PSG Annual Meeting

The PSG Annual Meeting was held on May 8 and 9 at the Coronado Island Marriott Resort in San Diego, California. There were 225 attendees that included special guests, industry representatives and research sponsors. Highlights included the PSG Biomarker Symposium in Honor of Clifford W. Shults, MD. Ellen Koutsky Shults said a few words about Cliff and brought a collage of pictures to share with everyone. Un Kang coordinated the symposium which brought together many experts in the field of biomarkers: Doug Galasko, Ken Marek, Kirk Frey, Nick Bohnen, David Eidelberg, Flint Beal, Michael Schwarzschild, Michael Schlossmacher, Jing Zhang, Clemens Scherzer, and Kalpana Merchant. Later that evening after the symposium, working group meetings were held with members from the Scientific Review Committee (SRC) and Mentoring Committee (MC) participating. Summaries of those meetings can be found on pages 2-4. Many members participated in the New Members Workshop and the GCP Training Session. Bright and early the next day, members participated in eRT/eDE basic and advanced training using the mobile training lab funded by the Parkinson’s Disease Foundation. At the PSG Membership Business Meeting, memorials for Leon Thal and Cliff Shults were given by Karl Kieburtz and Ira Shoulson. Donna Thal and Ellen Koutsky Shults participated. This was followed by honors to Aileen Shinaman and Alice Rudolph for their service on the PSG Executive Committee and all they have done for the PSG over many years. Research progress reports were given by Ergun Uc, Michael Schwarzschild, Jing Zhang, Connie Marras, Robert Hauser and Mike McDermott, Jay Nutt, and Tatiana Foroud. Members were impressed with the amount of research that is in progress and all presenters acknowledged the support of the Michael J. Fox Foundation, NIH, and the Parkinson’s Disease Foundation.

Tim Greenamyre and Cindy Comella gave brief reports on the SRC and MC, respectively, followed by a special research progress report given by Xiang Gao, the Mentored Clinical Research Awardee for 2007-2008. The meeting continued with study specific meetings and committee meetings all afternoon. To round out the meeting, an All Coordinators’ Meeting and an All Investigators’ Meeting were held. The coordinators discussed grant funding opportunities led by Mickie Welsh and site budgeting by Pat Donaghue. The investigators discussed the future competitiveness of the PSG and patient recruitment. The meeting ended with a joint reception for all meeting attendees hosted by the Executive Committee in honor of coordinators.

Special thanks goes out to Donna Moszkowicz for arranging all meeting rooms, meals, AV needs, etc. Her close attention to detail and expertise in meeting planning made all the difference in making the meeting a success and enjoyable by all. Mary Slough and Jill Lowell provided excellent support to Donna throughout the meeting and their hard work was appreciated, as well.

The next PSG Annual Meeting will be in the spring of 2009 - dates and locale to be announced soon.
Election Results

The PSG Election results were announced by Karen Rabinowtiz at the PSG Annual Meeting. Members elected Frederick Wooten and Jeana Jaglin to the PSG Executive Committee. This concluded terms for Ron Pfeiffer and Mickie Welsh on the committee and their hard work and dedication to this committee was acknowledged. We thank nominees Jorge Juncos, Deborah Fontaine and Barbara Fussell for accepting the nomination and acknowledge them for that honor. We want to thank all the PSG members who voted.

Training Modules

New this year at the PSG Annual Meeting were two training modules: “Developing a Single Center Study” given by Karl Kieburtz and Tom Guttuso and the other on “Training Mentors to be Mentors” given by Joel Perlmutter, Co-chair of the PSG Mentoring Committee. These were both well received. The training module on “Developing a Single Center Study” was audiotaped and is available on CD-ROM to anyone wishing to borrow it. We hope to be able to post this on the website in the near future for easy access for all. We thank those who provided ideas on the evaluation form for other topics they would like to see presented at future annual meetings.

Working Groups

The working groups met in person at the PSG Annual Meeting on May 8, 2008. This was the first in-person meeting for two working groups, the Functional Neurosurgery and Classic Motor groups. Members of the Mentoring and Scientific Review Committees attended to offer advice on research proposals in progress. The following is a brief summary of each meeting:

Biomarkers

The Biomarkers Working Group members were joined by faculty from the PSG Biomarker Symposium to follow up on issues raised during that session, and to brainstorm future directions in PD biomarker development. Discussion focused upon the questions of which biomarkers currently show greatest promise for further development, and how best to coordinate investigator’s efforts in neuroimaging and biochemical marker development. Progress over the previous year was reviewed, including (1) Dr. Jing Zhang’s proteomic analysis of CSF samples collected during the DATATOP trial (PDF/PSG funded), (2) Dr. Roger Kurlan’s proposal for testing various biomarker approaches in plasma to be collected in the QE3 trial (MJFF funded), and (3) Dr. Claire Henchcliffe’s study of MR spectroscopy as an ancillary study to the QE3 trial. Dr. Ivan Bodis-Wollner was invited to present promising data on optical coherence tomography. He will work with David Oakes to analyze his preliminary data and to perform power analysis upon which to base his design for a multicenter study.

Finally the Biomarkers and Cognitive Psychiatric Working Groups met jointly with the symposium speakers, given obviously overlapping interests, for exploratory discussions regarding the pressing need to look outside of the nigra and to develop biomarkers for cognitive and psychiatric symptoms in PD.
**Classic Motor**

The mission of the Classic Motor Working Group is to foster and develop research projects related to motor function in PD. This can include data mining projects, observational studies, interventional clinical trials, and other activities as appropriate. The Classic Motor Working Group met at the PSG meeting and discussed several proposals. A proposal was presented on behalf of Susan Fox regarding intravenous levodopa infusions as a means of assessing dyskinesia and wearing-off in phase II studies. Jay Nutt generously provided input and guidance based on his experience with levodopa infusions. There is interest in developing a small group of centers who will have the capacity to perform collaborative levodopa infusion studies.

Michelle Burack presented a proposal related to treatment of dyskinesia. She is interested in how we currently treat dyskinesia and how successful we are or are not. Allan Wu presented work on developing a more sensitive measure of motor function using a tapping device. Robert Hauser discussed a project to further define minimally relevant clinical changes. Interested individuals are encouraged to propose new projects and those interested in forming collaborations are encouraged to email the above individuals.

**Cognitive Psychiatric**

Dr. Uc briefly presented the results of the PDF funded study on the incidence and predictors of dementia and depression in the DATATOP trial. Dr. Chou summarized the efforts of the Cognitive Core Data Task Force to date. The task force has been considering adopting the cognitive component of the PD-DOC battery with some modifications, e.g., adding a visuospatial task. This was followed by a group discussion on the potential composition of a core battery and further meetings of the task force will be arranged to advance this initiative. Dr. Chou and colleagues will prepare a white paper on a proposed cognitive battery, which eventually will be presented to the PSG for consideration in upcoming studies. These presentations were followed by self-introduction of the attendees, describing their background, research interests, and suggestions for the working group.

At 9 pm, the Cognition/Behavior working group joined the Biomarker Group for a joint discussion with speakers of the Biomarkers symposium. Also, a brief discussion took place how to use the DATATOP repository for data-mining studies.

**Genetics/Environmental Risk**

The recently funded proposal “Vitamin D insufficiency: Prevalence and Clinical Correlates in the DATATOP Cohort” was discussed and the group will consider the following caveats: 1) the best use of the samples of the DATATOP study, and 2) the infrastructure of sample handling. A long-term goal should be making instruments available through the web, similar to what’s available on PD-DOC and regarding data collection standards. The group recommended looking into biosamples and minimal set of epi information. The members are also concerned about variations brought out by seasons, mobility, and sun exposure. These variables would affect the analysis of Vitamin D levels of study patients. The group noted that one unique feature of the PSG studies is that they could compare the current exposures to remote exposures due to the longitudinal nature of many of these studies. They also are considering developing/adopting some simple screening questions such as a “yes” or “no” to family history to start with.

**Functional Neurosurgical**

Dr.’s Okun, Fernandez and Kumar led a discussion of potential projects to be written up for formal proposals to the PSG Executive Committee. Based on the first phone call in 2007 and this in-person meeting, it was decided that 5 smaller working groups with one leader for each group would be formed. These groups will be charged with writing a proposal for the executive committee due on August 1. The group leaders are: 1) Zona Incerta - DBS for PD- group leader Robert Gross, Emory University; 2) Mood Fluctuations and DBS-group leader Tiffany Voss, U of R; 3) Earlier DBS- group
leader Rajeev Kumar, Colorado Neurological Institute; 4) PPN DBS- group leader Michael Okun, University of Florida; 5) Grounded Theory DBS- group leader Hubert Fernandez, University of Florida. These are the first five projects for 2008, and we will potentially reopen new ideas for 2009.

**Other Non-Motor Features**

The meeting focused on two projects in different stages of development. Dr. Peter Novak’s project “Evaluation of parasympathetic dysfunction in early PD” was discussed by Dr. Ivan Bodis-Wollner. General discussion praised the potential value of the proposed study. Dr. Novak and Bodis-Wollner will continue to work on this project. Dr. Theresa Zesiewicz’s project entitled: “URGE-PD: A Multi-Site, Double-Blind, Randomized, Placebo-Controlled Trial of Solifenacine Succinate (VESIcare) for the Treatment of Urinary Dysfunction in Parkinson’s Disease” was “workshopped” via a slide presentation with corrections and additions made based on suggestions by reviewers of the Scientific Review Committee (SRC). Dr. Zesiewicz plans to present the revised proposal to Astellas as a pilot study involving 3-4 sites. The revised protocol would also be concurrently presented to the SRC.

**Working Group Leaders’ meeting**

The following morning after all six working groups had held their meetings, the working group leaders got together for their first in-person meeting to share ideas for the operation of the working groups and to explore cross-working group collaborations. Each working group leader summarized their activities as the first step toward this goal. A suggestion was made to have two blocks of time for working group meetings next year, so that a member may be able to attend more than one working group meeting.

**Study Updates**

Study-specific meetings were held at the PSG Annual Meeting on May 8th and 9th. The following is a brief synopsis of each meeting:

**QE3**

*by Amy Beimler*

The QE3 Investigator and Coordinator meeting was successfully attended by the 65 plus sites participating in the US and Canada. Principal Investigators Flint Beal, MD and David Oakes, PhD and Co-Principal Investigator Ira Shoulson, MD led the presentations highlighting study updates, reviewing the study protocol and preparing sites for study start-up. After a series of past delays, the Steering Committee looks forward to a fall 2008 commencement as they remain committed to researching improved outcomes for PD patients with this treatment strategy. The objective of this study is to evaluate the safety and effectiveness of high dosages of CoQ (2400 mg and 1200 mg vs placebo) in slowing clinical decline in patients with early PD. Participants, who will be followed every four months over a 16 month period, must be diagnosed with PD within the last 5 years and not yet receiving dopaminergic therapy.

**PROGENI**

*by Cheryl Halter*

Dr. Tatiana Foroud from Indiana University welcomed current PROGENI investigators and coordinators to a presentation during which she shared progress from the past 2 years, since the last PSG annual meeting. Dr. Foroud opened the meeting to non-PROGENI investigators and coordinators and welcomed them to consider participating in the study. She reported that over the past 8 years PROGENI investigators have evaluated 1695 subjects at 60 PSG sites. Together with Dr. Nathan Pankratz, she discussed recent publications, particularly those investigating the role of LRRK2 in PD and findings about depression in PROGENI participants. Dr. Foroud also discussed the
recent Genome Wide Association study undertaken in collaboration with Dr. Richard Myers from Boston University. In conclusion, Dr. Foroud discussed recent recruitment expansion in the study. While PROGENI continues to recruit sibling pairs, enrollment has been expanded to include singletons that can document another first degree relative with PD. In addition, affected parent/child families are now being recruited for the study. Recent advances in analysis techniques have made the inclusion of these types of family possible for the study.

PramiBID
by Alice Rudolph

The Investigators and Coordinators for PramiBID (A randomized, double-blind, active and placebo controlled, efficacy study of pramipexole given 0.5 mg and 0.75 mg bid over a 12-week treatment phase in early Parkinson’s disease patients) met at the PSG Annual Meeting to discuss making a final recruitment effort in order to reach the enrollment goal of 296 subjects prior to June 30th. We are happy to report that, despite everyone’s concerns at the time of that meeting, sites were successful in enrolling a total of 311 subjects. The final subject visit is expected in late September and database lock will follow soon after.

SURE-PD
by Alice Rudolph

At the PSG Annual Meeting, SURE-PD (Safety of URate Elevation in Parkinson’s Disease) Investigators and Coordinators from the 11 sites gathered for the first time at a late-night informal meeting. SURE-PD is a randomized, double-blind, placebo-controlled, dose-ranging trial of oral inosine to assess safety and ability to elevate CSF urate in early Parkinson’s disease. The study is funded by the Michael J. Fox Foundation and is being led by Michael Schwarzschild from Mass General. In fall 2008 the study will hold its Orientation Meeting and begin enrollment of 90 subjects.

PostCEPT/PROBE
by Emily Flagg

The Investigators and Coordinators for the PostCEPT (A Longitudinal Observational Follow-up of the PRECEPT Study Cohort) and PROBE (Blood α-Synuclein, Gene Expression, and Smell Testing as Diagnostic and Prognostic Biomarkers in Parkinson’s Disease) studies had a joint meeting at the PSG Annual Meeting. The group reviewed the current status of the PostCEPT study that had a very successful enrollment of 537 subjects from the PRECEPT cohort at 54 sites. PostCEPT is finishing up the first year of follow up visits and the second year of follow up will be starting this summer. The PROBE study is moving along well and we plan to wrap up enrollment of 200 subjects (including PD, MSA, PSP and healthy controls) by August 2008. Planned analyses of the biomarker research labs will begin shortly thereafter.

Annual Symposium: Etiology, Pathogenesis, and Treatment of Parkinson’s Disease and Other Movement Disorders

The 22nd Annual Symposium on Etiology, Pathogenesis, and Treatment of PD and OMD will be held on Sunday, September 21, 2008 at The Grand America Hotel in Salt Lake City, Utah in association with the ANA meeting. The PSG and HSG Symposia Committee members (Andrew Siderowf, Jang-Ho Cha, Michael Schwarzschild, Roger Albin, Tanya Simuni, Guerry Peavy, Andrew Feigin, and Julie Stout) rated and selected regular and late-breaking research abstracts for platform and poster presentations. Web Ross and Jane Paulsen are the keynote speakers and will be addressing the challenges involved in early detection and potential treatment of Parkinson’s disease and Huntington’s disease. They will start off the program followed by a panel discussion with the audience and experts in the field. For more information and to view an abbreviated program, visit the PSG website at http://www.parkinson-study-group.org.
I joined the PSG in 1996 as a junior investigator at the recommendation of John Growdon at the end of my movement disorder fellowship at Massachusetts General Hospital. Although my research experience was laboratory-based (neurochemistry and molecular biology of dopaminergic systems), John encouraged clinical research exposure, even if modest, to open a door to future opportunities that might complement my basic science approach to Parkinson’s disease. This was good advice for me then, and I think it applies well to many junior investigators now. Upon joining I served as a site treating investigator for the ELLDOPA study.

In 1999, I attended the 12th annual PSG meeting in Las Vegas which featured a workshop by Stan Fahn entitled “From the Egg to the Golden Goose”, describing strategies for pursuing research ideas toward Parkinson’s disease trials. This drove home the PSG philosophy of encouraging junior investigators to pursue their ideas for novel clinical research in PD and inspired me to take it to heart. However, despite this encouragement, at the time junior investigators had limited access to discuss ideas with senior PSG investigators and Scientific Advisory Committee members. Considerable initiative was often required to obtain their advice at PSG meetings, usually by corralling them in the hallway between sessions, en route to the lavatory, on the shuttle bus to the airport, etc. In the last couple years, to further encourage investigator-initiated research projects, PSG mechanisms have been formalized for individual guidance (via the Mentorship Committee) and concept development (via Working Groups and Scientific Review Committee/Executive Committee review) under Karl’s and Karen’s leadership.

In 2000, I submitted a grant proposal to the PSG for a clinical research project, “Caffeine Consumption and Rates of Progression and Dyskinesia in PD”. Though the PSG did not fund the proposal they offered encouraging feedback. A revised version was submitted to the Michael J. Fox Foundation in 2001 in their inaugural call for research applications, and was funded permitting the development and administration of a caffeine questionnaire to the majority of the CALM-PD cohort as a PSG study (“CUPS of CALM-PD”). Over the past five or six years, I was fortunate to develop a productive interdisciplinary collaboration with Alberto Ascherio, MD, DrPH of the Harvard School of Public Health. Initially, my laboratory’s findings on adenosinergic mechanisms in mouse models of PD converged with those of his neuroepidemiology group on caffeine and PD risk. (Caffeine acts on the brain through blockade of adenosine receptors.) This collaboration led to insights into the mechanisms and epidemiology of PD, and also prompted us to consider whether newly identified factors linked to the risk of PD might also be associated with altered rates of disease progression. In 2005 Alberto’s group was beginning to uncover dramatic evidence that higher blood levels of the endogenous antioxidant urate are strongly associated with a reduced risk of developing PD, substantiating a less conclusive association that had been observed in a smaller earlier study. This prompted my posing with Alberto the hypothesis that higher urate levels are predictive of a slower rate of disease progression (as well as a lower risk of PD). We figured the easiest way to test the hypothesis would be to identify a completed or ongoing PSG trial that had collected baseline urate data and then rigorously characterized rates of disease progression.

We were initially unaware of any PSG study that had collected baseline blood urate data, and focused on the CSF samples analyses conducted in DATATOP. However, during the PRECEPT closeout meeting in 2005, my jaw dropped when I heard during a talk by Steve Schwid on the safety profile of the study drug CEP-1347 that it produced no significant effect on blood urate levels. Immediately appreciating that PRECEPT could offer that test we were seeking of our urate and PD progression hypothesis, I put together a quick inquiry to Ira Shoulson. Ira forwarded my questions to Steve Schwid on the safety profile of the study drug CEP-1347 that it produced no significant effect on blood urate levels. Immediately appreciating that PRECEPT could offer that test we were seeking of our urate and PD progression hypothesis, I put together a quick inquiry to Ira Shoulson. Ira forwarded my questions to Steve Schwid and we were on our way to further developing our research. This followed with work with David Oakes and his biostats group as well as Ira and the steering committees of the PRECEPT and the DATATOP studies. Alberto and I have obtained evidence strongly supporting the urate and PD progression hypothesis. These findings led to further data-mining studies and new mechanistic research, and prompted the development of our upcoming PSG trial to investigate inosine as a urate-elevating strategy in early PD. Regardless of whether urate elevation proves helpful, the discovery of a link between urate and Parkinson’s represents an important advance in our understanding of the disease.

Dr. Schwarzschild is an Associate Professor of Neurology, at Harvard Medical School, Massachusetts General Institute for Neurodegenerative Disease. For further reading on this topic, see “Serum Urate as a Predictor of Clinical and Radiographic Progression in PD”, Arch Neurol 2008 Jun;65(6):716–23.
Mentoring Committee News

Mentored Clinical Research Award

This year’s Mentored Clinical Research Award (MCRA) was awarded to Gregory Pontone, MD, Johns Hopkins University. His research is entitled “Prevalence and familial aggregation of panic disorder in patients with PD”. He will present his research at the next PSG Annual Meeting. The MCRA is an annual award program funded by a grant from the Parkinson’s Disease Foundation to the PSG. The purpose of this grant is to support a new investigator for a 1 year project in patient orientated research in PD or other parkinsonian disorders under the mentorship of an experienced investigator with the goal of making this individual an independent researcher.

Mentorship Lunch Symposium

The Mentoring Committee held a Mentorship Lunch Symposium on Tuesday, June 24th at the MDS meeting in Chicago entitled “Pearls from junior and senior mentors for new investigators: Opportunities and obstacles”. This was held jointly with MDS and involved a panel discussion with a panel of recently mentored colleagues who went on to successful careers and a panel of mentors who have had experience with the mentorship process. The symposium which was led by Cynthia Comella and moderated by Stan Fahn, included Connie Marras, Christine Klein, Ray Dorsey, and Birgit Högl representing the recently mentored faculty and Oscar Gershanik, Tony Lang, Karl Kieburztz, Yoshi Mizuno, Eduardo Tolosa, and Kimberly Gray representing the mentors with experience in the mentorship process. The audience of over 60 people enjoyed an informal discussion of the opportunities and obstacles for new investigators after the panel members shared what they thought was the most valuable pearl for them just beginning their career.

Standing Committees

The following members completed their terms on the following committees: Nominating Committee: Ron Pfeiffer, Lawrence Elmer, Joseph Friedman, Neal Hermanowicz, Maureen Lehey, John Morgan, Robert Rodnitzky, Cathi Thomas, and Theresa Zesiewicz; Standards Committee: David Standaert and Brad Racette; Study Budget Committee: Lisa Gauger, Christine Hunter, Meg Lannon, Bill Weiner; Symposia Committee: Andrew Siderowf completes his term after the symposium this year; Credentials Committee: Neal Hermanowicz, Jeana Jaglin, and Lauren Seeberger; Mentoring Committee: Connie Marras; Scientific Review Committee: Timothy Greenamyre, Chair. Many thanks goes out to them for their dedicated service. New members appointed are: Nominating Committee: Bill Weiner, Chair, Karen Blindauer, Brad Racette, and Oksana Suchowersky; Standards Committee: Joseph Jankovic was appointed Chair, Susan Fox and Eric Molho; Study Budget Committee: Stewart Factor will continue to serve as Chair for an extended term, Ron Pfeiffer will
extend his term, Pat Deppen, Mary Edna Parish, Mickie Welsh, and Theresa Zesiewicz; **Symposia Committee:** Roger Albin was appointed the next Chair and Michele Tagliati; **Credentials Committee:** Christine Hunter, Mark Lew, and Lin Zhang; **Mentoring Committee:** Gregory Pontone; **Scientific Review Committee:** Carlie Tanner, Co-chair, appointed new Chair.

Since the Mentoring Committee is a fairly new committee, Dr. Comella asked the members if they would be willing to extend their terms and continue to serve and they agreed. The Scientific Review Committee members have been asked if they would be willing to extend their terms, also, being in a similar situation as the Mentoring Committee. New terms have yet to be confirmed and Dr. Greenamyre will continue to serve on the committee.

We congratulate and welcome all the new committee members and look forward to working with them.

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**PSG SITE MAP**

_The PSG Site Map has been updated thanks to all of you who responded to our request for your contact information – 28 sites had not been listed and now they are – please let Roseanna know if any information is not correct or has changed. To view the site map go to [http://www.parkinson-study-group.org/psgmap/](http://www.parkinson-study-group.org/psgmap/)._

Remember to refer to the PSG website often for PSG up-to-date information on RFPs, studies, awards, and upcoming events.