motivation to participation in studies involving healthy volunteers. In this current study, however, financial compensation did not appear to be the primary motivation for participation. The participants' at all 3 sites stated that the main reason for their participation was the increased knowledge about their disease and the contribution to science. Negative experiences cited were primarily discomfort with blood draw, transportation, and parking logistics. Most importantly, a majority of the participants stated they would participate in future studies and would recommend a family member or a friend for a clinical study. In our sample, there was no difference in the favorable ratings as determined by race/ethnicity. In conclusion, the findings of this study inform the community with regard to how the research participants rate their experiences, and thus motivate others to participate in clinical research. Reasons for participants to withdraw from trials may be associated to their dissatisfaction with a trial or with the study staff. Thus, the degree of satisfaction with the research staff and the trial itself is crucial to reducing drop-out rates and increasing compliance with study procedures. Hence participant satisfaction is key to increasing participation in clinical trials, particularly among African Americans and other racial and ethnic minorities.

2530

Should all clinical research subjects pay the same?

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OBJECTIVES/SPECIFIC AIMS: Discuss ethical and policy issues that will impact clinical research. Raise awareness of the need to understand internal policies at home institutions Encourage further examination of ways to facilitate clinical research participation. METHODS/STUDY POPULATION: Ethical and policy analysis. RESULTS/ANTICIPATED RESULTS: Ideally, clinical research participants should not be required to pay to participate in research. However, if we go with an equity model, as opposed to an equality model, policies should be changed to allow equal access to research participation. This is a matter of justice and also will enhance the quality of the science. DISCUSSION/SIGNIFICANCE OF IMPACT: Unless steps are taken to make participation in clinical research less burdensome financially for participants, research may slow or results may be biased, because only those who can pay will be able to participate.

2533

Beyond "REACH": The Research, Education, And Community Health (REACH) coalition as an exemplar for broad-based stakeholder engagement

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OBJECTIVES/SPECIFIC AIMS: The Institute for Transnational Sciences (ITS) has developed novel methods to ethically engage stakeholders across the transnational research spectrum, up to and including public health practice and policy. METHODS/STUDY POPULATION: In 2014, the ITS co-founded The Research, Education, And Community Health (REACH), the mission of which was to facilitate communication, collaborative research, and service activities between faculty and scientists and area community leaders. The intent was to identify and meet the needs of our communities without gaps and/or redundancies, thus better leveraging time, funding, and efforts. RESULTS/ANTICIPATED RESULTS: REACH now boasts 23 Centers, Departments, and Institutes, as well as 39 community organizations, including public and mental health agencies, clinicians, policy makers, family service centers, cultural and faith-based organizations, business, and local schools/colleges. We offer 3 methods for consideration as best practices: (1) a comprehensive community health needs assessment, (2) an "Offer and Ask" community/campus partnership mechanism, and (3) Community Science Workshops, based on the European Union's Science Shops. DISCUSSION/SIGNIFICANCE OF IMPACT: Results of REACH's work have been used to provide guidance for enhanced, data-driven programs and allocation of resources for local and statewide initiatives. The organization has evolved into an independent coalition seeking 501(c)3 status and is planning to expand its scope to 5 counties. REACH thus serves as model for successful replication across applicable CTSA hubs.

2543

Participatory development of a CTSA-wide Community Advisory Board: Enhancing community engagement at the Michigan Institute for Clinical & Health Research

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OBJECTIVES/SPECIFIC AIMS: To describe how Michigan Institute for Clinical & Health Research (MICHR) has engaged communities in its leadership and governance structure. This presentation will describe these practices, how they are being evaluated, and future plans for institute-wide engagement of communities in translational research. METHODS/STUDY POPULATION: Engaged partners from various communities across Michigan in various ways within MICHR's Community Engagement Program. RESULTS/ANTICIPATED RESULTS: MICHR has utilized participatory practices in the development of the CAB to strengthen existing relationships and build new ones with potential partners. DISCUSSION/SIGNIFICANCE OF IMPACT: MICHR-wide Community Advisory Board (CAB) will ensure community voices are heard and utilized in leadership and strategic decisions for CTSA activities.

MECHANISTIC BASIC TO CLINICAL

2014

Identification of novel shared tumor antigens for the development of T-cell-based immunotherapies

Sherille Bradley and Greg Lizee

OBJECTIVES/SPECIFIC AIMS: The specific objective of this proposal is to identify and validate targetable tumor-associated antigens (TAAs) in ovarian and pancreatic cancer. It is our central hypothesis that the accurate identification and selection of appropriate TAAs will provide a foundation on which to develop of novel and effective cancer immunotherapies. We have formulated this hypothesis on the basis of preliminary results in which we have used high-throughput tandem mass spectrometry (MS) to successfully identify TAAs from melanoma patient tumors. We have subsequently generated TAA-specific T-cells that showed specific recognition and killing of tumor cells, and will form the basis of an upcoming clinical trial for our melanoma patients. We now have extended this antigen identification pipeline into ovarian cancer to accomplish our objective of developing effective T-cell-based immunotherapies for ovarian cancer and pancreatic patients. METHODS/STUDY POPULATION: We have collected patient tumor specimens, and we performed HLA immunoprecipitation, peptide elution, and completed high-throughput tandem MS on these eluted samples to identify TAAs. In addition, we have validated the safety of potential targets through the use of the publicly available RNA sequence data sources GTEX and TCGA. RESULTS/ANTICIPATED RESULTS: To date, we have successfully completed over 60 peptide elutions from ovarian and pancreatic patients samples. In total, we have found several potential novel tumor-associated targets. VGLL1, is one of these identified antigens, and in conjunction with our collaborators, we have successfully generated T-cells against it. Additionally, we have found that VGLL1 is a potential novel TAA for 3 other cancer types, including bladder, gastric, and triple negative breast cancers. We are now focusing our efforts on testing these T-cells against additional ovarian cancer cell lines and these cancer types to determine their specificity. We plan to continue the generation and testing other identified potential TAAs as well. We plan to use these T-cells directly in clinical trials in the future. DISCUSSION/SIGNIFICANCE OF IMPACT: The rationale for this proposal is that through the identification and validation of TAAs, we can open the door to a new world of therapies that can potentially increase the survival rate in a disease with a historically grim prognosis.

2064

Deconstructing the peptide specificity of TCR recognition

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OBJECTIVES/SPECIFIC AIMS: The off-target and organ-specific toxicities observed in cancer immunotherapy present an obstacle to T-cell-based therapeutics. A recent clinical trial underscored the need for improved

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methods to define TCR specificity after melanoma patients treated with TCR engineered T-cells suffered from fatal cardiovascular toxicity arising from the unpredicted recognition of a muscle-specific peptide. METHODS/STUDY POPULATION: To address this drawback to T-cell-based immunotherapies, we developed a novel protein engineering approach to define the peptide specificity of a given TCR. Here, directed evolution in a yeast display system produced a large scale peptide library, where recognition by the melanoma reactive DMF5 TCR acted as the guiding selective pressure. After this technique identified a panel of putative cross reactive peptides, sequence analysis and computational modeling followed by kinetic binding experiments and structural analysis determined the DMF5 TCR recognizes 2 distinct classes of peptides through chemically distinct mechanisms. RESULTS/ANTICIPATED RESULTS: This information led to the rational, structure-based design of additional cross reactive peptides and introduced a unique approach to screen the human proteome and identify the TCR targets which triggered undesired autoimmunity when this molecule was used in clinical trials. DISCUSSION/SIGNIFICANCE OF IMPACT: The distinct chemical nature of the 2 peptide classes suggest TCRs are more cross reactive than previously thought, presenting an obstacle to cell-based immunotherapy. Defining the peptide specificity of TCRs is of high interest to the immunology community, and will lead to improved approaches to designing engineered TCRs for cell therapy.

2074

Comparing the properties of human umbilical cord-derived mesenchymal stromal cells from preterm Versus full-term infants

Alvaro Moreira, Caitlyn Winter, Saloni Balgi, Shamimunisa Mustafa, Lauryn Winter and Peter Hornsby

OBJECTIVES/SPECIFIC AIMS: To compare functional differences in WJ-MSCs-derived from term Versus preterm infants. METHODS/STUDY POPULATION: WJ-MSCs were enzymatically digested from umbilical cord tissue from Term (gestational age ≥37 wk, n = 4) and Preterm (gestational age ≤32 wk, n = 5) neonates. Cells were characterized by (1) surface antigen markers using flow cytometry, (2) ability to differentiate into adipogenic, chondrogenic, and osteogenic lineages following in vitro stimulation, (3) colony forming unit efficiency, (4) proliferation rates, and (5) cell motility assay. RESULTS/ANTICIPATED RESULTS: WJ-MSCs were successfully isolated from both Preterm and Term groups. Cells adhered to plastic and displayed characteristic spindle-shaped morphology when cultured under standard conditions. WJ-MSCs from both groups expressed surface antigen markers CD73, CD90, and CD146 (≥90%) and did not express hematopoietic markers HLA-DR, CD79, or CD117 (<5%). Preterm and Term cells were capable of differentiating into osteogenic, chondrogenic, and adipogenic lineages. There were no significant differences between the groups when evaluated by colony forming efficiency, proliferation rates, or cell motility. DISCUSSION/SIGNIFICANCE OF IMPACT: These preliminary findings suggest that WJ-MSCs derived from full-term or preterm neonates have similar functional characteristics. Future studies will focus on the regenerative potential of WJ-MSCs from preterm and term infants following changes in the microenvironment (eg, oxygen tension, inflammatory stimulation).

2078

NGF and TNF-α contribute to oral cancer pain by regulating pro-inflammatory cytokines

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OBJECTIVES/SPECIFIC AIMS: We hypothesize that both NGF and TNF-α contribute to oral cancer pain by upregulating pro-nociceptive inflammatory cytokines. METHODS/STUDY POPULATION: In total, 48 oral cancer patients were evaluated and their pain scores were measured using a validated oral cancer pain questionnaire. Presence of perineural invasion (PNI) was identified from patients' pathology reports. We utilized The NIH Cancer Genome Atlas (TCGA) Head and Neck Cancer cohort to investigate the association between pain and genes related to NGF, TNF-α, and their receptors (TRKA, P75, TNF-α receptor 1, and TNF-α receptor 2) in oral cancer samples by employing PNI as a surrogate for pain. Demographic characteristics, clinical characteristics, and genes were analyzed using logistic regression models. A xenograft cancer pain model was created by inoculating human oral cancer cells (HSC-3) into the mouse hind paw. Mice (n = 6 per group) were treated with anti-NGF alone, anti-TNF-α alone, a combination of anti-NGF and anti-TNF-α, or PBS (vehicle control). Nociceptive behaviors were measured using an electronic paw withdrawal assay. Paw volume was measured using a plethysmometer. Cytokines in the paw tissues were measured using a multiplex assay kit with 28 cytokines. RESULTS/ANTICIPATED RESULTS: Oral cancer patients with PNI report significantly more pain compared with patients without PNI in our patient cohort ($p < 0.05$). From analysis of TCGA data, we found that PNI is significantly associated with lymphovascular invasion, pathological nodal invasion, and pathological tumor staging (all $p < 0.05$). In adjusted models, we observed that the NGF receptor p75NTR (NGFR) and the TNF-α receptor 1 (TNFRSF1A) were associated with PNI (both $p < 0.05$) and significantly correlated to each other ($r = 0.25$, $p < 0.001$). High levels of TNF-α were present in HSC-3 cell lines and the mouse xenograft cancers. In mice with cancer pain, combined treatment with anti-NGF and anti-TNF-α together provided more effective pain control compared with either anti-NGF or anti-TNF-α treatment alone ($p < 0.05$). We found significantly increased levels of MIP3a, IL-1b, IL-2, IL-4, IL-28b, IL-23, IL17a, IL-31, and IL-33 in cancer mice compared with normal mice (all $p < 0.05$). The combination therapy significantly reduced cytokines MIP3a, IL-1b, IL-4, IL-28b, IL-31, and IL-33 (all $p < 0.05$). DISCUSSION/SIGNIFICANCE OF IMPACT: We show that targeting both NGF and TNF-α provides more effective pain relief in an oral cancer model. These results suggest that therapeutic strategies aimed at both pathways could yield improved pain management for oral cancer patients.

2080

Therapeutic potential of mesenchymal stromal cells for hypoxic ischemic encephalopathy: A systematic review of preclinical studies

Alvaro Moreira, Jamie Archambault, Dawn McDaniel and Peter Hornsby

OBJECTIVES/SPECIFIC AIMS: To assess the efficacy of exogenous administration of MSCs in animal models of HIE. METHODS/STUDY POPULATION: Adhering to the Systematic Review Protocol for Animal Intervention Studies, a systematic search of English articles was performed using MEDLINE, Web of Science, CINAHL, and Google Scholar. Search term items included mesenchymal stem/stromal cell, hypoxic ischemic encephalopathy, asphyxia, cerebral ischemia, and neonatology. We selected randomized and nonrandomized studies that examined in vivo neonatal models of induced HIE. We excluded studies that combined MSCs with an adjunct therapy. Data were collected on study specifics, MSC characteristics, and outcome measurements. The primary outcome was efficacy of MSC treatment, assessed by functional neurologic measures (cognitive, motor, sensory). Risk of bias was assessed using the SYRCLE's risk of bias tool and we used the ARRIVE guidelines to describe the quality of study reporting. RESULTS/ANTICIPATED RESULTS: A total of 17 preclinical publications focusing on MSC therapy for HIE met our inclusion criteria. Fifteen of the studies (88%) induced HIE in rodents by ligating the common carotid artery followed by a period of hypoxic exposure. Nine (53%) studies derived their MSCs from rodent bone marrow, whereas the other investigators provided xenografts from human bone marrow or umbilical cord-derived MSCs. Range of MSC dose was between 0.25 and 3.5 × 106 cells with 71% of the experiments transplanting the MSCs intranasally or intracerebral. Three studies (18%) administered multiple doses. The cylinder rearing test was the most common (73%) sensorimotor functional outcome performed in the first month following the establishment of HIE. All studies demonstrated a reduction in asymmetrical paw preference after receiving MSC therapy. Lesional size was assessed, using neuroimaging or histologic evaluations, and the majority of studies showed a decreased insult following MSC therapy. DISCUSSION/SIGNIFICANCE OF IMPACT: MSC treatment demonstrates improved functional and structural outcomes that are encouraging for future translational studies.

2081

Phenotypic characterization of the CD4+ T-cell response during anti-CTLA4 therapy with ipilimumab in melanoma patients

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OBJECTIVES/SPECIFIC AIMS: To characterize the CD4+ T-cell response during CTLA-4 blockade immunotherapy with ipilimumab in patients with metastatic melanoma by correlating cytokine profiles with phenotypic changes in the intratumoral lymphocyte compartment of tumor biopsies obtained before and after treatment. METHODS/STUDY POPULATION: Peripheral

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