changes in the immunologic response at early (14 d) and tissue remodeling outcomes at late stages (90 and 180 d) of implantation. The mesh-tissue complex was removed from each rabbit and processed for histological staining as well as immunolabeling of immune cells, such as macrophages. Extracellular matrix protease assays and mechanical integrity of the tissue also evaluate the overall inflammatory response associated with each implant. METHODS/STUDY POPULATION: Commercially available polypropylene mesh was used to investigate the modulation of the immune response. An adapted radio frequency glow discharge method is used to create a stable negative charge on the surface of the mesh, followed by the sequential deposition of polycationic and polyanionic polymers to provide a stable, conformal, nanoscale coating. It is well known macrophages are characterized on a spectrum ranging from a proinflammatory M1 phenotype to an M2 anti-inflammatory phenotype. Interleukin-4, an immunomodulatory cytokine known to promote the M2 phenotype, is incorporated into the coating to be released in a controlled manner upon implantation. Utilizing a novel surgical technique in New Zealand white rabbits, we implant mesh using the "gold standard" abdominal sacrocolpopexy procedure and evaluate changes in the immunologic response at early (14 d) and tissue remodeling outcomes at late stages (90 and 180 d) of implantation. The procedure begins with an initial hysterectomy removing the uterus followed by creating space along the vaginal wall on both sides between the bladder and the rectum. Two 3 × 10 cm^2 pieces of mesh are secured along both sides of the vaginal wall. The remaining flaps at the top are then secured to a ligament in the sacral/lumbar space, creating the support to the pelvic organs. Upon closing the incision, a partial thickness defect is made in the abdominal wall, and mesh is implanted inside to repair the abdominal muscle. Both of these implantations of mesh allow for the assessment of the immune response in the pelvic area (relevant for prolapse patients) and in the abdominal area (relevant for translation from hernia repair).The mesh-tissue complex was removed from each rabbit and processed for histological staining as well as immunolabeling of immune cells, such as macrophages. Extracellular matrix protease assays and mechanical integrity of the tissue also evaluate the overall inflammatory response associated with each implant. RESULTS/ANTICIPATED RESULTS: The results of this study show that implants into vaginal tissues elicited an increased host inflammatory response at 14 days as compared with those in the abdominal wall. However, at chronic time points the inflammatory response in the vagina was reduced as compared to that in the abdominal cavity. The present study also demonstrates the scale-up of a previous methodology for a nanoscale coating. We present a nanometer thickness, tunable, and uniform coating capable of releasing bioactive interleukin-4. We evaluated the biological functionality of the coated mesh via bioactivity studies and in vivo implantation. An ideal mesh would provide mechanical support to the pelvic floor while decreasing the inflammatory response and increasing integration with the surrounding native tissue. DISCUSSION/SIGNIFICANCE OF IMPACT: We developed an in vivo model clinically relevant to understanding the early host response to mesh in an anatomically relevant area, the vaginal microenvironment. Previous studies have been conducted in a rodent abdominal defect model while other work has been done in a nonhuman primate vaginal model, but the host response is only observed at later time points (>3 mo). Thus, we developed a rabbit model to investigate early responses and a novel coating to actively working towards improved tissue integration.

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A CTSA External Reviewer Exchange Consortium: Description and lessons learned

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OBJECTIVES/SPECIFIC AIMS: To share the experience gained and lessons learned from a cross CTSA collaborative effort to improve the review process for Pilot Studies awards by exchanging external reviewers. METHODS/STUDY POPULATION: The CEREC process is managed by a web-based tracking system that enables all participating members to view at any time the status of reviewer invitations. This online tracking system is supplemented by monthly conference calls during which new calls for proposals are announced and best practices are identified. Each CTSA hub customized the CEREC model based on their individual pilot program needs and review process. Some hubs have supplemented their internal reviews by only posting proposals on CEREC that lack reviewers with significant expertise within their institutions. Other hubs have requested 1–3 external reviewers for each of their proposals or a selection of most promising proposals. In anticipation of potential scoring discrepancies, several hubs added a self-assessment of reviewer expertise and confidence at the end of each review. If a proposal is on the cusp of fundability, then the reviewers' self-assessment may be taken into account. In addition to the tracking data collected by the online system, a survey of CEREC reviewers was conducted using Qualtrics. RESULTS/ANTICIPATED RESULTS: Across the 144 proposals submitted for reviews, CEREC members issued a total of 396 email invitations to potential reviewers. The number of invitations required to yield a reviewer ranged from 1 to 17. A total of 224 invitations were accepted, for a response rate of 56%. An external reviewer was unable to be located for 5 proposals (3%). Ultimately, 196 completed reviews were submitted, for a completion rate of 87%. The most common reasons for non-completion after acceptance of an invitation included reviewer illness and discovery of a conflict of interest. CEREC members found the process extremely useful for locating qualified reviewers who were not in conflict with the proposal being reviewed and for identifying reviewers for proposals related to highly specialized topics. The survey of CEREC reviewers found that they generally found the process easy to navigate and intellectually rewarding. Most would be willing to review additional CEREC proposals in the future. External reviewer comments and scores were generally in agreement with internal reviewer comments and scores. Thus, hubs could factor in external reviewer scores equally to internal reviewer scores, without feeling compelled to calibrate external reviewer scores. Overall, through CEREC external reviewers, mainly due to the stronger matching of scientific expertise and reduction of potential bias, the quality of reviews appear to be higher and more pertinent. DISCUSSION/SIGNIFICANCE OF IMPACT: Some aspects of the process emerged that will be addressed in the future to make the system more efficient. One issue that arose was the burden on the system during multiple simultaneous calls for proposals. Future plans call for harmonizing review cycles to avoid these overlaps. Efficiency also will be improved by optimizing the timing of reviewer invitations to minimize the probability of obtaining more reviews than requested. In addition to the original objective of CEREC, the collaboration has led to additional exchange of information regarding methods and processes related to running the Pilot Funding programs. For example, one site developed a method using REDCap to manage their reviewer database; an innovation that is being shared with the other CEREC partners. Another site has a well-developed process for integrating community reviewers into their review process and is sharing their training materials with the remaining CEREC partners.

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A novel multi-photon microscopy method for neuronavigation in deep brain stimulation surgery

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OBJECTIVES/SPECIFIC AIMS: The goal for this project is to determine the feasibility of using a novel multi-photon fiber-coupled microscope to aid surgeons in localizing STN during surgeries. In order to accomplish this goal, we needed to identify the source of a strong autofluorescent signal in the STN and determine whether we could use image classification methods to automatically distinguish STN from surrounding brain regions. METHODS/STUDY POPULATION: We acquired 3 cadaveric brains from the University of Colorado Anschutz Medical Campus, Department of Pathology. Two of these brains were non-PD controls whereas 1 was diagnosed with PD. We dissected a 10 square centimeter region of midbrain surrounding STN, then prepared this tissue for slicing on a vibratome or cryostat. Samples were immuno-labeled for various cellular markers for identification, or left unlabeled in order to observe the autofluorescence for image classification. RESULTS/ANTICIPATED RESULTS: The border of STN is clearly visible based on the density of a strong autofluorescent signal. The autofluorescent signal is visible using 2-photon (850–1040 nm excitation) and conventional confocal microscopy (488–647 nm excitation). We were also able to visualize blood vessels with second harmonic generation. The autofluorescent signal is quenched by high concentrations of Sudan-black B (0.5%–5%), and is primarily localized in microtubule-associated protein-2 (MAP2) + cells, indicating that it is likely lipofuscin accumulation in neurons. Smaller lipofuscin particles also accumulate in microglia, identified based on ionized calcium binding adopter 1 (Iba1) + labeling. We anticipate that colocalization analysis will confirm these qualitative observations. Using 2-photon images of the endogenous autofluorescent signal in these samples, we trained a logistic regression-based image classifier using features derived from gray-level co-occurrence matrices. Preliminary testing indicates that our classifier performed well, with a mean accuracy of 0.89 (standard deviation of 0.11) and a Cohen's Kappa value of 0.76 (standard deviation of 0.24). We are currently using coherent anti-Stokes Raman scattering and third harmonic imaging to identify different features of myelin that can be used to distinguish between these regions and expect similar results. DISCUSSION/SIGNIFICANCE OF IMPACT: Traditional

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