Summary of Neurodegeneration Workshop Discussions (Dec 3rd, 2015)

**Introduction- (Gary Aston-Jones)**

Gary set out the goals for the workshop as (1) Specify the greatest opportunities for Center/PPG and T32 applications; (2) Identify missing elements that need to be provided to permit successful applications and (3) Identify potential subgroups within each focus area that could collaborate on a particular topic, e.g., PD, MS.

There is currently an effort underway at BHI with the help of James Millonig and John Pintar to assemble information from faculty about training history etc. So far ~44 faculty distributed across all Rutgers units have provided information. The goal is to identify strengths and develop targeted training grants. This effort could dovetail with the plans developed by the sub groups in each focus areas. Gary also announced the funds available for recruiting the Klein Endowed Chair in Alzheimer’s disease and Neurodegeneration as well as the Presidential support for diversity recruitment. He also described the support available from BHI for targeted faculty recruitment. The BHI recruitment model provides substantial support to host departments for start-up, space renovation, salary support and recruitment expenses. Thus significant resources are currently available for strengthening the Neurodegeneration and Injury focus area at Rutgers. For this focus area the goal of the BHI is to help obtain Center grants such as the Udall Center for PD, the National MS Society Center and P50’s or equivalent for TBI and SCI. NINDS also offers program project grants and multi-PI R01 opportunities as well as new translational grant mechanisms that are well-suited for multi-PI applications.

**Parkinson’s disease (Maral Mouradian)**

Maral mentioned that currently there are ~ 18 faculty listed on the BHI website (including basic and clinical) who are involved in various aspects of PD and motor disorders research at Rutgers. They use model systems that range from yeast to primates (off-site at Emory). Considering the current strengths at Rutgers, the 3 main questions in the PD field that could be addressed at Rutgers with a center or multi-PI approach are-

1. Molecular pathogenesis (a-synuclein, and other genes);
2. Identify disease modifying targets and

These questions could be addressed by utilizing in vitro models (yeast, cultured cells), patient-derived human iPSC’s (potential collaboration with Ron’s group), rodent models (various faculty) and primate models (currently off-site). For the latter, there is a need for a primate facility and specialized staff to support the facility at Rutgers (missing element). From a translational view point- preclinical testing of therapies in primate PD models is a key step towards moving to clinical trials and partnering with companies. Another missing element is the lack of brain/tissue bank and a neuropathologist to help with analysis. This bank and new faculty could be housed in the Pathology departments of the medical schools. It was mentioned that a new joint Chair has just been hired for the Pathology departments at NJMS & RWJMS- if the newly hired Chair has negotiated funds to hire new faculty, BHI could potentially coordinate with the Chair to hire a neuropathologist who would support research across multiple BHI focus areas. Maral also mentioned that she had unsatisfactory experience with the microarray services that she used at Rutgers in the past. Ron Hart recommended that she and others should approach him to use the excellent resources available at RUCDR.

**Multiple Sclerosis (Terri Wood)**

Terri described the strengths in basic and clinical MS research at Rutgers. There are currently two Endowed Chairs in MS at Rutgers. On the clinical side, there are two National MS society-recognized
centers at Rutgers; (1) NJMS MS Diagnosis & Treatment center at Newark (Directed by Dr. Stu Cook) and (2) the RWJ Center for MS at New Brunswick (Directed by Dr. Suhayl Dhib-Jalbut). Several MS clinical trials are being run out of these clinical centers. On the Basic Science side, Terri mentioned that over the past 5 years there were 90+ MS-related publications from Rutgers, 10 NIH and 14 non-NIH funded grants (based on 2014 data). The MS research at Rutgers can be broadly classified into “oligodendrocyte biology” & “immunology/therapeutics”. Based on these strengths, the group suggested the development of a Rutgers Glial Biology Center or Rutgers White Matter Research Center that could potentially span not only the research related to neurodegeneration and injury but also research related to the cognitive and neurodevelopment focus areas. Such a center could be initiated by funding from the NMSS Center grant which, although relatively small, could help to the development of P50 funded center. Terri mentioned that a recent application for such an NMSS center was not funded due to perceived lack of institutional commitment. This negative perception could be addressed by the new Rutgers focus on neuroscience as a Signature Area, the establishment of the BHI and potential for recruiting a new Klein Endowed Chair in Alzheimer's and Neurodegeneration and other BHI-faculty. The MS group discussion also highlighted the need for a brain/tissue bank and a neuropathologist. It was also pointed out that there was significant basic and clinical MS research at Kessler; while many of these faculty have a joint appointment at NJMS, collaborations with these Kessler faculty could be further strengthened. It will be important to reach out to these Kessler faculty as their expertise in cognitive and rehabilitation MS research would be an asset to any Center grant application.

**Traumatic Brain Injury (Bonnie Firestein); Traumatic Brain Injury/Epilepsy (Viji Santhakumar)**

The current state of TBI research at NB/Piscataway and Newark was covered by Bonnie and Viji, respectively. The major need in the field appears to be development of standardized and reproducible in vitro and in vivo models of TBI. Model development efforts are confounded by lack of reproducibility and consistency. TBI research encompasses in vitro stretch/injury models to several animal models. For the latter, while the faculty at NB/Piscataway use the lateral fluid percussion model and controlled cortical impact model (via external collaboration), the faculty in the Newark area use Blast Tube (NJIT- can accommodate large animal/cadaver & small animal), Drop Chute, Fluid Percussion Injury, Rate-Alterable FPI, Cortical Contusion Injury, Closed-head Pediatric TBI, Mechanical Retinal Injury. Also in development are -Rpt blast/impact TBI and Poly TBI. Geographic separation of model availability at different campuses hinders collaborations due to logistical problems in moving animals between campuses and buildings (Patrick Sinko mentioned that CMR was purchasing additional animal transport vehicles to address this). The major strength of TBI research at Rutgers is the larger number of faculty with funded research (over 15 Rutgers faculty) that already have strong collaborations with over 10 externally funded studies. To support and coordinate this research Smita Thakker-Varia (PI), Janet Alder with Co-PI Namas Chandra (NJIT) and Steve Levison (NJMS) have Proposed Rutgers-NJIT TBI Core Facility with a single manager and two locations (one in Newark and one in NB/Piscataway). So far ~49 faculty at Rutgers and NJIT have signed on as potential users. The core would offer services including, in vitro and in vivo models, tissue bank, immunohistology, behavior assays, neuroimaging (Steve Levison mentioned that an NIH application for a 7T magnet for small animal imaging at Newark received a fundable score but needs institutional support for installation), proteomics, therapeutic development etc. It was not clear if an application for the core facility has already been submitted. Regardless, given the broad scope of the services that will be offered by the core and potential overlap with existing core facilities, it might be necessary and advantageous to coordinate with Patrick Sinko’s ORAD office. The discussions lead to the suggestion
that recruiting a senior well-funded TBI faculty (with translational research experience) as a center director would be helpful in obtaining center and large PPG grants as several TBI researchers at Rutgers come from outside the TBI research field. The TBI research efforts at Rutgers could also be enhanced with availability of standardized models, functional imaging, behavioral core, Big Data computational expertise, enhanced exposure (booths at society & TBI-focused symposium at Rutgers) and targeted pilot funding to support collaborative projects. Given the recent interest in post-traumatic epilepsy and the presence of several NIH funded epilepsy researchers at Rutgers, epilepsy is another area that could be developed towards Multi-PI proposals using the suggested mechanisms.

**Spinal Cord Injury (Stella Elkabes)**

Stella covered the current state of SCI research in the Newark area. While there is significant strength in SCI at the Keck center on the NB/Piscataway campus, Stella highlighted both clinical and basic science research at NJMS, NJIT and Kessler. Majority of the SCI research is being done at the Tim Reynold’s foundation funded Spine Center. Dr. Robert Heary runs SCI related clinical trials and performs spinal decompression surgery while Stella oversees the basic science research. The major opportunities in SCI research include: Restoration of function/Quality of Life; Attenuation of Secondary injury/Neuroprotection; Repair/axonal regeneration/plasticity; Neuropathic pain. Many of these overlap with the questions that need to be addressed in TBI. The other under researched opportunity is the study of chronic effects of SCI, in the context of above opportunities. A unique issue facing SCI researchers is the lack of animal care staff to assist in the husbandry of the movement-compromised animals. Stella suggested the formation of a SCI consortium that could expand collaborations within Rutgers and with NJIT to include BME capabilities into SCI research. She also highlighted the role of glial scarring and axonal regeneration in SCI and how these research areas might overlap with the MS & TBI research areas. The above mentioned Glial Biology Center could incorporate these aspects of SCI research. SCI research at Rutgers has great patient community visibility and receives significant philanthropic support from the patient community. This could be leveraged to help obtain Center and PPG grants to support multi-campus SCI research.

**BME Resources (David Shreiber); IPSC’s/Stem Cell Resources (Ron Hart); NINDS Proteomics Core (Hong Li)**

David highlighted strengths of Rutgers BME faculty in Biomaterials / Tissue Engineering (for Peripheral nerve regeneration and scaffolds to control astrocyte reactivity), in Cellular therapies (biomaterials for implanting MSC’s and iPSC’s), Drug delivery / Devices, Brain-computer interface probes, prosthetics and Physiological monitoring. He highlighted the resources available in Joachim Kohn’s NJ Center for Biomaterials and Jeff Zahn’s BIOMEM facility for developing lab-on-chips. While not a classical “core facility” David mentioned that the BME faculty expertise is available for new collaborations.

Similarly, Ron Hart described the resources available at RUCDR for iPSC’s and Stem Cells generation based on an extensive genetic repository. The RUCDR hosts collection for NIDA, NIMH and recently NINDS. The RUCDR stem cell/iPSC resources are ideal for drug target and disease mechanism validation. These human normal and patient-derived cells represent a valuable intermediate screening step for therapy development to determine if mechanisms and targets identified in non-human models are applicable to human biology. RUCDR also performs CRISPR-based genome editing on these human lines and has superior bioinformatics,
RNAseq/ChIPseq/MeSeq/Microarray capabilities. While not a classical core facility, the RUCDR resources can be utilized by the neuroscience community- they need to approach Ron for help with this.

Hong Li described the NINDS P30 center grant funded proteomics core-facility at Rutgers. While the legacy UMDNJ core was funded by NINDS for 10 years, the latest award (2015-2019) is managed by Hong at Newark and Peter Lobel at Piscataway. The proteomics core provides research support to NINDS funded investigators on both campuses (particular expertise in studying post-translational modification of proteins). Hong described his experience putting together and administering a P30 center grant at Rutgers. He mentioned that there is a need for administrative support to put together these large center grants (something that BHI can provide) and also a clear indication of institutional commitment (in terms of supplementary financial and administrative resources, pilot funding etc.)

ORED & ORAD core facilities/services (Patrick Sinko)

The workshop concluded with a presentation by the Associate vice-president for Research Advancement, Dr. Patrick Sinko, who gave the group an overview of the resources and core facilities through Rutgers ORED. Pat mentioned that there is a university-wide initiative underway to determine the various core-facilities available and their operations. This might result in changes over the next few years in the core facilities on campus. Pat suggested that new core facility plans should be developed in consultation with his office as they might have resources and be able to reduce the impact of RCM costs. He also asked to bring to his attention needs for new core services (for e.g. a viral vector core would be very useful to support research in various disciplines). Currently ORED “core facilities” offer several new services that the community might not be aware of but is directly relevant to translational research. These include-Molecular Design and Synthesis; Molecular Imaging Center, Animal Research Pathology Services (through office of Rutgers Translational Sciences- Dr. David Kimble). Chemical Biology Core Facility; Genome Editing Core Facility; and Pharmacokinetics/ADME Services (through office of Research Advancement- Dr. Sinko). Currently all these services are highly subsidized. Pat’s office also oversees Comparative Medicine Resources (animal facility) and mentioned that there are plans underway to renovate the animal facility in the Research Tower.

Overall Impressions and future plans-

1. There appears to be a need for a tissue/brain bank with a neuropathologist for PD, MS & TBI. The newly hired Chair of pathology (presumably with new faculty positions) might be amenable to hiring a neuropathologist with BHI’s assistance.

2. A Glial Biology or White Matter Research Center that encompasses basic and clinical white matter research in MS, TBI/SCI, cognitive, developmental dysfunction. Initiate the center by reapplying for the NMSS center grant with clear documentation of institutional support from BHI/Rutgers. Follow up with a P50 funded center.

3. A core facility for TBI & SCI as proposed by Smita et al. Its services could be a bit more narrowly defined than shown in the current slide and avoid overlap with existing facilities. The primary focus could be on developing standardized TBI/SCI models for research purposes and coupling it with animal husbandry services, functional imaging (Steve’s 7T magnet) and a behavioral core. To minimize the logistical issue with animal transport, the core should be located in a dedicated space in a CMR facility on the two campuses. This core could be
associated with a new Center for Brain and Spinal Cord Injury with a newly hired Director with translational experience and significant extramural funding in TBI.

4. Need for a better integration of BME, RUCDR, Proteomics expertise and ORED core facilities into Center grant applications.

5. Formation of working subgroups for PD, MS, TBI/SCI areas or a “White Matter” sub group with a specific goal of developing Center grants, Core grants and T32 grants (in coordination with BHI, Millonig’s & Pintar’s on-going efforts). The subgroups should also identify the need for faculty recruitment and pilot funding to advance the development of the above applications.

6. Closer interaction with Patrick Sinko’s ORAD and Brittany Barkow at Rutgers Foundation to identify administrative, research and funding resources to support the above initiatives.