Overview

*Robert Sokol, M.D. – Director*

**Introduction**

During the past several years our efforts have been directed towards achieving and maintaining a preeminent position in Reproductive Sciences Research in the nation, now and, more importantly, into the future. This has been a demanding and protracted process, as would be expected for a Center of this magnitude and research productivity and during a period of nearly unprecedented fiscal constraint, particularly in the Detroit area. Despite these challenges, **we are building new area(s) and program(s) for the Mott consistent with the needs for a balanced research portfolio spanning areas of reproductive and perinatal science.**

**The Big News for 2013**

With the assistance of many other individuals and university officers, including the Dean of the School of Medicine, the President of the University and the Board of Governors, **Doctors Sokol and Hassan of the Department of Ob/Gyn were once again awarded as Project Site Managers a 10-year contract to house the Perinatology Research Branch of the NIH on the 3rd floor of the C.S. Mott Center for Human Growth and Development and at Hutzel Hospital.** Over 10 years 3 months, this large award, including provision for space for the work of the Branch and collaborating Wayne faculty, has already helped and will help set strategic directions for recruitment and ongoing research in the Department of ObGyn and at the Mott Center and will have an impact on research planning and execution for the entire University and investigators, not only at Wayne State, but also at the University of Michigan, Michigan State and the Henry Ford Health System.

**Site Visit(s) – NIH, CAP, CLIA**

In preparation for several site visits held throughout 2013, many preliminary steps to reconfigure or renovate portions of the building were focused on. This included reconfiguring major areas on the third floor in support of the PRB and perinatal research, as well as on the 2nd floor to accommodate the research program that houses some of the WRHR scholar research. Substantial movement of laboratory personnel and laboratory equipment to reorganize the research space throughout the building was planned and accomplished in early 2014 in preparation for new faculty joining the Mott and a third site visit to the PRB.

A CAP CLIA site visit was also held in 2013 for the AGTC Core Laboratory Facility. For the AGTC to provide specialized clinically applicable laboratory services for the future, it was imperative that CAP certification was approved. This process was very long with many steps and overall took approximately 2 years from the initial steps to completion. **ISO and CAP accreditations were achieved opening the way to proceed with our Personalized (Precision) Medicine initiative, in conjunction with the Karmanos Cancer Institute.**

**Where We Are Scientifically**

During 2013, the Mott Internal Advisory Committee continued to be chaired by Dr. Joseph Dunbar, Associate Vice President for Research; and the External Advisory Committee also continued to be chaired by Dr. Gloria Heppner, Associate Vice President for Research. Both the chairs and their committees contribute immensely to guiding and enhancing the Mott’s operation and development. We continue to update membership on both committees to assure appropriate representation of Mott stakeholders.

The Mott Center continues to broaden collaboration by increasing interdisciplinary and multidisciplinary research in areas that include genomics, bioinformatics, perinatal epidemiology,
reproductive sciences and genetics. Partnership with the PRB continues and extends to other centers and departments in Wayne State University, e.g., the Center for Molecular Medicine and Genetics and the Merrill Palmer Skillman Institute.

**Publications:** We continue to demonstrate excellent productivity as measured by publications, with 118 refereed articles published and in press this year. In other words, that's about one referred paper from the Mott every three days!

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**Grants and Contracts:** Grant and contract support is also in reasonable shape. Of course, with NIH paylines as unfavorable as they’ve ever been, maintaining an acceptable level of funding is a major challenge. Further, several of our investigators derive substantial support for their labs from the PRB contract (as they were recruited to do), though they also seek external grant support. As of the date of writing, based on information gleaned from the ObGyn Department, investigators’ CVs and related documentation, these faculty members have the listed number of pending grant requests --

- Abu-Soud – 2
- Awonuga – 1
- Belotte - 2
- Chen – 1
The total direct costs requested by Mott personnel is approximately $11.8 million in 28 requests. Over the calendar year, >50 grant requests were submitted. Last year at the time of this writing we had requests out for ~$12.5 million.

At the time of this writing in April, 2014, Mott faculty is involved with 40 active research grant with a total value of $4,183,535. At this time last year, this was figure was ~$2.5 million. If one includes the PRB contract, this year’s grant and contract figure climbs to $20,683,535.

The Clinical Research Center (CRC)
A first floor patient-oriented CRC was renovated and reactivated, after having served as the base for WSU’s participation in the Women’s Health Initiative, a few years ago as part of our commitment to translational research. This area continues to be fully operational, and has many on-going interdepartmental and inter-institutional clinical research projects. These include –

1) Human Skeletal Muscle Proteome and Phosphoproteome in Obesity and Type 2 Diabetes (College of Pharmacy and Health Sciences, Zhengping Yi - PI);
2) Asthma Phenotypes in the Inner City (HFHS, Edward M. Zoratti - PI);
3) A Biomarker-Based Pilot Study of Cockroach Sublingual Immunotherapy in Cockroach Sensitive Children with Asthma and/or Perennial Allergic Rhinitis (HFHS - Edward M. Zoratti - PI);
4) The Role of Epigenetics in Inner City Asthma (HFHS – Edward M. Zoratti, PI);
5) Registry for Asthma Characterization and Recruitment (HFHS, Edward M. Zoratti - PI);
6) Preventative Omalizumab or Step-Up Therapy for Severe Fall Exacerbations (HFHS, Edward M. Zoratti - PI);
7) A Phase 3/4, Multi-Center, Randomized, Double-Blind, Placebo-Controlled, 52-Week Study to Evaluate the Efficacy and Safety of Belimumab (HGS1006) in Adult Subjects of Black Race with Systemic Lupus Erythematosus (SLE) (Dept. Internal Medicine, Josephine P. Dhar - PI);
8) Phase I, Safety and Immunogenicity of Gardasil in Systemic Lupus Erythematosus (Dept. Internal Medicine, Josephine P. Dhar - PI);
9) A Randomized, Double-Blind, Placebo-Controlled 52-Week Study to Assess Adverse Events of Special Interest in Adults with Active, Autoantibody-positive Systemic Lupus (Dept. Internal Medicine, Josephine P. Dhar – PI);
10) A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Belimumab Plus Standard of Care vs. Placebo Plus Standard of…. (Dept. Internal Medicine, Josephine P. Dhar - PI);
11) Uses of Propranolol to Block Memory Reconsolidation to Female OIF/OEF Veterans (Dept. Psychiatry, Deane Aikins – PI);
12) A Phase-3, Open Label, Randomized, Multi-Center Study to Assess the Safety and Tolerability of an Induction, Titration, And Maintenance Dose Regimen of BMN 165 Self (Department Pediatrics, Robert Conway – PI);
13) Adjunct Vitamin D Therapy as a Means to Reduce the Disparity in Subclinical Target Organ Cardiac Damage Among Vulnerable Hypertensive Patients (Dept. Emergency Medicine, Philip Levy – PI);
14) Achieve BP (Department Emergency Medicine, Julie Gleason-Comstock – PI).

For 2013, the CRC supported 14 research studies with a total of 676 consented and enrolled subjects. One half were NIH funded and the other one half were pharmaceutical related.

Graduate Program
The Department’s doctoral program is housed in the Department of Physiology and noted as a concentration in Reproductive Sciences. The Reproductive Science Concentration represents an integrated Ph.D. program incorporating the teaching, research and physical resources of two departments, Obstetrics/Gynecology and Physiology. Program specific courses are taught by Ob/Gyn teaching faculty and dissertation research is performed in our departmental basic science laboratories at the Mott Center. The program presently offers 10 courses totaling 20 credit hours which cover a range of topics in the Reproductive Sciences field. In 2013, during the summer PSL 7710 was offered with a new course director (A. Awonuga, M.D.) for 1 credit, and the following courses that are offered every other year was PSL 7730 in the Fall semester - 3 credits (JH Hannigan, Ph.D.) and PSL 7700 in the winter semester - 3 credits with a new course director (DR Armant, Ph.D.). In 2014 were are offering an online course on Embryo Physics.

In addition, the program’s emphasis on bioinformatics was expanded by cross-listing 2 curriculum courses from the new Bioinformatics & Computational Biology Concentration offered by the Department of Computer Science and Center for Molecular Medicine and Genetics. This program had also been expanded for individuals with Medical Degrees to earn their Ph.D.’s through the Reproductive Sciences Concentration. This effort is directed primarily at our young M.D.s currently participating in clinical fellowships in Maternal Fetal Medicine (MFM), Reproductive Endocrinology and Infertility (REI), and Gynecologic Oncology, as well as Research Fellows in the Perinatology Research Branch (PRB). Juan Gonzalez, M.D. (Mentor: Roberto Romero, M.D. with Robert Sokol, M.D.) is ready to defend his dissertation. Jimmy Belotte, M.D., is now in his second year; Rani Fritz, D.O., is the third individual to enter this program and he is in his first year. Our program expanded in 2013 by three, to include eight students. Overall, there are 19 faculty that participate in this program with a total of 10 faculty that have mentored Reproductive Sciences graduate students. This is an increase in mentorship by seven since 2011.

In 2013, one student graduated with a Ph.D. Nicole Fletcher-King (Mentor: Ghassan Saed, Ph.D.) successfully defended her Ph.D. dissertation in July 2013. The thesis focused on “The Role of Oxidative Stress in the Pathogenesis of Epithelial Ovarian Cancer.” She will continue her postdoctoral training in Dr. Ghassan Saed’s laboratory. The total number of students who have graduated from this program now number eight.

Selected “News”

The goal in this very selective reporting of what’s new and what is happening at the Mott is to provide some flavor of the day to day activities which contribute to moving the Center forward strategically.

Seminar Series and Journal Clubs: In 2013, the Mott Center continued to have one on-going seminar series and a journal club. The faculty member “Brown Bag” seminar series continued monthly presentations through June. The Reproductive Biology journal club joined Chromatin, Computers and Reproduction journal club and meets weekly.

Mott Center Scientific Retreat: Over the past few years, the Mott Center has held a yearly scientific retreat. This encompasses faculty and invited guests, including select faculty from other departments within WSU and outside WSU. All fellows, students and laboratory personnel are encouraged to attend. The purpose of the retreats are to foster interdisciplinary collaboration to initiate new research projects. The scientific retreat for 2013 was again held at the Detroit Yacht Club on Belle Isle. This time, there were 62 attendees, with 11 presentations and one keynote speaker. The theme for this year’s retreat focused on the new and/or junior faculty and the presentations spanned from Immunology – Genetics – Computational Genomics to Disease Pathways and Intervention. At this retreat, Dr. S.K. Dey, Lova Riekerat Chair and Professor of Pediatrics, Cancer and Cell Biology, Cincinnati Children’s Hospital Medical Center served as guest reviewer and keynote speaker. The keynote presentation was “Gene-Environment Interactions in Preterm Birth.” The 2014 retreat is planned for May.

MARTS (Michigan Alliance for Reproductive Technologies and Science) Symposium: The Michigan Alliance for Reproductive Technologies and Science was created approximately five years ago. This is a
consortium between of the three research universities to accelerate growth of the reproductive sciences in Michigan. It is focused on enhancing the communication and collaboration among researchers, clinicians, and educators. The alliance fosters a supportive environment for basic research, technological development, translational studies, and clinical implementation. University of Michigan hosted the 2013 event, as it was their turn in the rotation. The Mott, which hosted this meeting the previous year, participated actively and will again participate in 2014.

Honors/Awards/Highlights: The Mott Center investigators were very active this past year and were recognized by a number of rewards or events in the Year 2013. Some highlights, honors, awards, and events are as follows:

1. Ghassan Saed, Ph.D., Associate Professor, had an article on MDLinx “Uterine fibroids are characterized by an impaired antioxidant cellular system: Potential role of hypoxia in the pathophysiology of uterine fibroids”. This was featured on July 16 and published in the Journal of Assisted Reproduction and Genetics. Dr. Saed also received the 2013 ASRM Star Award. This award is for the reproductive health care professional who has presented at 9 out of 10 ASRM annual meetings.
2. Robert Freedman, Ph.D., and Vaibhav Diwadkar, Ph.D. had “Temporal Sequencing of Brain Activations during Naturally Occurring Thermoregulatory Events” published in the June issue of Cerebral Cortex (an Oxford University Press journal).
3. An article published in Fertility and Sterility 100:578-584, Aug. 2013 with J Banerjee, M.D. as lead author “Peroxy-nitrite affects the cumulus cell defense of metaphase II mouse oocytes leading to disruption of the spindle structure in vitro” became part of the discussion forum for this journal.
4. Dr. HM Abu-Soud had a Fulbright Scholar, Dr. Iyad Ali, Ph.D., join his laboratory on May 1, 2013 for one year. This Fulbright Scholar was fully funded for the entire year. Dr. Iyad Ali is an Assistant Professor of Biochemistry, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus, Palestine.
5. Kang Chen, Ph.D., Assistant Professor published “Mucus Enhances Gut Homeostasis and Oral Tolerance by Delivering Immunoregulatory Signals” in Science. This was a collaboration between his current laboratory and former laboratory. This article was also broadcast by the BBC.
6. Dr. Daniel Rappolee’s published article “Stress induces AMPK-dependent loss of potency factors Id2 and Cdx2 in early embryos and stem cells” was the featured journal cover in “Stem Cells and Development” (May 15, 2013).
7. Dr. Stephen Krawetz continued to welcome a Visiting Scholar from India. With co-authors, Dr Krawetz published in Human Reproduction Update “The presence, role and clinical use of spermatozoal RNA’s.” This was featured on the cover for the November/December 2013 issue. He was also quoted in April, 2014 as a world expert in sperm RNA in a commentary in Nature.
8. Dr. D. Randall Armant published a major review paper on embryonic implantation in a special issue of Molecular Aspects of Medicine (high impact journal – IF: 10.8). He also organized a very successful satellite meeting at Society for Gynecologic Investigation – Mar. 2013.

New Faculty News: At the beginning of 2013, we welcomed Sascha Drewlo, Ph.D., Assistant Professor, who joined the Mott Center (University of Toronto) as the newest faculty member. Dr. Drewlo’s research interests focuses on molecular mechanisms of placenta related pregnancy disorders and the development of in vitro models of disease and intervention strategies. By the end of the year, Dr. Drewlo had a fully functioning laboratory in place.

In addition, we welcomed two adjunct faculty members. Susan Dombrowski, Ph.D., Adjunct Assistant Professor, is a senior Next Generation Sequencing (NGS) scientist at Genomatix Software, Inc. which is a leading supplier of technologies to analyze and interpret genomic data. Dr. Dombrowski’s research interests focus on the analysis of microarray and NGS data, such as RNA-Seq and DNA-Seq. Richard Gordon, Ph.D., Adjunct Professor, is a theoretical biologist who had an extensive and prominent academic
career at the University of Manitoba, and recently established the Embryogenesis Center at the Gulf Specimen Marine Laboratory in Panacea, Florida. Dr. Gordon’s research focuses on algal biofuels, diatom nanotechnology, embryo physics, breast cancer detection and HIV/AIDS prevention. Both are contributing to our education programs.

**The Perinatal Initiative:** As a continuation of the Perinatology Research Initiative for Year 2013, two more junior faculty and one more senior faculty have been hired and will be joining us this summer on the third floor of the Mott Center. This initiative is one of the primary reasons that all the building space reconfiguration process has commenced. Overall, the Perinatal Initiative, funded by the WSU Board of Governors, instituted by Dr. Roberto Romero and managed by Dr. Sonia Hassan, has led to a rebalancing of research at the Mott with increased emphasis in perinatal research and a net increase in five PIs at the Mott.

**Where Should We Go? – A Strategic Reassessment of Future Directions**

A strategic view toward making the Mott and its scientists more competitive in an increasingly competitive funding environment was undertaken about nine years ago and has engendered a large number of steps, all of which have been described in previous summaries. We started with administrative structure, physical plant, fixed and major equipment and have proceeded to program enhancement and creation of the graduate program concentration and M.D./Ph.D. program. Indeed, we updated the plan in moving toward Systems Biology in the Reproductive Sciences about five years ago, as we moved the Applied Genomics Technology Center and some epigenomic expertise to the Mott and activated a named endowed Chair in bioinformatics, now held by Sorin Draghici, Ph.D. We have closely related the AGTC to the PRB, as well as to the Karmanos Cancer Institute, upgraded our Next Generation Sequencing capabilities and have moved toward our vision of Personalized Medicine by attaining CAP certification for the genomics facility and working with KCI in profiling lung cancers.

The Systems Biology Program initiative was and is only possible because of the continued support of the School of Medicine, the Office of the Vice President for Research and the Provost. Just as important to this effort are our partners in the Karmanos Cancer Center, the Center for Molecular Medicine and Genetics, the Department of Computer Sciences, Computer and Information Technology, the Department of Physiology and several other academic areas.

The future success of the Mott will be grounded in its interdisciplinarity and cooperation and collaboration with the National Institute of Child Health and Human Development, across Wayne State University, our sister institutions in Michigan and the new initiatives that will be spun from our current and planned research endeavors. BUT, times have changed. Recruitment of new talent is likely nearly complete and there are major environmental limitations nationally and locally for medical schools and academic health systems. We await a new Reproductive Endocrinology and Infertility Division Director and continue to experience a lack of clear emerging themes both in some areas of our team research and our graduate concentration. The current challenge will be to create a strategic thinking and action process sensitive to our stakeholders, specifically and primarily the Department of Obstetrics and Gynecology and the Perinatology Research Branch, as well as our Advisory Committees and most importantly our Scientists.