1) **Biomarkers** by Jennifer Goldman, MD, MS, Chair and Roy N. Alcalay, MD, MS, Co-chair.

The Biomarker WG met on Saturday Sept 17, 2016 at 1:30-3 PM. The meeting was well attended and facilitated by Jennifer G. Goldman (Chair) and Roy Alcalay.

The participants introduced themselves and described their interest in biomarkers. Biomarker interests were diverse, ranging from biological specimens to imaging among others, and many attendees bring clinical skills to the biomarker WG.

The introduction was followed by a presentation by Dr. Michael Schwarzschild. Dr. Schwarzschild presented an inspiring story of uric acid, from biomarker studies to the development and implementation of an NIH funded interventional trial. He further elaborated on the importance of the biomarker aspects of SURE-PD (e.g. to confirm target engagement).

Dr. Goldman reviewed the existing biomarker efforts from NIH and Michael J. Fox Foundation (MJFF) and provided an update on the Biotie/MJFF SYNAPSE PD Dementia pharmacogenomic sub-study).

Dr. Ivan Bodis-Wollner joined the group by phone and presented his preliminary data on retinal changes in Parkinson’s disease.

Lastly, the Biomarkers WG joined the Classic Motor WG meeting to hear a presentation by Dr. Alberto Espay outlining a project centered on developing biomarker-driven phenotyping (as opposed to the prevailing model of phenotype-driven biomarker development) that is under development.

2) **Cognitive/Psychiatric (Behavior)** by Jorge Juncos, MD, Chair and Jessica Freshour, PhD, Co-Chair.

Many attended the work group meeting on September 17, 2016. Laura Marsh, MD, Chair, stepped down from her position and Jorge Juncos assumed the Chair. Jessica (Calleo) Freshour was unable to attend due to a recent delivery of her baby.

Ongoing studies in cognitive and behavioral aspects of PD were given updates such as a Phase IV study of primavanserin and serotonin agonist in demetia. Ideas for potential funding were discussed for projects such as TMS in PD, DBS for depression, Ketamine infusion, and Lamotrigine. The group will meet again this fall 2017 in Florida and the PSG Annual Meeting.
3) **Genetics/Environmental Risk** by David Simon, MD, PhD, Chair and Anne-Marie Wills, MD, Co-chair.

Summary of the meeting of the Genetics and Environmental Risk Working Group meeting at the Annual PSG meeting in Portland, OR, 9-17-16: There were 32 in attendance.

The meeting opened with introduction of Anne-Marie Wills, who is our new co-Chair, joining Xiang Gao who will take over as Chair in January when David Simon steps down. David Simon briefly summarized the mandate, goals, and past accomplishments of this working group.

We next heard a presentation from Connie Marras regarding a new naming system for genetically determined movement disorders, as well as her collaborative work to establish the Movement Disorders Genetic Mutation Database (MDSGene).

Jim Boyd next gave an update on the NIC-PD study, as well as the current status of a study in the planning stages of a nicotine agonist to treat levodopa-induced dyskinesias (several members of this working group are involved).

Vanessa Arnedo from the Michael J. Fox Foundation presented data on a survey that assesses the impact of genetic counseling on genetic mutation carriers and at-risk subjects in the PPMI study.

Karlin Schroeder from the Parkinson Foundation (formerly NPF and PDF) briefly informed us about the PDF Leadership Awards for working with PDF “PAIRS” at early stages of clinical research.

The meeting closed with a reminder from David Simon for working group members to encourage others, especially junior investigators, to use the "Discussion/Review request form" (available on the PSG website) for advanced or early-stage ideas to take advantage of the expertise of our working group to facilitate clinical studies of relevance to our group.

4) **Classic Motor** by Alberto Espay, MD, MSC, Chair and Tiago Mestre, MD, Co-chair.

After a brief welcoming, the group reviewed the mission statement and goals for the Working Group.

**Update on ongoing studies:**
Alberto Espay provided an update on the works of the Task Force on Technology in PD and announced the statement of need on the use of technology-based objective measures (TOMs). The main statement paper was published in this month’s issue of *Movement Disorders*.

The proliferation of new technologies and technology developers has ushered the need for their integration into a single open-access platform to allow synchronized, closed-loop multi-channel data. Work toward such integration is under development in collaboration with the Carnegie Mellon University.

Integration of telemedicine was discussed. There will be combined efforts of both technology and telemedicine task forces by next year at the MDS annual meeting.
**Discussion of proposals for PD studies:**
The placebo data from a fetal transplant study was presented by Cyndy McRae, PhD. She has access to data from early stem cell transplant studies, and is particularly interested in further data-mining the placebo effect based on the one-year double-blind period, based on a prior report that the perceived allocation to real vs sham surgery affected the outcome more robustly than the actual treatment effect. She will be answering several questions, including the medical and psychosocial predictors of perceived treatment at 4, 8, and 12 months.

Low-dose lithium as adjunct treatment for PD in motor fluctuators was presented by Tom Guttuso, Jr., MD. He reviewed his open label data (which was recently published in letter form) which suggested that low-dose lithium may be beneficial in PD motor fluctuators otherwise considered optimal surgical candidates. The discussion centered on the logistical challenges of determining the dose that may be not low enough to actually induce parkinsonism (literature reviewed) and the extent to which pharmacogenomics techniques may be used to recognize whether there is a genotype (in or beyond the GSK3beta receptors presumed to be targeted by lithium) to distinguish those who would benefit from those who may be harmed. Dr. Guttuso will communicate with GSK3beta expert from NIH and explore potential funding sources for further development.

The last 20 minutes were devoted to the shifting concept in biomarker development in combination with the Biomarker WG. We discussed the current phenotype-driven biomarker development and the need for a complementary but reversed biomarker-driven phenotyping if we are to make strides in validating targets and subpopulations amenable to disease modifying therapies. This model of biomarker development will be incorporated in an upcoming large biomarker-development study with foundation support.

5) **Other Non-Motor Features of PD** by Aleks Videnovic, MD, Chair, Leslie Cloud and Pinky Agarwal, Co-chairs.

Dr. Ron Pfeiffer opened the meeting with a presentation related to gastrointestinal physiology/pathology in PD. He reviewed available data that suggest early GI involvement in PD that may start in the enteric nervous system and progress along the Vagus nerve to the lower brainstem. He also discussed influences that CNS has on GI dysfunction in PD and talked about changes in the gut microbiome in PD.

Four members of the workgroup subsequently gave focused presentations of research projects:

- Dr. Leslie Cloud discussed the current study of RQ-10 for gastroparesis and constipation in PD. RQ-10 is a novel 5HT4-receptor partial agonist. In this 3-year study, which is funded by the MJFF, the safety, tolerability, pharmacokinetics, and effects on gastric emptying of single and multiple doses of RQ-10 in PD will be tested.

- Dr. Tiago Mestre discussed his upcoming study of glycopyrrolate for sialorrhea in PD. This is a phase 2 double-blind placebo controlled trial in 2 sites in Canada. He hopes this may lead to a larger multicenter study down the road.

- Dr. David Shprecher discussed an upcoming expansion of the Banner Health Brain & Body Donation Program to include patients with idiopathic RBD. Patients with idiopathic RBD will undergo annual physical, neurological and cognitive exams. They will also be consented for whole
body donation after their death. This study has the potential to shed new light on the relationship between RBD and synucleinopathies.

- Dr. Pinky Agarwal discussed 2 studies of overactive bladder in PD. One study in collaboration with radiology division of U PENN involves assessing for increased neural activity in areas of the brain processing emotion in patients with OAB using functional BOLD MRI. The second study will assess efficacy and safety profile of beta 3 adrenergic agonist drug Mirabegron in patients with OAB.

Formal presentations were concluded with a discussion of a brief PSG survey developed by Dr. Aleks Videnovic. This brief 3-question survey was circulated recently via e-mail to PSG investigators to gauge their interest and capabilities for collaborative multicenter PSG studies of RBD. The survey results confirm a high level of interest for this initiative, and follow up activities will be planned based on this initial outreach.

The meeting was very well attended and agenda topics stimulated lively discussion. Time limitations limited discussion about potential new collaborative projects and brainstorming. Ongoing e-mail communication within the members of the workgroup after this meeting will be utilized as a platform to explore mutual interests of the members and collaborative projects.

6) **Health/Care Outcomes & Disparities** by Allison Willis, MD, MS, Chair and Lisa Shulman, MD, MS, Co-chair.

**Summary**: The Health Care Outcomes and Disparities Working group had a productive year, culminating in the 2016 PSG meeting. Below we describe the 2015-2016 year activities, plan for the 2016-2017 year, and introduce the progress made toward the 2016-2017 goals thusfar.

**Review of 2015-2016 Activities**: The HCODWG produced data on physiotherapy use in PD, and on sex differences in comorbid disease and health care use. Two manuscripts were co-authored by the HCODWG members:

1. **“Gender Disparities in Health and Health Care Utilization after Parkinson Diagnosis- Rethinking PD Associated Disability”**. This paper is current under review for publication
2. **“Utilization of Rehabilitation Therapy Services in Parkinson’s disease in the United States”**. This paper was submitted and favorably reviewed at a leading neurology journal. Revisions have been invited. We hope for an acceptance within the next 30 days.

**Planned Activities, HCODWG 2016-2017.**

1. As a result of discussions that began at the PSG annual Meeting in Portland, we have designated a theme for this year- Deep Brain Stimulation. Our primary research/writing activities will focus on collaborating with the Functional Neurosurgery Group, as they work to plan a PSG lead DBS registry. Specific HCODWG activities as they relate to this collaborative effort are as follows
   a. HCODWG members will provide expertise on the registry design, outcome selections.
   b. The HCODWG will produce national data on health care utilization after DBS, including perioperative complications, mortality, readmissions. These data currently do not exist on a national level.
2. We will also produce national data on health care shortage areas for Parkinson Disease, using an approach similar to what is currently used to guide federal budgeting for health care provider shortages. We think these data will be helpful to all PD foundations.
Progress on HCODWG activities to date (3/14/17).

1. HCODWG members have been involved in the design of the RAD-PD registry
2. We have completed the analysis for the first manuscript from this year, which examines national rates of DBS complications and unplanned admissions after DBS. Manuscript writing will be in in the next two weeks, with a planned submission date of July 1, 2017.
3. PD shortage area project: background and methodology research for this project will begin in April 2017.

7) **Functional Neurosurgical** by Elena Moro, MD, PhD, Chair.

The three leaders of the FNWG (E. Moro, J. Schwalb, J. Jimenez-Shahed) were all present in person. Thirty-two members attended the meeting.

The FNWG welcomed all members, who briefly introduced themselves. The main working group objectives and the meeting agenda were briefly reviewed by E. Moro.

J. Jimenez-Shahed updated the members on the RAD-PD project. The main news is the MJFF has supported a planning grant to establish a protocol for a Registry for DBS PD patients.

M. Burack suggested to investigate the impact of Duopa therapy compared to DBS. She presented some data of 21 pts at UofR (see her abstract). None chose Duopa over DBS as initial treatment. Pts who had previously refused DBs did not want Duopa (no surgery). One postop DBS pt has undergone Duopa therapy. There is different practice between countries in Europe and North America, with cultural and neurologist related biases, together with stigma of feeding tube in US and France. We could look at cost in US. Obviously some bias based on self-selection of people in the room. A survey of what is going on across US and patient/physician preferences might be interesting. A focused group?

D. Kern proposed a study with interleaving stimulation during the last group meeting. He is willing to lead the project together with F Farrokhi. He provided systematic review of interleaving and the Toronto experience. Not a lot of data and not much benefit in TO but there is some benefit on dyskinesia. Some centers would like to be involved in a trial to better investigate this programming tool.

K. Mills and A. Butala intervened on behalf of Z. Mari (excused). They presented some results from a survey on DBS practice done with the help of the NPF and the MDS. Only 59 centers replied. Does DBS volume inversely correlate with number of trials for medications at that site? The Chairs recommend adapt survey for PSG, but need to see all data first.

C. McRae would like to have some collaboration from the group to collect more data from the patients involved in the fetal transplantation trial more than 15 years ago.

Some previously proposed projects (Studies comparing DBS using intraoperative MRI versus awake surgeries with MER; Expert consensus: STN vs GPi target selection referrals (survey?); Neuroethics and DBS (patients and caregivers’ perspectives, surveys, etc.; Parkinson Alliance might help); Multi-center prospective investigation of ICDs following DBS) were not discussed, especially because of lacking of time.