such as presence of T_H2 cytokines IL-4 or IL-13 *in vitro* (Martinenaite *et al*, 2019, DOI: 10.1038/s41423-019-0231-3 and DOI: 10.1007/s00262-019-02425-6).

Methods and Results In order to explore if arginase-1-specific T cells have a potential role in modulation of immune homeostasis, human arginase-1-specific memory T cells were isolated and expanded for functional characterization. We show that arginase-1-specific T cells specifically recognize arginase-1 expressing cells, such as mRNA transfected autologous dendritic cells (DCs) and B cells as well as M2 polarized macrophages in vitro. In addition, activated arginase-1-specific T cells produce pro-inflammatory cytokines IFNγ and TNFα. Secretion of TH1 cytokines by these T cells suggests potential role as potent immune modulators in the tumor microenvironment, since many arginase-1 expressing myeloid cells are not terminally differentiated and they can be re-polarized to an immunostimulatory, M1-like phenotype. We also observed that targeting of M2-polarized arginase-1 expressing monocytic leukemia cell line THP-1 with arginase-1-specific CD4+ T cells induces upregulation of PD-L1 on the THP-1 cells. Furthermore, we demonstrate that an arginase-1-derive peptide vaccine has a therapeutic effect in syngeneic mouse tumor models (B16 and MC38), both as monotherapy and in combination with anti-PD-1 treatment. The therapeutic effect was associated with increased immune infiltration in the peptide vaccinated mice compared to the control.

Conclusions Our study provides evidence that immune modulatory vaccination targeting arginase-1 is an intriguing way of targeting the immune suppressive microenvironment.

Disclosure Information E. Martinenaite: A. Employment (full or part-time); Significant; IO Biotech. **M. Aaboe Joergensen:** None. **R.E. Johansson Mortensen:** None. **S. Munir Ahmad:** None. **S.E. Weis-Banke:** None. **M. Orebo Holmström:** None. **A. Wakatsuki Pedersen:** A. Employment (full or part-time); Significant; IO Biotech. **Ö. Met:** None. **I.M. Svane:** F. Consultant/Advisory Board; Significant; IO Biotech. **M. Hald Andersen:** A. Employment (full or part-time); Significant; IO Biotech.

P04.06 MUCOSAL IMMUNIZATION WITH A CDC1-TARGETED CTA1 ADJUVANT VACCINE CONFERS PROTECTION AGAINST MELANOMA METASTASIS

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10.1136/jitc-2020-ITOC7.75

Background Specific targeting of anti-cancer vaccines to dendritic cells (DCs) has been shown to mount efficient immune responses against tumor cells. Classical $CD103^+$dendritic cells (also called cDC1) have an inherent ability to cross-present antigens to $CD8^+$ cytotoxic T cells. Here we have explored an anti-tumor vaccine that specifically targets cDC1 cells for protection against and elimination of metastatic melanoma. The vaccine contains the cholera toxin A1 subunit (CTA1) adjuvant and is targeted to cDC1 cells through an anti-CD103 single chain antibody (CD103 scFv).

Material and Methods C57BL/6 mice were injected with wild type or ovalbumin (OVA) expressing B16 melanoma cells either subcutaneously (s.c.) to establish solid tumors, or intravenously (i.v.) to allow the formation of pulmonary metastases. Before or after establishment of tumors, mice were intranasally inoculated with a vaccine composed of a CD103 scFv element fused to the adjuvant CTA1 and the MHC I H2kd-restricted OVA epitope SIINFEKL together with the MHC II H2kd-restricted OVA epitope p323 or just the p323 peptide alone (*i.e.* CTA1-SIINFEKL-p323-CD103 and CTA1-p323-CD103, respectively). Control mice were inoculated with PBS. The growth of solid tumors was carefully monitored and the development of pulmonary metastases was determined 2–3 weeks after tumor cell injection. In addition, antigen-specific T cell immunity following intranasal immunization was evaluated.

Results Targeting MHC I and MHC II tumor cell epitopes to cDC1, via CD103 ScFv, in conjunction with the CTA1 adjuvant elicited strong tumor specific and protective $CD8^+$ T cell responses as well as $CD4^+$ T cell immunity. Immunization with the CTA1-SIINFEKL-p323-CD103 vaccine significantly reduced the growth of established solid B16F1-OVA melanomas ($P<0.001$) and potently prevented metastasis formation ($P<0.01$). Control immunizations with the CTA1-p323-CD103 vaccine tended to reduce metastasis, but tumor-specific $CD8^+$ T cells were required for full therapeutic protection.

Conclusion Targeting tumor specific $CD8^+$ T cell epitopes to cDC1, in the context of a powerful adjuvant such as CTA1, leads to the development of efficient anti-tumor immune responses. Our results point towards the utility of cDC1-targeted vaccines in the treatment of established tumors or as a means to prevent metastasis formation.

Disclosure Information M. Arabpour: None. **S. Paul:** None. **R. Kiffin:** None. **H.G. Wiktorin:** None. **K. Hellstrand:** None. **N. Lycke:** None. **A. Martner:** None.

P04.07 ABSTRACT WITHDRAWN

P04.08 VIRUS LIKE VACCINES: A NOVEL IMMUNOTHERAPY STRATEGY AGAINST THE CANCER-ASSOCIATED ENDOGENOUS RETROVIRUS

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10.1136/jitc-2020-ITOC7.76

In face of the necessity of broadly acting and highly effective vaccines capable of eliminating/preventing human cancers with insufficient mutated antigens, we introduced the concept of Virus-Like Vaccines (VLVs). This strategy combines a replication-deficient retrovirus encoding virus structural proteins. These proteins assemble into secreted virus-like particles (VLPs) that deliver the target antigen to the immune system rising both humoral and cellular immune responses. Here, we use an adenoviral vector encoding the group specific antigen (Gag) and the glycoprotein of the viral envelope (Env) from endogenous retrovirus (ERV). Since ERV Env is reported to have immunosuppressive properties that support tumor establishment and development, we designed a modified vaccine that includes a mutation on the Env immunosuppressive domain (ISD) that

prevents the vaccine from being immunosuppressive itself. In our studies, we demonstrate that VLVs are able to induce strong, broad, and long-lasting ERV Env specific CD8+ T cell by flow cytometry and antibody responses by ELISA in mice. Furthermore, the modified vaccine is of special interest to future research as it proved to significantly delay mouse tumor growth in a therapeutic setup. Nevertheless, we now need to address the principal host related developmental uncertainties in translating our achievements into the clinical setting. This goal can be accomplished by raising human T cells capable of targeting human cancers *ex vivo*. Furthermore, to support the translation of our work, we tested the ability to rise adaptive responses upon vaccination in non-human primates (NHP) which endogenously express ERVs similar to humans (in collaboration with IPB University, Indonesia). Fellowship granted by Innovation Fund Denmark.

Disclosure Information J. Daradoumis: A. Employment (full or part-time); Significant; InProTher Aps. B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; Innovation Fund Denmark. **P.J. Holst:** A. Employment (full or part-time); Significant; InProTher Aps. E. Ownership Interest (stock, stock options, patent or other intellectual property); Significant; InProTher. **K.N. Nielsen:** A. Employment (full or part-time); Significant; InProTher Aps.

P04.09 DEVELOPMENT OF A DENDRITIC CELL VACCINE AGAINST HEPATOCELLULAR CARCINOMA USING VSV-NDV

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10.1136/jitc-2020-ITOC7.77

Background Activated **Dendritic cells (DC)** are the immune system's allrounder: they initiate innate and adaptive immune responses; they induce instant immune reactions as well as immunologic memory. Therefore, there is growing interest in using them as a potential anticancer vaccine.[1] Here we use the beneficial immune-stimulatory properties of the novel oncolytic hybrid virus **VSV-NDV** to create a DC vaccine against hepatocellular carcinoma.[2]

In our therapeutic approach, a sample of the patient's tumor cells is lysed *in vitro* with VSV-NDV (=oncolysate). The patient's DCs are then co-cultured *in vitro* with the oncolysate in order to activate them and load them with tumor antigens. In the end, the stimulated DCs are injected into the patient, where they can lead to a personalized and broad anti-tumor immune response.

Materials and Methods To investigate the potential of the approach in a cell culture system, human monocyte-derived dendritic cells were generated from PBMCs of healthy donors and incubated with VSV-NDV-lysed HepG2 hepatoma cells. Afterwards their state of activation was investigated via flow cytometry and cytokine measurement, whereas their functionality was assessed in co-culture with T-cells. In a murine system, dendritic cells were generated from bone marrow stem cells, incubated with a VSV-NDV-lysed murine HCC clone and investigated as in the human system.

Results Flow cytometry of oncolysate-stimulated DCs showed a significant upregulation of the activation markers CD86, MHC-I, MHC-II and PD-L1 ($p < 0.05$). Moreover, these stimulated DCs released increased amounts of cytokines. Upon co-culture of the DCs with T-cells, an elevated secretion of IFNγ by the T-cells, as well as an upregulation of T-cell activation markers could be shown, demonstrating the functional potential of the oncolysate-stimulated DCs. These results apply to both the human and the murine system.

Conclusions Our *in vitro* data demonstrates that the oncolysate-stimulated human and murine DCs are not only activated, but furthermore have a high functional potential. Further *in vitro*-experiments will be necessary to translate the process to patient-derived samples, whereas murine *in vivo*-experiments will give further insights into the effect of the therapeutic approach.

REFERENCES

1. Lichtenegger FS, Rothe M, Schnorfeil FM, Deiser K, Krupka C, Augsberger C, Schluter M, Neitz J, Subklewe M. Targeting LAG-3 and PD-1 to Enhance T Cell Activation by Antigen-Presenting Cells. *Front Immunol* 2018.
2. Abdullahi S, Jäkel M, Behrend SJ, Steiger K, Topping G, Krabbe T, Colombo A, Sandig V, Schiergens TS, Thasler WE, Werner J, Lichtenthaler SF, Schmid RM, Ebert O, Altomonte J. A Novel Chimeric Oncolytic Virus Vector for Improved Safety and Efficacy as a Platform for the Treatment of Hepatocellular Carcinoma. *J Virol* 2018.

Disclosure Information J. Gold: None. **L. Hanesch:** None. **T. Krabbe:** None. **C. Lozano-Simon:** None. **G. Hänel:** None. **M. Rothe:** None. **A. Klopp:** None. **S. Göttert:** None. **S. Heidegger:** None. **U. Protzer:** None. **M. Subklewe:** None. **J. Altomonte:** None.

P05 Precision Medicine Meets Immunotherapy (Immuno-Monitoring)

P05.01 COMPARATIVE ANALYSIS OF RNA VERSUS DNA AS INPUT MATERIAL FOR IGH REPERTOIRE SEQUENCING PANELS FOR IMMUNO-ONCOLOGY APPLICATIONS AND RARE CLONE DETECTION

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10.1136/jitc-2020-ITOC7.78

Background Recent progress in tumor immunotherapies have shown the importance of next generation sequencing (NGS) T cell repertoire profiling to characterize T cell immune response to treatment. Understanding the role of the B cell repertoire upon stimulation of the immune system by checkpoint blockade is paramount for immunotherapeutic approaches in treatment of B cell malignancies, as well as understanding B cell function within traditional I/O strategies. The ability to detect low frequency B cell clones enables numerous hematology/oncology research applications, including identification of potential biomarkers and minimal residual disease (MRD) research. Historically, efforts to track the frequency of malignant B cells by IGH chain sequencing have utilized DNA input given potential challenges in accurately quantifying