be used as a monotherapy or in combination with tumor-targeting monoclonal antibodies to trigger induction of anti-cancer immunity. DSP107 is currently tested in IND-enabling studies and clinical development is planned to commence in 2020.

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IFNY SECRETION OF ADAPTIVE AND INNATE IMMUNE RESPONSES IN AML

E. Bremer: Significant; KAHR Medical.

A. Chajut: None.

Y. Pereg: A. Employment (full or part-time); Significant; KAHR Medical.

Background Myeloid leukemic blasts can be converted into leukemia derived dendritic cells (DCleu) with blastmodulatory Kit-I and Kit-M, which have the competence to regularly activate T and immunoreactive cells to gain anti-leukemic activity or rather cytotoxicity. As innate and adaptive immune responses are notably promoted by the cytokine interferon gamma (IFNy), we hypothesised that the IFNy secretion could be a suitable parameter to display DC/DCleu mediated immunologic activity and even anti-leukemic cytotoxicity.

Materials and Methods DC/DCleu were generated from leukaemic WB with Kit-I (GM-CSF + OK-432) and Kit-M (GM-CSF + PGE1) and used to stimulate T cell enriched immunoreactive cells. Initiated anti-leukemic cytotoxicity was investigated with a cytotoxicity fluoroscopy assay (CTX). Initiated IFNy secretion of innate and adaptive immune cells (T cells, \( \tau^{CD4} \) +, \( \tau^{CD8} \) +, NK, \( \tau^{CD56} \) +, NK, \( \tau^{CD161} \) +, CIK, \( \tau^{CD56} \) +, CIK and iNKT) was investigated with a cytokine secretion assay (CSA). In some cases IFNy production was additionally evaluated with an intracellular cytokine assay (ICA). Conclusively, the IFNy secretion of immunoreactive cells was correlated with the anti-leukemic cytotoxicity.

Results Significant amounts of DC and DCleu as well as migratory DC and DCleu could be generated with Kit-I and Kit-M without induction of blast proliferation. T cell enriched immunoreactive cells stimulated with DC/DCleu showed an increased anti-leukemic cytotoxicity and an increased IFNy secretion of TN and NK and CIK cells compared to control. Both the CSA and ICA yielded comparable amounts of IFNy positive innate and adaptive immune cells. The correlation between the IFNy secretion of immunoreactive cells and the anti-leukemic cytotoxicity showed a positive relationship in T cells, \( \tau^{CD8} \) +, \( \tau^{CD56} \) + and NKCD56+ cells.

Conclusions We found blastmodulatory Kit-I and Kit-M competent to generate DC/DCleu from leukaemic WB. Stimulation of T cell enriched immunoreactive cells with DC/DCleu regularly resulted in an increased anti-leukemic cytotoxicity and an increased IFNy dependent immunological activity of TN, NK and CIK cells compared to control. Moreover the anti-leukemic cytotoxicity positively correlated with the IFNy secretion in T cells, \( \tau^{CD4} \) +, \( \tau^{CD8} \) +, NKCD56+ cells. We therefore consider the IFNy secretion of innate and adaptive immune cells to be a suitable parameter to assess the efficacy of in vitro and potentially in vivo AML immunotherapy. The CSA in this regard proved to be a convenient and reproducible technique to detect and phenotypically characterise IFNy secreting cells of the innate and adaptive immune system.

pretreated vs -untreated WB, suggesting a production/activation of (potentially leukemia-specific) cells after kit-stimulation. Moreover kit-pretreated WB regularly and significantly improved provision, activation as well as antileukemic and leukemia-specifically directed immune reactive cells after MLC. TEM showed exosome-like structures with a typically cup-shaped appearance without any differences between healthy and AML samples. iNTA revealed average vesicle sizes of 177 ±23 nm (healthy) and 178±17 nm (AML). Higher levels of EVs were detectable in AML samples compared to healthy controls in serum and after DC-culture, but lower levels after MLC independent of culture conditions.Interestingly, the number of EVs increased during cultivation of DC of AML and healthy samples, but not in AML-derived MLC samples.

Conclusions We will provide data in AML patients and healthy volunteers about a potential role of DCs- and MLC-derived exosomes as biomarkers in immune responses, malignant progression or as potential therapeutic targets for AML patients.


P01.12 IMPACT OF COMPLEMENTARY SUBSTANCES ON IMMUNE CELL ACTIVITY
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Background Natural substances and micronutrients are more and more included in anti-cancer therapy. However, benefit and harm both are reported from one and the same substance. This emphasizes the urgent need for the systematic analysis of a personalized approach which patient will profit from which substance.

Materials and Methods Risk analysis was performed using PBMCs isolated from patients diagnosed with advanced solid cancer. Benefit was analyzed using 3D-microtumors directly from which substance.

Results In 80% of the patients natural substances induced a metabolic inhibition (mean: 16.4%, range: 5.2–42.8%) immunotoxicity mediated by chemotherapy. Analysis of the 3D-microtumors indicated that natural substances can mediate an antitumor effect, which was most obvious in relapsed tumors heavily pretreated with chemotherapeutic drugs. In addition, natural substances were identified as chemosensitizer. For example, curcumin was found to increase efficacy of Mitomycin C in breast cancer, Bicalutamid in prostate cancer and 5-FU combined with Cisplatin in gastric cancer.

Conclusions Complementary substances have a different effect depending on dosing, timing, cell type and cell characteristics. Therefore preclinical testing is required to identify the most effective complementary substances for the individual cancer patient analyzing both immune cells and cancer cells.