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

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