disease and a high rate of relapse following initial therapy. Immunotherapy in combination with standard treatment modalities has emerged as an encouraging treatment approach to surmount this unmet medical need. DCP-001 is a cancer relapse vaccine derived from the DCOne human leukemic cell line and is currently progressing through clinical trials in hematological malignancies. During manufacturing, DCOne cells are shifted towards a mature dendritic cell phenotype, rendering the cells highly immunogenic and providing the basis for DCP-001, which is administered as an intradermal vaccine. DCOne cells express multiple common tumor associated antigens (TAA) such as WT-1, RHAMM, PRAME and MUC-1, which have been documented as potential target antigens in ovarian cancer. This observation suggests that DCP-001 vaccination may also have an anti-tumor effect in OC. To support this hypothesis, we assessed the capacity of DCP-001 to induce immune responses against OC in human peripheral blood mononuclear cells (PBMCs) and a humanized mouse model for OC.

Methods The effect of DCP-001 on T cells from OC patients or healthy donors was evaluated after a 3 week culture of peripheral blood mononuclear cells (PBMCs) with or without DCP-001. Cytotoxic activity was analysed by specific IFNg production and CD107a expression when these cells were subsequently cultured with the OC cell line SKOV3. The effect of DCP-001 vaccination in vivo was evaluated in humanised NCG mouse subcutaneously engrafted with SKOV3 OC cells. Mice received intra-peritoneal (i.p.) vaccination with DCP-001 either after or prior to SKOV3 engraftment and tumor size was measured to evaluate the efficacy of DCP-001.

Results In vitro, DCP-001 was shown to activate both CD4+ as well as CD8+ T cells and to induce formation of memory T cells. Importantly, DCP-001-stimulated CD8+ T cells from OC patients were shown to exert a HLA class I dependent, cytotoxic immune response to OC cells. In vivo, in an ovarian tumor mouse model, significant reduction of tumor growth rate and partial or even complete tumor regressions were observed in mice vaccinated with DCP-001, particularly when administered as relapse vaccine (prior to tumor engraftment), as compared to PBS treated mice.

Conclusions These pre-clinical in vitro and in vivo results support the potential use of DCP-001 as a cancer relapse vaccine in ovarian cancer, with the aim to reduce disease recurrence following initial standard of care therapy.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0171

172 INCREASING ACTIVATION OF HUMAN TUMOR-REACTIVE T CELLS (CD39+CD103+CD8+) BY GENE SILENCING OF PD1 WITH SELF-DELIVERING RNAI INTASYL(TM)

[1]Colin Thalhofer*, [1]Ryan Montler, [2]Melissa Maxwell, [2]Dingxue Yan, [2]James Cardia, [2]Simon Fricker, [1]Jacob Moses, [1]Joshua Rios, [3]Tarsem Moudgil, [3]Bernard Fox, [1]Nick Morris, [3]B Bell, [4]Andrew Weinberg. *[1]Agonox Inc., Portland, OR, USA; [2]Phio Pharmaceuticals, Marlborough, MA, USA; [3]EACRI, Providence Cancer Center, Portland, OR, USA; [4]AgonOx, EACRI Providence Cancer Center, Portland, Oregon, USA*

Background Tumor Infiltrating Lymphocyte (TIL) therapy has proven effective for patients with stage IV melanoma, however there are critical issues that can limit the efficacy of standard TIL therapy across a wide range of different malignancies. We and others have shown that some tumor types contain a low percentage of tumor-specific T cells. We hypothesize that most of the patients that do not respond to TIL therapy are likely receiving a low percentage of tumor-reactive T cells and therefore a high percentage of non-therapeutic bystander TIL. We have developed a streamlined method that expands a highly enriched fraction of tumor-reactive T cells contained within the CD39+CD103+CD8+ TIL in greater than 90% of patient samples from a wide variety of malignancies (melanoma, colon cancer, head and neck cancer, etc.). This TIL product displays a broad repertoire of tumor-specific TCRs. The expanded CD39/CD103 TIL can kill autologous tumors in vitro, but the possibility remains that they could revert to a suppressed or exhausted state when they reach the tumor microenvironment upon transfer back into patients. To mitigate the suppressive effects of the tumor microenvironment we have evaluated Phio Pharmaceutical's self-delivering RNAi INTASYL(TM) platform to silence PD-1 in the expanded TIL product.

Methods The TIL product was treated during the rapid expansion phase of the protocol with either nontargeting control compounds or PD-1 targeting INTASYL™ compounds. PD-1 protein levels and TIL functionality were assessed via flow cytometry and cytokine bead array.

Results Silencing of PD-1 expression in the expanded TIL product was obtained by adding the self-delivering RNAi compounds to the cell culture media, without needing transfection media, delivery formulations or electroporation. The RNAi-treated TIL product showed increased IFN-?? TNF-α and Granzyme B expression.

Conclusions These data highlight a promising combination to improve the activity of tumor-reactive TIL in future human clinical trials.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0172

173 AN IN VIVO CRISPR/CAS9 SCREENING PLATFORM TO IDENTIFY T CELL ENHANCING EDITS IN DISTINCT SOLID TUMOR MICROENVIRONMENTS

Amy Becker*, Troy Luster, Ishina Balwani, Nachiket Shevale, Jingwei Sun, Erica Del Aguila, Jeff Jones, Srijani Sridhar, Nishit Patel, Daniel O'Connell, Reynald Lescarbeau, Birgit Schultes. *Intellia Therapeutics, Cambridge, MA, USA*

Background Chimeric antigen receptor (CAR)-based T cell therapy and other forms of adoptive cell therapies (ACTs) have shown remarkable success in the treatment of hematologic malignancies; however, reports of clinical activity in solid tumors are limited to date. One key therapeutic challenge presented by solid tumors is the immunosuppressive tumor microenvironment (TME). Adding to the complexity, it is becoming increasingly clear that TMEs are heterogeneous (broadly classified as 'inflamed,' 'immune excluded' and 'immune dessert'), utilizing different mechanisms of immunosuppression. Instrumental to overcoming the barriers presented by solid tumors will be the development of T cells with immune- enhancing edits that improve penetration, potency and persistence, while also preventing exhaustion in hostile TMEs. T cells with these properties may help in the development of ACTs in solid tumors.

Methods CRISPR/Cas9-based functional genetic screens in T cells can enable prioritization of known targets and uncover novel targets to improve the design of genetically reprogrammed cell therapies, in an unbiased fashion. Most CRISPR screens to date have been performed in vitro with tumor cells due to the complexity of setting up CRISPR screens in primary T cells, particularly for in vivo target discovery. Here,