and acute myeloid leukemic (AML) patients' ex vivo cell cultures, we correlated the cell biological data with the profiles of cell culture supernatants derived VOCs.

Materials and Methods DC/DCleu from leukemic or healthy whole blood (WB) were generated without (Control) or with immunomodulatory Kit M (Granulocyte-macrophage-colony-stimulating-factor (GM-CSF) + prostaglandin E1 (PGE1)) in dendritic cell cultures (DC culture). Kit pretreated/not pretreated WB was used to stimulate T cell enriched immunoreactive cells in mixed lymphocyte cultures (MLC culture). Leukemia-specific adaptive and innate immune cells were detected with degranulation assay (Deg) and an intracellular assay (InCyt). Anti-leukemic cytotoxicity was explored with a cytotoxicity fluorolysis assay (CTX). VOCs collected from DC- and MLC culture supernatants (with vs. without Kit M pretreatment and before vs. after culture) were measured by eNose.

Results Compared to Control (without treatment) a Kit M pretreated leukemia and healthy WB gave rise to higher frequencies of mature (leukemia derived) DC subtypes and activated and memory T cells after MLC. Moreover, antigen (leukemia) specific cells of several lines (innate and adaptive immunity cells) were induced giving rise to blast lysing cells. The eNose could significantly distinguish between healthy and leukemic patients' serum-, DC- and MLC-culture supernatants derived volatile phases and could significantly separate several supernatants (with vs. without Kit M treatment, cultured vs. uncultured) derived VOCs within subgroups (healthy DC or leukemic DC or healthy MLC or leukemic MLC supernatants). Interestingly, the eNose could indicate a Kit M and culture associated effect.

Conclusions The eNose might be a prospective option for a deduction of a VOC based profiling strategy using serum or cell culture supernatants and could be a useful diagnostic tool to recognize AML illness.

REFERENCES

1. Biehl, W., Hattesohl, A., Jorres, R. A., *et al*. VOC pattern recognition of lung cancer: a comparative evaluation of different dog- and eNose-based strategies using different sampling materials. *Acta Oncologica* 2019;**58:** 1216–1224.
2. Amberger, DC, Doraneh-Gard, F, Gunsilius, C., *et al*. PGE1-Containing Protocols Generate Mature (Leukemia-Derived) Dendritic Cells Directly from Leukemic Whole Blood. *International Journal of Molecular Sciences* 2019;**20:**4590.

Disclosure Information T. Baudrexler: None. **T. Boeselt:** None. **S. Bohlscheid:** None. **L. Li:** None. **C. Schmid:** None. **A. Rank:** None. **J. Schmohl:** None. **H.M. Schmetzer:** E. Ownership Interest (stock, stock options, patent or other intellectual property); Modest; Modiblast Pharma GmbH, Oberhaching, European Patent 15 801 987.7–1118.

P04.02 A HIGH SENSITIVITY, TUMOR-INFORMED LIQUID BIOPSY PLATFORM, DESIGNED TO DETECT MINIMUM RESIDUAL DISEASE AT PART PER MILLION RESOLUTION

M Pruess*, E Newburn, SM Boyle, D Norton, RM Pyke, F Navarro, J West, R Chen. *Personalis, Inc., Menlo Park, CA, USA*

10.1136/jitc-2022-ITOC9.38

Background While circulating tumor-derived DNA (ctDNA) is an emerging biomarker for many cancers, the limited sensitivity of current detection methods reduces its utility for diagnosing Molecular Residual Disease (MRD) across a variety of clinical applications. Sensitive detection and quantification of MRD remains a key challenge, particularly in early-stage cancers, where timely detection of small micrometastatic lesions may enable treatment that prevents progression to advanced metastatic, incurable disease. To address these challenges, NeXT Personal was developed to deliver industry-leading MRD sensitivity in the range of 1–3 parts per million (PPM) representing a 10–100X increase over other available methods, while requiring only a single tube of blood (4 mL plasma/15ng cfDNA), and 1mm^3 of FFPE tumor tissue.

Materials and Methods NeXT Personal leverages tumor/normal whole genome sequencing (WGS) to design personalized, targeted MRD liquid biopsy panels for each patient. The MRD portion of the panel is composed of up to 1800 somatic tumor variants, enabling higher sensitivity MRD detection in plasma through tracking of high quality and lower noise variants. Additionally, further content included in the panel design enables simultaneous tracking of clinically-relevant, individual variants longitudinally to enable a deeper understanding of tumor biology and its dynamic response to therapy.

Results Performance characterization using cell line dilution series and clinical samples revealed the linearity of tumor signal down to the 1–3 PPM range. Orthogonal confirmation using droplet digital PCR (ddPCR) demonstrated near-perfect concordance down to ddPCR LOD. Further, an input titration curve showed consistent performance using 5 to 50 ng of input cfDNA material from patient samples. Additionally, NeXT Personal achieved 100% MRD specificity when tested on healthy donor plasma samples.

Conclusions NeXT Personal achieved highly sensitive and specific MRD detection, reproducibly demonstrating a LOD down to 1 PPM in different cancer indications, patient sample dilutions, and cell line dilutions. The high sensitivity of NeXT Personal potentially enables MRD detection across a broad variety of cancers and stages, including typically challenging early stage, low mutational burden, and low shedding cancers. In addition to MRD, NeXT Personal tracks and annotates individual variants to advance knowledge of tumor biology and observe emergence of known clinical and resistance hotspots.

Disclosure Information M. Pruess: A. Employment (full or part-time); Significant; Personalis, Inc. **E. Newburn:** A. Employment (full or part-time); Significant; Personalis, Inc. **S. M. Boyle:** A. Employment (full or part-time); Significant; Personalis, Inc. **D. Norton:** A. Employment (full or part-time); Significant; Personalis, Inc. **R.M. Pyke:** A. Employment (full or part-time); Significant; Personalis, Inc. **F. Navarro:** A. Employment (full or part-time); Significant; Personalis, Inc. **J. West:** A. Employment (full or part-time); Significant; Personalis, Inc.. E. Ownership Interest (stock, stock options, patent or other intellectual property); Significant; Personalis, Inc. **R. Chen:** A. Employment (full or part-time); Significant; Personalis, Inc.. E. Ownership Interest (stock, stock options, patent or other intellectual property); Significant; Personalis, Inc..

P04.03 CANCER IMMUNOTHERAPIES, COMPANION DIAGNOSTICS AND PRECISION MEDICINE

N Cascante-Estepa*, S Mayrhofer, H Enzmann. *Federal Institute for Drugs and Medical Devices (BAM), Bonn, Germany*

10.1136/jitc-2022-ITOC9.39

For decades, basic research and clinical trials have aimed to establish a meaningful cancer immunotherapy. An unprecedented number of medicinal products for cancer immunotherapy are currently being authorised. For this success, the selection of the right molecular targets for immunotherapy has been crucial. Monoclonal antibodies targeting cell surface receptors for growth factors were successfully introduced in clinical routine for the treatment of common solid tumours more than 10 years ago. Since then, however, the focus of cancer immunotherapy has shifted. More recently, many authorized medicines targeting growth factors receptors in solid tumours are no longer based on antibodies, but on small molecule protein kinase inhibitors. Currently, medicines with recent European marketing authorizations for the immunotherapy of cancer come from three major categories: (1) monoclonal antibodies targeting blood cell surface antigens; (2) CAR-T cells for the therapy of haematological neoplasia; and, with broader use including solid tumours, (3) checkpoint inhibitors. For the successful use of many of these medicines, the appropriate companion diagnostics (CDx) are required. Therefore, precision medicine also means selecting precisely the patients who will profit from a specific treatment (using, for example, a CDx). But, how can an informed choice be made with regards to CDx? We will give an overview on the cancer immunotherapies that depend on CDx and outline what to look for when choosing a suitable CDx.

Disclosure Information N. Cascante-Estepa: None. **S. Mayrhofer:** None. **H. Enzmann:** None.

P05 Reverse translation

P05.01 PLATELETS ROLE IN IMMUNOTHERAPY RESPONSE IN NON-SMALL CELL LUNG CANCER

C Colarusso*, M Terlizzi, A Pinto, R Sorrentino. *University of Salerno, Fisciano, Italy*

10.1136/jitc-2022-ITOC9.40

Background Immunotherapy has revolutionized the therapeutic landscape of non-small cell lung cancer (NSCLC). In particular, therapy based on immune checkpoint inhibitors (ICIs), such us monoclonal antibodies (mAbs) targeting programmed cell death protein 1 (PD-1) pathway, has changed the survival rate of NSCLC patients. However, a subset of patients is responsive to ICIs and another subset develops acquired resistance to ICIs. In the past few decades, increasing studies have highlighted that high platelets (PLTs) count is associated with poor prognosis of NSCLC patients. Therefore, the aim of this research was to investigate the contribution of PLTs in response to immunotherapy.

Materials and Methods Blood samples from advanced (non-resectable, stage IV) NSCLC patients treated with Atezolizumab were collected at the baseline (T0, prior to the first cycle) and at disease progression (PD). PLTs were isolated by PLT-rich plasma by centrifugation. PD-L1 and Fc gamma receptors (FcγR) PLTs expression were analyzed, and the release of activated PLTs-associated mediators were measured.

Results We found that PLTs count was higher in NSCLC patients at stage IV than earlier stages. These PLTs showed higher levels of PD-L1 than early stages. Moreover, although not in a statistical manner, ICI-non responder NSCLC patients had slightly higher levels of PD-L1. No differences were found in terms of FcγRIII (CD64), FcγRII (CD32) and FcγRI (CD16) expression on isolated PLTs either at baseline or after treatment. In order to better understand whether drug treatment with atezolizumab could alter PLTs activity, the isolated cells were treated in vitro with the mAb (1 μg/mL) to evaluate the release of mediators associated with PLTs activation. We found that differently than healthy PLTs, the stimulation of PLTs derived by NSCLC non-treated patients with Atezolizumab for 30 minutes induced the release of platelet factor 4 (CXCL4). Similarly, the challenge with Atezolizumab was able to trigger the release of TGF-β from NSCLC-derived PLTs after 5 hours of treatment; nevertheless, we observed that PLTs collected from patients who did not respond to treatment (PD) secreted higher amount of TGF-β at earlier time point (1 hour after Atezolizumab addition).

Conclusions Currently simple and robust biomarkers to predict therapy responses towards ICIs are still missing. Our data suggest that the PLTs expression of PD-L1 at PD may reflect the reduced drug efficacy due to the interaction and binding of mAbs (such as Atezolizumab) to the surface PD-L1 by limiting the drug which is not able to exhibit its pharmacological activity on tumor tissues or innate tumor-infiltrated immune cells.

Disclosure Information C. Colarusso: None. **M. Terlizzi:** None. **A. Pinto:** None. **R. Sorrentino:** None.

P06 Cell therapy in solid tumors

P06.01 ROR1-CAR T-CELLS AS NOVEL TREATMENT STRATEGY FOR ANAPLASTIC THYROID CARCINOMA

[1]D Chernyakov*, [1]O Skorobohatko, [2]B Edemir, [1]K Nerger, [1]T Müller, [1]M Binder, [1]B Trojanowicz, [1]K Lorenz, [3]S Hüttelmaier, [1]M Alb, [4]M Hudecek, [1]C Dierks. *[1]Universitätsklinikum Halle (Saale), Halle (Saale), Germany; [2]Universität Witten/Herdecke, Witten, Germany; [3]Institut für Molekulare Medizin, Halle (Saale), Germany; [4]Universitätsklinikum Würzburg, Würzburg, Germany*

10.1136/jitc-2022-ITOC9.41

Background Anaplastic thyroid carcinoma (ATC) and poorly differentiated thyroid carcinoma (PDTC) are rare thyroid malignancies with an extremely poor prognosis. Current therapies include operation, radiochemotherapy and kinase inhibitors, but finally most patients relapse and require further treatments. Thus, new therapeutic strategies are needed. CAR-T (chimeric antigen receptor) therapy is a modern approach to manipulate and target the patient's own T cells against a specific marker on tumor cells. The Receptor Tyrosine Kinase Like Orphan Receptor 1 (ROR1) is an essential transmembrane receptor during embryonic development and is associated with the non-canonical Wnt signaling pathway. ROR1 is barely expressed in adult healthy tissue, but can be re-upregulated on specific tumor cell types. In this study we investigated ROR1 as a potential target for CAR T-cell therapies in thyroid carcinoma.

Materials and Methods Initially, the expression of the ROR1 receptor was determined in primary ATC/PDTC and compared to non-malignant thyroid tissue. *ROR1* mRNA expression on ATC cell lines was correlated with ROR1 surface expression