Meeting Report

Cancer Immunology Research

Translating Science into Survival: Report on the Second International Cancer Immunotherapy Conference

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Abstract

On September 25–28, 2016, in New York City, the Second International Cancer Immunotherapy Conference was cohosted by the Cancer Research Institute, the American Association for Cancer Research, the Association for Cancer Immunotherapy, and the European Academy of Tumor Immunology. This exciting conference brought together more than 1,400 participants, including scientists, clinicians, investors, and regulators, to discuss the latest scientific advances within the field of cancer immunotherapy. This conference report reviews the chief themes that emerged during the 4-day meeting. *Cancer Immunol Res; 4(12); 996–1000. ©2016 AACR.*

Introduction

Last year, because of the success of the Inaugural International Cancer Immunotherapy Conference, the Cancer Research Institute (CRI), the American Association for Cancer Research (AACR), the Association for Cancer Immunotherapy (CIMT), and the European Academy of Tumor Immunology (EATI) worked together again to host another cancer immunotherapy conference. Notably, nearly half of the attendees represented the pharmaceutical and biotechnology industries, demonstrating the clinical and practical relevance of the meeting. The conference—which included 50 speakers in 8 sessions in addition to nearly 300 poster presentations—covered the entire spectrum from basic tumor immunology to clinical cancer immunotherapy.

Topics covered included antigens and vaccines, the tumor microenvironment (TME), microbiota, new checkpoints, mechanistic merging of treatment modalities, non-checkpoint immunotherapies, new agents and their mode of action, and emerging technologies. In this meeting report, we review some of the key topics that emerged during the 4-day meeting, with a focus on new research areas.

How Mutations Could Be Used to Develop Personalized Immunotherapies

Emerging clinical evidence suggests that tumor-specific neoantigens that arise as a consequence of mutations within the tumor can be recognized by cytotoxic T cells, potentially allowing for antitumor activity (1). Identifying neoantigens is technically challenging though, so this year's conference focused on improving neoantigen discovery and identification to enhance cancer immunotherapy in the clinic.

Experts discuss current benefits and future potential of cancer immunotherapies. From left to right: Philip D. Greenberg, Jill O'Donnell-Tormey, Elizabeth M. Jaffee, Alexander Huang, and Aung Naing. Photo courtesy of CRI.

The field of cancer immunotherapy encompasses more than just scientists, clinicians, regulators, drug developers, and patient advocates. As Jeffrey Hammerbacher of the Icahn School of Medicine at Mount Sinai stated, data scientists and software developers also perform crucial roles. Hammerbacher uses emerging data science technologies to improve tumor neoepitope selection. Collaboration with clinicians enables access to patient samples/data and his laboratory provides bioinformatics analysis tools, including the publicly available Epidisco-web (http://epidis.co), a web interface platform to submit sequences for algorithm-based analysis with respect to mutated proteins (pyensembl and varcode), variant-specific isoform expression (isovar), unified interface to pMHC predictors (mhctools) and minimal epitopes, and vaccine peptide ranking (topiary and vaxrank).

Increasing focus has been placed on determining which neoepitopes T cells recognize. Improved functional assays are necessary to separate out small populations of (nonexpanded) neoepitope-specific T cells from tumor-infiltrating lymphocytes (TIL), or even peripheral blood mononuclear cells (PBMC). James

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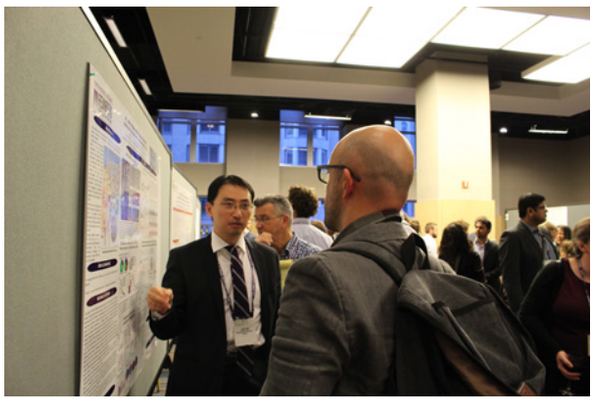

Lively poster session brings together physicians, researchers, and students to showcase and discuss all aspects of cancer immunology and immunotherapy. Photo courtesy of CRI.

Heath, of the California Institute of Technology, pioneered a novel method based on Ton Schumacher's protocol for identifying neoantigens using multiplex flow cytometry (2), using nanoparticle–barcoded Nucleic Acid Cell Sorting (NP-barcoded NACS), in which a photo-cleavable neoantigen:MHC complex binds to a cysteine-labeled streptavidin assembled on a tetramer. Each neoantigen–barcode–MHC:peptide tetramer is then mixed and loaded on a microfluidics chip with TILs or PBMCs to isolate neoantigen-specific T cells from tumors or whole blood. These cells are then separated for sequencing or isolated in the capture region for reading out the barcodes via microchip. To validate this method, Heath worked with Antoni Ribas, University of California, Los Angeles, to obtain tissue from patients with anti–PD-1-treated melanoma. They found similar neoantigens in PBMCs and TILs from individuals. They isolated neoantigen-specific T cells and sequenced their *TCRA*/*TCRB* genes to identify and measure the number of clonotypes. His team is currently working to accommodate higher throughput sequencing of individual TCRs.

Robert Schreiber of Washington University in St. Louis, already a pioneer in immunoediting and neoantigen identification, described work investigating whether neoepitopes influence each other in the T3-MCA sarcoma mouse model. Neoepitopes did influence the T-cell response to other neoepitopes, which showed that immunodominance exists. They did this by "repairing" one of the dominant mutant neoepitopes in the parental line back to its unmutated state and determining if repaired T3 tumor lines still retained sufficient immunogenicity for effective checkpoint blockade responses. When mice bearing single "repaired" T3 tumors were treated with PD-1 or CTLA-4 blockade, established tumors were rejected. Furthermore, $CD8^+$ T cells specific for remaining neoantigens were still present intratumorally, and T-cell responses were skewed toward the remaining dominant neoantigen. Additionally, this immunodominance may mask some antigen responses, meaning that subdominant neoepitopes can potentially induce protective effects.

Patrick Ott, from the Dana Farber Cancer Institute, used neoantigen identification to make personalized multi-epitope vaccines capable of expanding preexisting tumor-reactive T cells, stimulate tumor-reactive T cells, and broaden the antitumor T-cell repertoire. His group chose high-risk melanoma patients (stage III or IV), typically characterized by a high mutation rate, immune responsiveness, easy tumor access, and responsive to surgery. To develop the vaccine, they examined DNA and RNA sequences from TILs and matched PBMCs, performed neoepitope prediction via NetMHCpan and RNA expression, synthesized roughly 20 synthetic long peptides (20–30 mers) per patient, and then administered the vaccine along with the adjuvant poly-ICLC. Early clinical data demonstrated that the vaccine's safety and tolerability. Initial results indicate that significant *ex vivo* IFNγ was secreted (ELISPOT), and $CD4^+$ and $CD8^+$ T cells can recognize and respond to neoepitope peptide pools. Although the long-term benefits of this approach must be determined, neoepitope-specific vaccines seem feasible, well tolerated, and can generate immunologic responses.

Ughur Sahin from BioNTech Biopharmaceutical discussed personalized vaccine development using engineered RNA immunotherapy. His method takes advantage of both local and systemic dendritic cells: a liposomal mRNA (RNA-LPX) vaccine is delivered *in vivo* to dendritic cells (DC), which in mouse models triggered the innate immune receptor TLR7 and mediated a type-I IFN response from plasmacytoid DCs and macrophages, inducing tumor responses. Sahin's group is testing their neoantigen vaccine in the clinic through a phase I trial in patients with malignant melanoma who have had metastatic lesions resected, to study the safety, tolerability, and immunogenicity of their IVAC MUTANOME mRNA vaccine. In the first 11 patients treated, all demonstrated T-cell responses against at least 3 of 10 vaccine neoepitopes. Remarkably, several patients who had high-risk melanoma prevaccination remain relapse free in observation (8–27 months follow-up).

The Effects of Epigenetics on the Immune System

Epigenetic regulation also influences antitumor immune responses. E. John Wherry of the University of Pennsylvania, the winner of CRI's Frederick W. Alt Award this year, has long investigated $CD8^+$ T-cell exhaustion, and at the conference he explored the epigenetics of exhaustion. Although PD-1 blockade has improved outcomes by reinvigorating previously exhausted $CD8^+$ T cells (T_{ex} cells), how this happens remains unclear. Wherry wanted to determine if any differentiation occurs in T_{ex} cells during PD-1 blockade: Do T_{ex} cells transform into T effector (T_{eff}) cells, T memory (T_{mem}) cells, or another subset altogether (3)? In a murine lymphocytic choriomeningitis virus (LCMV) model, numerous transcriptional changes occurred during T_{ex}'s temporary reinvigoration after PD-1 blockade, but they did not develop immunologic memory and became re-exhausted if antigen levels remained high.

When chromatin accessibility and methylation patterns were analyzed, the T_{ex} cells had roughly 18,000 enhancers that differed from naïve T cells, and their epigenetic landscape also differed from T_{eff} and T_{mem}. Furthermore, 8,000 of these differences were unique to T_{ex}, including some associated with the *Ifng* and *Pdcd1* genes. PD-1 blockade altered 600 enhancers and temporarily reinvigorated T_{ex}, but, unfortunately, neither globally reprogrammed epigenetic patterns nor enabled memory acquisition.

Alexander Huang, also at the University of Pennsylvania, revealed a link between reinvigorated T cells and tumor burden, from a new study that tracked antitumor T cells in the peripheral blood before, during, and after pembrolizumab treatment in stage IV melanoma patients. Interestingly, immunological responses

(78%) were more common than clinical responses (38%), which correlated better with the magnitude of reinvigoration. Proliferation (Ki67 positivity) and tumor burden appeared to reflect, and even predict, overall survival (OS) as early as 6 weeks after treatment. In short, the larger the tumor, the more reinvigoration was needed for an effective response. These findings were confirmed via a second patient cohort conducted at the Memorial Sloan Kettering Cancer Center, under Michael Postow and Jedd Wolchok.

Weiping Zou of the University of Michigan examined the epigenetic regulation of Th1-type cytokines in ovarian and colon cancer cells, and found that the histone-modifying methyltransferase EZH2 and DNA-methyltransferase 1 (DNMT1) repress Th1-type chemokine production, affecting T_{eff} migration and antitumor immunity. These epigenetic regulators showed synergy, suggesting independent and nonredundant activity. Their activity also inversely correlated with the amount of $CD8^+$ TILs, with better survival associated with more $CD8^+$ TILs and low EZH2/DNMT1 expression. In a spontaneous animal cancer model, poor T-cell infiltration due to low CXCL9/10 expression prevented responses against tumor antigens, PD-L1 blockade, and adoptive cell transfer (ACT).

Metabolism in the TME

Susan Kaech of Yale University next explored metabolic factors in the TME and explained how switching from mitochondrial oxidation to aerobic glycolysis is crucial for T-cell development and function. Glucose deprivation alone suppressed effector functions of Th1-type cells and promoted production of the immunosuppressive TGFβ. Kaech posited that the TME's decreased glucose and increased lactate and fatty acid (FA) concentrations promoted T-cell dysfunction through "metabolic editing" of TILs. This environment upregulates inhibitory receptors on T cells, increases T-cell death, and decreases expression of IFNγ, TNFα, and IL2.

Increased tumor glucose consumption appears to promote T-cell dysfunction, as deprivation inhibited TCR-induced accumulation of cytoplasmic Ca^{2+} by activating SERCA (sarco/endoplasmic reticulum Ca^{2+}-ATPase)-mediated uptake by the endoplasmic reticulum. FAs—often found at elevated levels intratumorally—also affect T-cell activity (4, 5). Certain FAs (oleic and linoleic acid) decreased IFNγ and TNFα production and increased PD-1 expression. CD36 was identified as a $CD8^+$ T-cell FA transporter that promotes FA uptake, PD-1 expression, and tumor growth.

High lactate production by tumors also hinders antitumor immunity, as Taha Merghoub of the Memorial Sloan Kettering Cancer Center discussed. In the phase Ib Keynote-012 trial, triple-negative breast cancer (TNBC) patients with high lactate dehydrogenase (LDH) expression did not benefit from pembrolizumab. Merghoub hypothesized that tumor glycolytic activity and lactate production promote an aggressive breast cancer TME, which blocks TIL survival, expansion, and function. Therefore, preventing high lactate concentrations should increase TILs and checkpoint blockade's effectiveness, according to the inverse correlation between tumor expression of glycolysis-related genes like *LDH-A* and *LDH-B* and metastasis-free survival. Analysis of 731 invasive breast carcinoma patients from The Cancer Genome Atlas (TCGA) revealed mutually exclusive expression of glycolysis and immune-associated genes. Knocking down *LDH-A* in the TNBC mouse model decreased primary tumor growth and increased TILs, antitumor effects, and survival. In a coculture system (tumor and T cells), inhibiting the lactate transporters MCT1 and MCT4 lowered the lactate/glucose ratio, reversed lactate-mediated immunosuppression of T cells, enhanced their proliferation, and increased production of IFNγ and TNFα.

As Greg Delgoffe of the University of Pittsburgh discussed, T-cell activation depends on significant biosynthetic activity, but TILs (irrespective of PD-1 expression) often possess fewer, diminished mitochondria. Expression of mitochondrial biogenesis cofactor PGC1α was significantly lower in $CD8^+$ TILs; the loss occurred progressively and independently of PD-1. Akt dynamically regulates PGC1α but is chronically elevated in cancers; T cells with the highest Akt concentrations had the lowest PGC1α levels, and inhibiting Akt increased both PGC1α expression and mitochondrial mass in TILs, increasing their antitumor function.

The diabetes drug metformin, which is associated with a reduced risk of cancer, inhibits mitochondrial complex 1 and decreases tumor oxygen consumption rates (OCR) as well as TME hypoxia. Because metformin must be actively transported into cells and only tumor cells express high amounts of OCT1, a metformin transporter, T-cell effects must be indirect. In *ex vivo* experiments, lowering tumor OCR increased TILs OCR and improved their antitumor potential (Tim-3 expression). Metformin synergized with PD-1 blockade in mice, improving TIL proliferation and decreasing tumor growth, with better results achieved when metformin was administered first.

The Immune Contexture within the TME

The next topic focused on the tumor immune microenvironment (TIME). Colorectal cancer is generally resistant to PD-1 blockade, except for microsatellite instability–high (MSI-H) subtypes with DNA mismatch-repair defects that are typically associated with higher mutational burdens and increased T-cell infiltration (6). Drew Pardoll's group found that myeloid cells at the invasive front express PD-L1 in MSI-H but not microsatellite stable (MSS) colorectal cancer, and that infiltrating T cells in MSI-H patients contain $PD\text{-}1^{hi}/IFN^{hi}$ populations of $CD4^+$ and $CD8^+$ T cells (7). As Pardoll pointed out, 14% of MSS tumors exhibit "MSI-like" TME, which could explain why some MSS patients stabilized (~16%).

Next, Wolf Fridman from INSERM used RNA expression profiling to show that some colorectal cancers with a high lymphoid gene signature are associated with poor prognosis, and that this is coupled with mesenchymal and myeloid infiltration, not antitumor $CD8^+$ TILs. Conversely, a common signature was present in both MSI-H and "MSI-like" colorectal cancer that is associated with better prognosis, specifically when accompanied by cytolytic $CD8^+$ TILs (8). Clearly, not all immune infiltrates are equal. Poorly prognostic mesenchymal tumors have high lymphoid infiltrates, but of the wrong (immunosuppressive) type. Eventually, these immune classifications could guide strategies to turn "cold" tumors into "hot" tumors and make them more responsive to immunotherapy.

Shannon Turley of Genentech covered fibroblastic reticular cells (FRC), a group of immune-associated cells that lay down a conduit system through which lymph flows and to which FRCs adhere. FRCs are crucial for lymph node organization and T- and B cell–mediated immunity. Ablating the FRCs in lymph nodes in an influenza mouse model prevented antiviral $CD4^+$ T cells from

forming and B-cell production of virus-specific antibodies. FRCs were also critical for B-cell homeostasis and follicle identity, apparently through production of prosurvival B-cell activating factor (BAFF). FRC podoplanin (PDPN) is involved in their contractility and in DC motility over them. When DC CLEC-2 engages FRC podoplanin, it inhibits FRC contraction and the cells remain elongated. DCs that lacked CLEC-2 could not prevent FRC contraction and lymph node stiffness. Blocking PDPN directly relaxes the FRCs, which increases the spaces within the node available for T-cell activation by DCs, minimizing contact from the suppressive influence of the reticular network.

Elizabeth Jaffee, from Johns Hopkins, is developing ways to enhance T-cell infiltration into checkpoint blockade–resistant pancreatic adenocarcinoma (PDAC) tumors. Jaffe's group utilized GVAX, a whole tumor cell vaccine designed to boost DCs and antigen presentation, LADD Listeria (live attenuated *Listeria monocytogenes*), and nivolumab in metastatic PDAC patients who progressed after chemotherapy. Some patients experienced partial remissions, but they took at least 6 months to manifest. In addition, vaccination increased Eomes expression, which enhances T-cell infiltration and is associated with less exhausted $CD8^+$ TILs. Furthermore, IDO (indoleamine 2,3-dioxygenase) was expressed in the tumor epithelia and lymphocytes in human pancreatic cancer after vaccination. This is relevant for therapy, as IDO expression is associated with increased regulatory T cells (Treg) and decreased cytotoxic T cells. Thus, an IDO inhibitor might complement the vaccine/checkpoint blockade treatments and enhance T_{eff} while depleting Tregs.

Adenosine is another immunosuppressive factor elevated in the TME. First, Stephen Willingham of Corvus Pharmaceuticals discussed CPI-444, a selective inhibitor of the adenosine receptor $A_{2A}R$, which is highly expressed on $CD8^+$ T cells. In mouse models, CPI-444 protected against colorectal cancer formation and synergized with PD-1/PD-L1 blockade. CPI-444 depended on $CD8^+$, but not $CD4^+$, T cells for its efficacy and is being tested in a phase I trial against several solid cancer types, both alone and in combination with the anti–PD-L1 atezolizumab. Thus far, the optimal dose (100 mg) elicited sustained $A_{2A}R$ inhibition in peripheral blood lymphocytes and increased the frequency of activated $CD8^+$ lymphocytes as measured by PD-1 expression.

An emerging area that appears relevant to the TIME is the microbiome. Work on the microbiome by Lawrence Zitvogel, from Gustave Roussy in Paris, France, demonstrated that two intestinal commensals (*E. hirae* and *Barnesiella intestinihominis*) enhance cyclophosphamide's therapeutic effects. *E. hirae* induced systemic Th17 cell responses associated with tumor antigen–specific activation of cytotoxic T cells, whereas *B. intestinihominis* boosted systemic polyfunctional T-cell responses via intratumoral, IFNγ-producing γδ T cells. All of these activities depend on intestinal innate immune receptor NOD2. Furthermore, the immune responses toward these two commensals could predict progression-free survival in metastatic cancer patients (9).

New Targets for Immunotherapy

In addition to vaccination and checkpoint blockade, other efforts, such as oncolytic virus therapy, are focused on enhancing antitumor immune responses. David Reese of Amgen discussed Talimogene laherparepvec (T-Vec), a modified, oncolytic herpes virus. Specifically, he discussed work that characterized the potential mechanisms of action of the mouse version of T-Vec ($OncoVEX^{mGM\text{-}CSF}$) using an A20 contralateral syngeneic tumor model. Although 10 of 10 injected tumors responded, only 5 of 10 of the uninjected tumors responded. Furthermore, whereas the virus was not detected in the uninjected tumors, increased $CD3^+$ T cells were. $CD8^+$ T cells were crucial for these antitumor effects; when they were depleted, tumors grew much larger. Oncolytic virus therapy also synergized with CTLA-4 blockade and improved responses against uninjected tumors. A phase Ib trial is testing this combination of T-Vec and ipilimumab in previously untreated patients with unresectable, stage IIIb to IV melanoma (10), and 13 of 18 patients who received T-Vec followed by ipilimumab showed no disease progression. Four patients had complete responses, and another 5 had partial responses. Another trial, MASTERKEY-265, is testing T-Vec in combination with pembrolizumab in a similar group of melanoma patients. Here, too, pembrolizumab was administered after T-Vec, and of the 21 patients treated, 5 patients experienced complete responses and 3 had their disease stabilize. Notably, cases of pseudo-progression were seen in both trials. The phase III portion of its MASTERKEY-265 study, which will treat 660 patients with either T-Vec alone or in combination with pembrolizumab, is now moving forward.

Martin Oft, from ARMO Biosciences, discussed a novel role for IL10, which can curb inflammatory responses but can also promote antitumor activity. Oft's group developed a PEGylated-IL10 called AM0010 and are testing it alone and in combination with PD-1 blockade against several cancer types in a phase I/Ib basket trial. Thus far, it has been well tolerated in 324 patients both alone and in combination. In kidney cancer patients treated with AM0010 and pembrolizumab, 4 of 8 patients responded, including two complete responses. In lung cancer patients treated with the same combination, 2 of 5 responded. Future data will help determine the durability of these responses.

Whereas checkpoint blockade "releases the brakes," another approach seeks to "hit the gas" by activating T cells. Patrick Mayes of GlaxoSmithKline (GSK) discussed one such agonist, the inducible T-cell costimulator (ICOS). The IgG4 isotype was used as the base for the ICOS-agonist antibody because, although it binds to the inhibitory FcγRIIb, it does not induce antibody-dependent cell-mediated cytotoxicity through activating FcγRs. Thus far, H2L5—GSK's humanized, ICOS agonist—has enhanced the survival, proliferation, and activity of antigen-activated T cells. In mice, an ICOS agonist provided protection against colorectal and breast cancer. It also increased the ratio of $CD8^+$ T cells/Tregs and induced PD-1/PD-L1 expression in the TME, providing a rationale for combining ICOS agonists with PD-1 blockade. In syngeneic mouse tumor models, the combination enhanced IFNγ production and significantly improved survival. It also increased IFNγ production in T cells from healthy donor blood as well as TILs from non–small cell lung carcinoma patients. GSK will be testing its ICOS-agonist antibody H2L5 alone and in combination in the upcoming ICOS FTIH study.

Ton Schumacher of the Netherlands Cancer Institute, a 2016 CRI Coley Award winner, characterized other factors influencing PD-L1 expression. By applying a gene trap on haploid cells (HAP1), Schumacher discovered two previously unidentified PD-L1 regulators. The first, PD-L1M1, is a poorly characterized protein with several transmembrane domains. Although it is widely expressed, it has no known functions. After shRNA knockdown of PD-L1M1, surface expression of PD-L1 decreased in melanoma and lung cancer cells *in vitro*; with thyroid cancer cells, not even IFNγ

signaling restored PD-L1 expression. CRISPR/Cas9 deletion of the *PD-L1M1* gene corroborated its role in PD-L1 expression. However, when PD-L1M1 was knocked out in HAP1 cells, a "backup" protein, PD-L1M2, emerged. Moving forward, Schumacher stressed the necessity of investigating tissue and tumor-specific expression of PD-L1M1 and PD-L1M2, to develop approaches that can overcome PD-L1–mediated immunosuppression.

Phillip Greenberg of the Fred Hutchinson Cancer Research Center discussed two clinical trials with engineered T cells for acute myeloid leukemia (AML) patients who have undergone stem cell transplantation (SCT). T cells transduced with anti-WT1 TCRs were tested in two groups of AML patients: those at high risk of relapse after SCT (prevention) and those with relapsed and persistent disease after SCT (therapeutic).

In the prevention group, Epstein–Barr virus (EBV)–specific $CD8^+$ T cells were used because they reduce GvHD risk and enable *in vivo* tracking. They also contain both T_{eff} and central T_{mem} cells capable of self-renewal and persistence, which the virus may boost *in vivo*. With a median time since infusion of 19 months, none of the 10 patients have relapsed yet, and the EBV-specific T cells demonstrated sustained memory and effector responses. In the therapeutic group, $CD8^+$ T cells specific for cytomegalovirus (CMV) were used in addition to EBV-specific T cells, and they demonstrated clear evidence of therapeutic, antileukemic activity.

Moving beyond TCRs, immunomodulatory fusion proteins (IFP) can also enhance cell-based immunotherapies: The inhibitory PD-1 surface receptor (CD200R) was modified and attached to the intracellular portion of the costimulatory CD28 domain. In this way, surface PD-1 stimulation promotes activation instead of inhibition. Construct size was crucial to the new CD200R IFP's function: the insertion of 9 amino acids best preserved the T cell–tumor cell synapse distance and enabled proper migration upon recognition. $CD8^+$ T cells expressing this CD200R IFP produced more cytokines and better eliminated targets, both *in vitro* and in mouse models, after exposure.

ACT approaches against other antigens are also being developed for PDAC. In an engineered B6 KPC ($Kras^{LSL\text{-}G12D+;}$ $Trp53^{LSL\text{-}R172H+}$;p48-Cre) mouse model that shares PDAC's characteristics, mesothelin-targeting T cells remodeled the stroma and increased blood vessel access. These T cells induced tumor cell apoptosis, but their anticancer function declined over time as they upregulated inhibitory surface receptors, including PD-1, Tim3, Lag3, 2B4, and BTLA. Fortunately, providing these T cells every 2 weeks increased survival in mice with established tumors. After comparing naïve (T_{naive}) and central memory T cells (T_{CM}), Greenberg showed that T_{CM} are superior to T_{naive}, in terms of IFNγ production. T_{CM} also outcompeted T_{naive} and showed sustained production of IFNγ, TNFα, and IL2. The engineered T_{CM} also physically interacted with tumor cells and formed cell clusters that may be responsible for enhancing their antitumor activity, which was still maintained 22 days after transfer. A clinical trial testing this ACT approach using anti-WT1 and/or antimesothelin cells in PDAC patients is scheduled to begin within the next year.

Conclusion

The second International Cancer Immunotherapy Conference, entitled "Translating Science into Survival," brought together clinicians, scientists, amongst others, to discuss advances in cancer immunotherapy. Significant new immunological approaches, promising clinical results, and ideas for future study were presented. The third International Cancer Immunotherapy Conference, cohosted by the same four nonprofits, will be held on September 6–9, 2017, in Mainz/Frankfurt, Germany.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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