will be associated with enhanced mucosal HIV susceptibility in the explant challenge model. DISCUSSION/SIGNIFICANCE OF IMPACT: There is a paucity of information regarding the mechanisms of rectal HIV transmission, and no studies to date investigate the immunologic effects of aging on transmission in the rectal mucosa. The results from this study will provide important information regarding age-related differences in the immune cell composition of the rectal mucosa as a critical step in better understanding immunologic factors that influence rectal HIV transmission.

3285

Toxicity of Released B Cell Products in Multiple Sclerosis: Effects on Neurons and Oligodendrocytes

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OBJECTIVES/SPECIFIC AIMS: We previously demonstrated that products released by cultured B cells from patients with Multiple Sclerosis (MS) are cytotoxic to neurons and oligodendrocytes, while minimal toxicity was observed in response to B cell secretory products from age- and sex-matched normal controls. The goal of this proposal is to identify the range of brain cells susceptible to MS B cell-mediated cytotoxicity, to define the cytotoxic factor(s) released by MS B cells, and to determine whether particular subset(s) of MS B cells harbor the greatest pathogenic potential. METHODS/STUDY POPULATION: The toxicity of B cell products will be demonstrated by incubating primary rat cultures of neurons, oligodendrocytes, and oligodendrocyte progenitor cells (OPCs) with B cell supernatants. B cells will be isolated from the peripheral circulation of untreated relapse-remitting MS (RRMS) patients and age- and sex-matched normal controls. The identification of specific toxic factor(s) in MS B cell supernatants will be achieved through a combination of exosome-depletion/enrichment of conditioned media, proteomics, next generation sequencing, and lipidomics. Determining pathogenic B cell subsets will be achieved by cell sorting into memory and naïve B cell subsets prior to collection of supernatants. RESULTS/ANTICIPATED RESULTS: We hypothesize that the toxicity of MS B cell products is mediated, at least in part, by extracellular vesicles, such as exosomes. We expect depletion of these exosomes from the B cell conditioned media or inhibition of their biogenesis will mitigate the observed toxicity. Furthermore, differences in B cell-derived exosomal content, such as proteins, (mi)RNAs, or lipids, likely explain the differences in observed toxicity. Lastly, we hypothesize that memory B cells, which are enriched in the CNS of MS patients and demonstrate a more pro-inflammatory profile than naïve B cells, are responsible for the toxicity observed in supernatants of total B cells. DISCUSSION/SIGNIFICANCE OF IMPACT: MS is the most prevalent chronic inflammatory disease of the CNS, affecting more than 2 million people worldwide. Although over a dozen disease-modifying therapies are approved for the treatment of RRMS, none are meaningfully effective at limiting disease progression. This proposal will provide new insight into immune-CNS interactions in progressive MS and provide much-needed novel targets for therapeutic intervention, either via blocking identified toxic molecule(s) or by selectively depleting pathogenic B cell subsets.

Regulatory Science & Translational Methods

3202

Columbia University's Personalized IRB Liaison Service: Evaluation over its initial 2.5 years

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OBJECTIVES/SPECIFIC AIMS: National concerns about IRB-related research delays have led to re-assessment of IRB review processes at institutional levels. We sought to address whether a dedicated IRB Liaison Service at the Irving Institute's central location could provide additional useful staff support to the investigator community for interactions with the IRB at various levels of protocol submission. METHODS/STUDY POPULATION: We evaluated the results of a user satisfaction survey and performed a focused in-depth analysis of Liaison Service impact. An online tracking and satisfaction survey was implemented for researchers to complete following each consultation. The goal was to gauge the uses, user types and usefulness of the Service, and to follow-up with researchers who might have additional questions. Data was gathered about users of the Service and their affiliations, and the topics and questions that were discussed. A terse summary was drafted to categorize each consultation that was conducted during office hour sessions. Additionally, surveys were emailed to researchers to gauge their experience with the Service and their overall satisfaction. Users completed the survey either in person at the end of the consultation, or by email request sent immediately following each in-person consultation. The impact of the IRB Liaison Service on IRB protocol approval times was analyzed for a random sub-sample of protocols for which consultations were provided. Consultations for studies with an associated IRB protocol number (i.e., at least initially submitted) from May 2015-June 2017 had been assigned a number in an Excel file. Using a randomization formula, a subset of 90 protocols was identified for further analysis. Protocols that did not result in an IRB submission and duplicate entries were removed. The final dataset consisted of 67 protocols. Those protocols were assessed by type of review process (expedited versus full board review), by status (new submission, first return, second return, etc.), and by which of the seven IRB committees completed the review. Consultations for each protocol included in this subset were reviewed using the notes about that consultation. IRB records in Columbia's online research oversight system, Rascal, were also reviewed to assess the timing of and issues raised in subsequent IRB review. Factors examined included whether the protocol was approved at next submission and if not, whether questions raised in subsequent IRB returns were related to the topics discussed in the consultation. RESULTS/ANTICIPATED RESULTS: Since its inception in January 2015 through June 2017 (2.5 years), a total of 501 in-person consultations have been performed, usually 25-30 per month. Users were primarily study coordinators and investigators. Most requests concerned new protocol development, policy questions or assistance in addressing IRB comments from submitted protocols. Survey response rate was 43%. Results of 215 competed satisfaction surveys were 100% positive. Of 67 unique protocols analyzed for outcomes of the consultation, 73% were subsequently approved within 14 days. DISCUSSION/SIGNIFICANCE OF IMPACT: Overall, we

have found the Liaison Service to be a popular addition to research support, and plan to continue the service. We will continue to evaluate its user satisfaction and usefulness. Additional focus will be placed on whether the Service can improve approval times for human subjects research for protocols using the Liaison Service.

3080

Ensuring Quality in Investigator-Initiated Clinical Trials through Monitoring Concepts Training

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OBJECTIVES/SPECIFIC AIMS: Because clinical trial results are instrumental in the approval of a new drug or changes to the practice of medicine, ensuring the accuracy and validity of collected data is critical in the clinical trial process. This function, routinely carried out by clinical trial monitors in industry-sponsored trials, is often lacking in investigator-initiated trials (IITs) conducted in academia. To address this challenge, we have developed a self-study module that can be used to cross-train academic researchers in essential concepts and practical approaches to monitoring. Furthermore, we are applying a framework drawn from implementation science in the development and launch of this initiative. This framework, as used in other educational programs, is employed here to close the gap between initiative and practice, thereby effectively disseminating this training would improve the quality of clinical trials in academia. METHODS/STUDY POPULATION: This research project applied exploration, installation and implementation stages of the implementation science process by 1) exploring the need for a new initiative, 2) disseminating results, 3) engaging stakeholders, 4) creating standard operating procedures (SOPs) for installation and implementation, 5) studying user satisfaction and effectiveness, 6) addressing feedback and 7) conducting implementation. RESULTS/ANTICIPATED RESULTS: From literature review and internet searches we determined that although numerous GCP training resources exist, most are too broad and lack the practical approaches to meet the complex requirements of monitoring. Moreover, most of the offerings identified are costly or inaccessible. With only about 65% of IITs reported as being monitored (Figures 1 and 2), it appears that there is a clear need for training tools that are easily available to a broader audience. And because monitoring skills are substantially different from those associated with research coordination, it is not surprising that research professionals believed that they would need additional training to become proficient. To address this need, we began developing a monitoring module. We engaged key stakeholders from academia and industry to gain insights into their needs. The results indicated that although our training module was effective, supplementary information on the fundamentals of clinical trials should be included for those new to the field. After incorporating suggested changes and completing the module, we conducted user testing to determine if our module is ready to be broadly disseminated (Figures 3 and 4). Following positive feedback from the group, we are currently in the process of disseminating our module and studying its impact. DISCUSSION/SIGNIFICANCE OF IMPACT: IITs are instrumental in translating academic research into product development. Deficiencies in the quality control of these trials can lead to inadequacies in data accuracy and validity that could lead to significant delays in bringing innovative therapies to patients. Recent NIH policies require data and safety monitoring for all of the trials it supports. The latest addendum to ICH GCP, E6(R2), discusses a need for quality management across the clinical trial lifecycle. As we continue to disseminate and share information during the development of our self-study monitoring module, we are engaging key stakeholders from academia, government, and private institutions to understand and address quality challenges in conducting clinical trials. Finally, this research informs dissemination and implementation research, specifically for creating training for academic research professionals.

3076

Findings from the first year of California's Workplace Violence Prevention in Healthcare standard (Title 8, Section 3342)

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OBJECTIVES/SPECIFIC AIMS: This research project aims to: 1) describe the incidents of workplace violence that have been reported to CalOSHA through the Workplace Violent Incident Reporting System for Hospitals; 2) determine if there are any relationships between the types of violent incidents reported and the unit or hospital where the event occurred; 3) describe what mitigation strategies facility representatives report having utilized immediately following a violent incident, such as changes to practice or involvement of law enforcement. METHODS/STUDY POPULATION: Reports submitted to CalOSHA pursuant to the Workplace Violent Incident Reporting System for Hospitals are considered public record and are available through the state's Public Records Act (PRA) mandate. Records from 7/1/17 – 9/30/18 were obtained through the CalOSHA PRA request process. Descriptive statistics and correlations were calculated using Stata. RESULTS/ANTICIPATED RESULTS: Records reporting 11,116 individual events of violence were analyzed. These results do not include reports submitted by the five California State Hospitals, a group of facilities which treated nearly 13,000 patients in 2017, many of whom have a psychiatric diagnosis and are undergoing treatment mandated by judicial decision. For each record, 111 variables were reported, including description of the event itself, characteristics of the workers involved, factors which may have triggered the event, and what measures were taken to mitigate the situation during and after the incident. All events identified an aggressor; 10,357 (93%) described this individual as a patient. 11,048 reports had a unit or hospital location listed to describe where the incident occurred. Of these, 9393 (84.5%) were inpatient, behavioral health, or surgical units. A physical injury was reported in 3672 events (33%) and stress/psychological impairment was reported in 536 (5%) of the incidents. Police officers were deployed to the scene following the incident in 1122 (10%) of reported events, resulting in arrest of the perpetrator in 402 (3.6%) of the reported incidents. DISCUSSION/SIGNIFICANCE OF IMPACT: While the impulse to address the high prevalence of workplace violence towards healthcare providers has led to deserved attention from policy makers, safety regulators, and healthcare unions, plans for ensuring that new initiatives are achieving their desired effect for workers have yet to fully materialize. An ongoing concern is that incidents are known to be under-reported through official mechanisms, leading to challenges in determining the scope of the problem itself and evaluating the efficacy of interventions to address it. CalOSHA's new reporting requirement and online interface provides a new channel for improving validity of prevalence data, as early findings indicate that less serious events are being reported through the system. In addition, information describing how hospital leaders report