capacity to specifically recognize subtle alterations in glycoproteins on the cell surface lectins are increasingly being used in diagnostic (for identification of malignant or premalignant cells) and therapeutic purposes (for targeted drug delivery).

Materials and Methods We have previously isolated and biochemically characterized a fungal lectin Clitocybe nebularis lectin (CNL) . We have synthesized recombinant form of CNL and tested its effects on different human cell lines and primary cells using various biochemical and molecular biological assays.

Results CNL is a GalNAcβ1–4GlcNAc-binding lectin that shows an antiproliferative effect solely on the leukemic Jurkat T cells. Furthermore, recombinant CNL treated Jurkat T cells exhibited archetypal features of early apoptosis, homotypic agglutination but lacked the activation of initiating and executing caspases since none of the features of CNL-induced cell death was effectively blocked with the pan-caspase inhibitor or different peptidase inhibitors. In addition, CNL binding induced Jurkat cells to release the endogenous damage-associated molecular pattern molecule high-mobility group box 1 (HMGB1), which is typically associated with necroptosis. We have identified CD45 and CD43 cell surface glycoproteins as main binding targets on the cell surface of Jurkat cells. However, the blockade of CD45 phosphatase activity failed to block either CNL-induced homotypic agglutination or cell death. Remarkably, a plant lectin, Wisteria floribunda agglutinin (WFA), which shows similar specificity in ligand binding, showed less selective cytotoxicity and induced cell death in Jurkat cells, Tall-104 acute lymphoblastic leukemia, and Hut-