

## **ORWH CAREER DEVELOPMENT PROGRAMS FOR FY 2004**

A major part of the ORWH mandate is to develop opportunities and support for the recruitment, retention, re-entry, and advancement of women in biomedical careers. To accomplish these goals, ORWH held a public hearing and major career development workshop in 1992. ORWH invited and interacted with the scientific and medical communities, organizations with an interest in women's health, the Congress, and other components of Government about NIH's programs related to women's health as well as the public.

The ORWH initiated a number of programs to nurture the participation and advancement of women in biomedical careers in order to ensure that interest and priorities in women's health remain at the forefront of our nation's research agenda. ORWH has developed strategies and programs to implement the recommendations made at this workshop and to address career issues, barriers, and concerns of women and minorities in science. These programs include support for mentored research training in areas related to women's health; support for biomedical scientists who have interrupted careers in research in order to fulfill family obligations to re-start their research careers; outreach to young girls and women who have an interest in pursuing careers in biomedical science; and collaboration with professional societies to encourage their support of the career advancement of women scientists.

### **A. ACHIEVING EXCELLENCE IN SCIENCE AXXS - 2004**

#### Partnership Meetings

- The Core ACTeam has made proposals and been accepted to conduct Partnership Meetings in conjunction with the Society for Neuroscience (October, 2004) and the American Society for Cell Biology (December, 2004). These interactive meetings will present a history of AXXS, current statistics related to women in science, and discussions about the role of the society in the advancement of the careers of women.
- The meeting topics are presented by a panel from the Core ACTeam and members of the partner society. Each is tailored to meet the needs of the partner society.
- These Partnership Meetings are an initiative launched by the Core ACTeam this year. They are a vehicle to partner with a society to both help the society assess its current programs to assist the careers of women and to share knowledge/information/initiatives that are part of the AXXS network.
- The Core ACTeam is currently negotiating with additional societies to plan for Partnership Meetings for FY'05.

#### ORWH/AXXS Website

- The website is currently being upgraded to expand from its original scope of a report on AXXS'99 to include current AXXS-related information and

“Effective Practices” that scientific societies have submitted to describe their initiatives to advance the careers of women in science.

#### ORWH/IOM Roundtable

- The Core ACTeam has worked with Dr. Pinn and Joyce Rudick to develop topics that could be addressed by a joint Roundtable sponsored by ORWH and IOM. Core ACTeam members will consult with the ORWH and the IOM to develop and facilitate these roundtables focused on the careers of women in science.

#### Self-Assessment Tool (SAT)

- The Core ACTeam, under the guidance of Sue Shafer, has begun the development of a tool for societies to assess themselves in terms of: participation of women scientists in society activities, climate for women in the society, and identifying current or potential “value added” for women members of the society. This effort is being managed so that the development of this tool is done cooperatively with societies that are interested in piloting and using the tool.
- Preliminary discussion of the SAT and what might be in it will be part of each of the Partnership Meetings to be held in the upcoming year.

#### “Effective Practices”

- The “Sixteen Effective Practices” have been updated and are being printed for Partnership Meetings and posted on the AXXS Website.
- Both new publications call for additional effective practices and include directions for submitting such practices.

#### Future AXXS Meetings

- The Core ACTeam has presented proposals to Dr. Pinn for future AXXS Conferences.
- The Team will continue to support ORWH in planning and implementing future conferences as part of ORWH’s strategy and outreach.

### **ORWH-FAES-NIH High School Student Summer Program - 2004**

In the summer of 2004, the program had 24 new high school students and 13 returning students. There were 22 women and 15 men, including 13 minorities (3 African-American women and 1 Hispanic man), coming from both public and private schools in Maryland, Virginia, and the District of Columbia. The summer started with an informational meeting on June 23 at which the students learned the history of the program, heard about the structure of the NIH, the Intramural Research Program, and the Office of Research on Women’s Health, and received guidance on how to make research presentations. Each week from June 30 until August 4 the students met as a group for a lunchtime session at which 6-8 of them made presentations on their research to each other. Included in the audience were their preceptors, a few of the high school teachers in

the HHMI-NIH Summer Teachers' Program, some of the advisors for the program (all members of the NIH scientific staff), and either Dr. Michael Gottesman, Deputy Director for Intramural Research or his Assistant Director, Dr. Joan Schwartz. The presence of these NIH senior scientific staff ensured a lively discussion of each presentation, and put each research project into a broader biomedical context. One of the returning students continued her work on "Gynecologic Manifestation of Hereditary Leiomyomatosis and Renal Cell Cancer in Families in North America", in Dr. Jorge Toro's laboratory, NCI. All the students also presented posters at the NIH Summer Student Poster Presentations day, August 5. They thus learned not only how to carry out a research project, how to ask important questions and how to design experiments to answer those questions, but also how to communicate their results to other scientists.

**Course: Formula for Achieving Management Excellence Leadership Development Initiative - FDA** **\$30,000**

The purpose of this collaboration is to create a web-based course designed to give the student a basic scientific understanding of the major physiological differences between the sexes, the influence these differences have on illness and health outcomes, and the implications for policy, medical research, and health care. This is a joint collaboration between FDA, OWH, and ORWH.

**Course Learning Objectives:**

The Introductory course is intended to increase the learner's awareness of fundamental issues related to the differences and similarities in the basic biology of the sexes as they apply to drug research, development and regulatory review management. Specifically:

- Definition of Sex and Gender
- Legislative Framework (FDA/NIH/HHS)
- Cell Physiology
- Developmental Biology
- Pharmacodynamics and pharmacokinetics

**BUILDING INTERDISCIPLINARY RESEARCH CAREERS IN WOMEN'S HEALTH (BIRCWH I and II)**

The Office of Research on Women's Health (ORWH) developed an institutional career development award for Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Career Development Programs. These Programs support research career development of junior faculty members, known as Interdisciplinary Women's Health Research (IWHR) Scholars, who have recently completed clinical training or postdoctoral fellowships, and who are commencing basic, translational, clinical and/or health services research relevant to women's health.

The goal of this initiative is to promote the performance of research and transfer of findings that will benefit the health of women. The Programs accomplish these goals by bridging advanced training with research independence, as well as bridging scientific disciplines or areas of interest. This will increase the number and skills of investigators at

awardee institutions through a mentored research experience leading to an independent scientific career addressing women's health concerns. This RFA uses the NIH Mentored Research Scientist Development Program Award (K12) mechanism. To date over 110 scholars have been in the program in the following areas:

### **BIRCWH I SCHOLAR RESEARCH AREAS**

#### **UCLA**

Catherine McLean MD, PhD -Utilization of services/pattern care for women with rheumatoid arthritis

Helene Bernstein MD, PhD - Neonatal NK cells produce chemokines & suppress HIV replication

Larissa Rodriguez, MD - Vaginal physiology and the pathophysiology of vaginal prolapse

#### **Program Graduates:**

Karol Watson, MD, PhD – Received K01: Estrogen and angiogenesis

Michael Broder, MD, MS – Improving patient outcomes for hysterectomy& myomectomy

#### **UNC**

Beverly Rockhill, PhD - Primary prevention breast cancer

Sue Brown MD - Risk of bone loss during pregnancy in adolescents

Eliana Perrin, MD – Obesity and eating disorders in adolescents

Guadalupe Ayala PhD – Management of asthma & diabetes among latino families

Nancy DeMore, MD - Micrometastases and breast cancer

Karen Grewen PhD - Outcomes related to the role of relationships to lowering stress

Denniz Zolnoun MD - Developing treatments for chronic neuropathic vulvar pain syndromes

#### **Program Graduates:**

Kim Boggess, MD – K08 HD 43284-01: Effect of chronic infection on placental development

Elizabeth Claire Dees MD – K23 RR 16536-01: Phenotype and chemotherapy toxicity in the elderly

Angela Kashuba, Pharm D – K23 AI 054980: Antiretroviral pharmacology in the genital tract (PS 162)

Penny Gordon-Larsen, PhD – K01 HD 044263-01: Obesity and the environment - transition to adulthood (PS 134)

Kathy Hartmann, MD, PhD – R01 HD 43883 (PS 0.2%): Consequences and course of uterine fibroids in pregnancy

R01 HL 075645-01 (PS 9.6%): pending council review

Joan Taylor, PhD – R01 HL 071054001: Adhesion signaling in vascular growth and development

Rolf Craven, MD – R03 AG 002700-01: Phosphatase inhibitor of telomere signaling

Stephan Moll, MD – Pregnancy loss and factor V; 11 IRB approved clinical trial protocols; Co-PI CDC grant

## **BAYLOR**

Aleks Rajkovic, MD - Mouse models of premature ovarian failure

Laura Goetzl, MD - Epidural-related fever and maternal serum IL-6 levels

Aparna Kamat, MD - Genetics of endometriosis (using tissue microarrays)

Matthew Anderson, MD, PhD - HPV associated neoplasia

### **Program Graduates:**

Susan Brundage, MD, MPH – Academic position, Stanford University

## **UAB**

Yu-Ying Chen, MD, PhD - CV risk in women with Spinal Cord Injury

Craig Hoesley, MD - Molecular epidemiology HPV in women with HIV

Michelle Martin, PhD - Hypertension in African Americans, effects of exercise

Huan Nguyen, PhD - Immune responses to HPV and other factors in surveillance cervical cancer

Patrick Ramsey MD - Antecedents of fetal lung dysplasia

## **UCONN**

Francisco Sylvester, MD - Role for activated T lymphs in bone loss in Crohn's, sex differences

Catherine Lewis, MD - Health services in HIV infected incarcerated women

Yu-Hsiung Wang, DDS, PhD - Assessment effects of PTH on primary osteoprogenitor cells; Received R03, NIDCR

Julie Wagner, PhD - Knowledge of risk for coronary heart disease among diabetics, relationship to gender/ethnicity

John Meyer, MD - Occupational exposures and pregnancy complications (including preterm delivery and low birth weight)

Thomas Trojian, MD - Supplemental estrogen and progesterone effects on the anterior cruciate ligament

Sharon Yang, MD - Effects of estrogen depletion & replacement on systemic and cerebrovascular inflammation

### **Program Graduates:**

Kristen Kelly, PhD – HIV risk perception

Crystal Park, PhD – Recovery from MI

## **WASHINGTON UNIVERSITY**

Bettina Mittendorfer, PhD - Sexual dimorphism in reguln metabolism

Linda Peterson, MD – Obesity and heart metabolism

Reina Villareal, MD - Role of polymorphisms cyt P450 enzymes in estrogen metabolism in postmenopausal women

Prabha Ranganatha, MD - Frequency of polymorphisms in 5 enzymes involved in methotrexate metabolism in rheumatoid arthritis

Fanxin Long, PhD - Osteogenesis in Hedgehog (gene chip mRNA technology)

Consuelo Hopkins, MD - Frequency of Vitamin D deficiency, osteopenia/osteoporosis in elderly persons with Alzheimer's disease

**Program Graduates:**

Timothy Schaiff, PhD – Fatty acid transport in trophoblasts

Michael Jakoby, MD – Lipids, diabetes

**UMDNJ**

Javier Torrens, MD - Ethnic differences in insulin insensitivity and B cell function

Hartmut Hanauske-Abel, MD, PhD - Eukaryotic translation factor 5A as a molecular target (cervical ca)

Gloria Perez, PhD - Oocyte genomic instability in aging and chemotherapy

Lin Yan, PhD – Aging and gender differences in cardiovascular disease (premenopausal women vs. postmenopausal women vs. men)

**U MICHIGAN**

Josephine Kasa-Vubu, MD - Exercise, amenorrhea, stress and bone health

Jane Banaszak-Hall, PhD - Importance gender, nursing home resident & long term care

Vanessa Dalton, MD - Contraception/Behavior; Management of Early Pregnancy Loss

Jonathan Metzl, MD, PhD - Impact of SSRI on women's depressive illness

Matthew Wishart, PhD - Molecular mechanism of MTMR protein function in lipid signaling (myotubularins)

Nancy Fultz, PhD - Urinary incontinence body weight and cognitive function

**Program graduates:**

Lilia Cortina, PhD – Sexual Harassment and psychological health of women

Lisa Kane-Low, CNM, PhD - Birth related outcomes

**UCSF**

Alka Kanaya, MD - Type II diabetes in women

Elad Ziv, MD - Genetic epidemiology of breast Ca

Rachel Whitmer, PhD - Cognitive function, dementia

John Shepherd, PhD – Breast density and breast cancer risk

Jeffrey Tice, MD – Breast cancer prevention

Shelley Hwang, MD – Ductal carcinoma in situ

Lisa Barcellos, PhD - Genetics of multiple sclerosis

Monica Gandhi, MD – Epidemiologic and clinical studies on HIV infection in women

**Program Graduates:**

Erica Gunderson, PhD – K01: Pregnancy and risk factors for cardiovascular disease and Type II DM

**U KENTUCKY**

Alice Thornton, MD - Epidemiology and host response to trichomoniasis

Paul Dassow, MD - Increasing colorectal cancer screening among Kentucky women with use of mailed education prompts

Subbu Apparsudaram, PhD - Estrogen modulation of central cholinergic and dopaminergic fuxn

Anita Fernander, PhD – Influence of stress& coping on smoking status and smoking behavior among disadvantaged African-American women

Michael Kilgore, PhD - Transcriptional control of breast cancer through peroxisome-activated receptor gamma

Joan Griffith, MD - Adolescent female obesity, depression and high risk behavior

**Program Graduates:**

Mariana Nikolova-K'ian, PhD – R01: Ceramide and acute phase proteins elevation during aging;

Jane Joseph, PhD – Received R01

Melinda Wilson, PhD – R01: HIV protease inhibitors, macrophage function/estrogen;

R03 AG 22122: Estrogen and HIV dementia

Jody Clasey, PhD - Relationship between insulin sensitivity & measures of body composition in obese prepubescents & adolescents

**VCU**

Paulina Essah, MD – Obesity and Type II DM in women, including racial differences in weight loss; insulin metabolism in obese women with insulin resistance

Gayle Roux, PhD – Resilience in women at risk for chronic health conditions

Donna Miles, PhD - Gender differences in the etiology of substance abuse, including tobacco use, in adolescent twins

Kristen Jacobsen, PhD - Sex differences in antisocial behavior

Maria Iuorno, MD - PCOS: role leptin & gonadotropin secretion, and insulin resistance: Received R03 HD 44455, “Coupling of D-chiro-inositol in PCOS”

Charles Cook, PhD - Sex differences in opioid analgesia

Robert McKallip, PhD – Cannabinoid receptors as novel targets for breast cancer treatment; HPV and cervical cancer in DES offspring

**YALE**

Wendy Lynch, PhD – Effect of sex and hormones on cocaine self-administration

Idil Cavus, MD, PhD - Effect of menstrual cycle phase and nicotine on cognition, neurochem& neurophys

Ann Rassmusson, MD - Nicotine addiction in women with PTSD

Therese Kosten, PhD – Neurobehavioral responses to cocaine: interactions of gender with genetics & environment

**Program Graduates:**

Rajita Sinha, PhD – P50, SCOR: Gender differences in the relationship of stress and addictive processes

**BIRCWH II SCHOLAR RESEARCH AREAS**

**BOSTON UNIV**

Tracy Battaglia, MD, MPH - Risk perception on breast and colorectal cancer screening in a multi-ethnic population

Julie Keysor, PhD - Gender differences in relationships among environment, attitudes & disability

Irene Tien, MD, MSc - Welfare issues for mothers of children referred to child protective team

Michele David, MD, MPH, MBA - Social and cultural factors in managing chronic diseases in Caribbean immigrants

### **BROWN UNIV**

Joseph Harwell, MD - HIV in Cambodian women

Jessica Whitely, PhD - Smoking Cessation Rates for women with abnormal PAP smears

Mark Schleinitz, MD, MPH – Quality of Life for women with breast cancer

#### Program graduates:

Maureen Phipps, MD, MPH – HHS, Center of Excellence in Women's Health - PI

### **DOWNSTATE**

Nia Jiang Liu, PhD - Gender-based analgesia (ovarian sex steroid)

Elizabeth Boskey, PhD - Female hygiene habits and effects on the local immune system

John Shin, MD - Mechanism by which diabetes contributes to cardiovascular disease

David Klemer, PhD, MD - NIR Tomography for early breast cancer detection and characterization

Jun Zhong, PhD - Role of BC1 in estrogen-mediated pain responsiveness

Elena Braznik, PhD - Hormonal changes induced by seizure activity in rats, feedback circuits

### **DUKE**

Andra James, MD, MPH - Impact of fetal sickle cell disease on pregnancy outcome

### **MAGEE**

Kathleen McTigue, MD, MPH - Environmental approaches to obesity prevention in women

Judy Chang, MD – Communication & power dynamics of female patients and their healthcare providers

Debra Bogen, MD - Role of maternal depression on women's breast feeding decisions

Jeyabalan, Arundhathi, MD - Role of vascular gelatinase in pregnancy and relaxin-mediated renal vasodilation.

### **U MARYLAND**

Jenny Jones, PhD - Regulation of plasminogen activation system in breast cancer

William Romani, PhD, PT - Estrogen receptors in the rat anterior cruciate ligament

Jessica Mong, PhD - Estradiol regulation of L-PGDs expression involves neuronal-glia interactions

Vasana Cheanvechai, MD – Vascular disease in women

### **OREGON**

Erin Blanc, MD, MPH - Hormone replacement therapy and effects on cognition

Karen Eden, PhD - Innovative approach to childbirth decision-making using a mathematical model



Nancy Glass, RN, PhD, MPH - Emergency department screening and treatment intervention to improve safety & health of battered women

Tanja Pejovic, MD, PhD - Causes and consequences of genetic instability in ovarian cancer (microarrays)

Paco Herson, PhD - Gender-specific susceptibility to neurological dysfunctions

### **UPENN**

Susan Domcheck, MD - Universal breast ca antigens as targets linking early detection & therapeutic vaccination

Eunkyung Kauh, MD, PhD - TGF-Beta 1 function in mammary carcinogenesis

Virginia Chang, MD, PhD - Obesity in African American & Hispanic women (role of social context)

Salli Tazuke, MD - Genes regulating ovarian function

Ronald Buckanovich, MD, PhD - Ovarian cancer (epithelial) - immunogenic vs. non-immunogenic profiles

### **STANFORD**

Chrysoula Dosiou, MD - NK cell gene expression in normal pregnancy vs. recurrent miscarriages

Latha Palaniappan, MD - Insulin sensitivity and pregnancy related weight gain

### **TULANE**

Arnold Alper, MD, MPH - Hypertension and renal disease (clinical)

Jing Chen, MD - Cardiovascular disease & chronic kidney disease (modifiable environmental risk factors and genetic determinants)

Karen DeSalvo, MD, MPH - Properties of a single item global health measure for predicting patient outcomes in CVD

### **UTAH**

Colleen Hough, PhD - Genetics of ovarian cancer (identifying promoter genes using mouse models)

Robin Marcus, PhD, PT - Effects of a novel countermeasure high force lengthening muscle contractor to stimulate muscle growth

Marga Massey, MD - Breast cancer, mechanisms of ischemia reperfusion injury and ischemia preconditioning

Beth Scholand, MD - Genetic factors that contribute to nicotine addiction and to the development of COPD

Kathryn Swoboda, MD - Effect of gender on phenotype in a subset of disorders, neurotransmitter deficiency disorder

### **VANDERBILT**

Kaylon Bruner-Tran, PhD - Expression & regulation of TGF-Beta 2 in the human endometrium

Nancy Keller, PhD - Role of estrogen in the pathophysiology of orthostatic intolerance

Neerajah Peterson, MD - Modifiable risk factors for ovarian cancer.

Examples of Selected topics include:

**Mental Health:**

- Assessing the impact of SSRI antidepressants on popular notion of women's depressive illness
- Sexual harassment and psychological health of women
- Emergency department screening and treatment intervention to improve the safety and health of battered women
- Examining communication and power dynamics of female patients and their health care providers
- Role of maternal depression on women's breastfeeding decisions

**Diabetes:**

- Ethnic differences in insulin insensitivity and B cell function
- Knowledge of risk for heart disease among people with diabetes: relations to gender, ethnicity and diabetes treatment regimen
- Mechanism by which diabetes contributes to CVD

**Cardiovascular Health:**

- Ceramide in circulating lipoprotein and vascular-endothelium
- Estrogen and angiogenesis
- Coronary heart disease risk in women with spinal cord dysfunction
- Primary and Secondary Prevention -Cardiovascular Disease associated with mental health risk factors
  - Cardiovascular disease and chronic kidney disease(determine the modifiable environmental risk factors and genetic risk determinants for CVD)
- Study of the properties of a single item global health measure for predicting patient outcomes and high risk CVD
- Vascular Disease in Women

**Arthritis/Musculoskeletal Health:**

- Utilization of services and patterns of specialty care for women with rheumatoid arthritis
- Exercise, amenorrhea, stress and bone health
- A role for activated T lymphocytes in the bone loss associated with Crohn's Disease
- Pharmacogenetics of methotrexate toxicity and efficacy in Rheumatoid Arthritis

**Neurological Disorders:**

- Gender susceptibility to neurological dysfunctions by altering GABA receptor signaling
- Effect of gender and phenotype in a subset of disorders: neurotransmitter deficiency related disorders
- Hormone changes induced by seizure activity in rats

**Menopausal Hormone Therapy:**

- Estrogen and angiogenesis
- Effects of estrogen on cardiac fibrosis after MI
- HRT and effects on cognition

**Sex/Gender**

- Sex differences in substance abuse
- Importance of gender and social supports in the nursing home setting
- Sex differences in HIV therapies

Substance use:

- Sex differences in the etiology of substance abuse
- Gender-specific pathways linking stress and cocaine relapse
- Sex differences in vulnerability to cocaine addiction
- Smoking cessation rates for women with abnormal PAPs

#### **Reproductive Health:**

- Risk factors for sexually transmitted infections among women in an Alabama HIV clinic
- Increased vaginal levels of a marker of collagen synthesis and preterm birth
- Epidural-related fever and maternal serum interleukin 6 levels
- Synchrony between LH and leptin pulsatile secretion in women with polycystic ovary syndrome
- Mouse models of premature ovarian failure
- Innovative approach to childbirth decision-making using mathematical model
- NK cell gene expression in normal pregnancy vs. recurrent spontaneous miscarriage
- Insulin sensitivity and pregnancy related weight gain
- Development of a decision aid for patients considering treatment for endometriosis pain

#### **Cancer Research:**

- Identifying low-penetrance breast cancer susceptibility genes
- Quantifying breast composition for breast cancer risk using X-ray absorptiometry
- Ovarian Cancer -- immunogenic vs. non-immunogenic profiles
- Causes and consequences of genetic instability in Ovarian Cancer
- Breast cancer -- mechanisms of ischemia, reperfusion injury and ischemic preconditioning
- Universal breast cancer antigens as targets linking early detection and therapeutic vaccination

#### **Molecular Biology/Genetics:**

- Genetics of endometriosis (using microarrays)
- Genetics of breast cancer

#### **Health Services/Disparities:**

- Hypertension in African American Women and the effects of exercise
- Health services in HIV infected incarcerated women
- Improving health outcomes for women with chronic illness
- Effect of risk perception on breast cancer and colorectal cancer screening
- Social and cultural factors of significance in managing chronic diseases in Caribbean immigrants

#### **Molecular Biology/Genetics**

- Genetics of endometriosis (using microarrays)
- Genetics of breast cancer

#### **Trauma**

- Estrogen and prolactin in septic shock

#### **Research Independence**

- Global Metric beyond individual achievement looking at how much collaborative research is generated by the BIRCWH centers
- Assessment of scholars based on their individual baseline level when they entered the program as they are a diverse group of researchers

- Percentage of scholars who continue to conduct research in women's health post-BIRCWH
- Publications – high impact vs. low impact journals
- Number of grants submitted per scholar compared to the number funded
- Percentage who go into Academia
- Number of scholars teaching clinical research methods (recognition for teaching)
- Number publications, positions held, awards, honors and oral presentations

**WOMEN'S REPRODUCTIVE HEALTH RESEARCH CAREER CENTERS (WRHR)  
NICHD            \$800,000**

ORWH joined NICHD in the development of a Request For Applications (RFA) to invite institutional career award applications for Women's Reproductive Health Research Career Development Centers in FYs 98 and 99. These Centers support research career development of obstetrician-gynecologists, known as Women's Reproductive Health Research (WRHR) scholars, who recently completed postgraduate clinical training, and were commencing basic, translational and/or clinical research relevant to women's health. The goal of this initiative is to promote the performance of research on women's reproductive health and transfer findings that will benefit the health of women.

In FY 98 12 Centers were funded: Magee-Women's Hospital Pittsburgh, Oregon Health Sciences University, Stanford University, University of California, San Francisco, University of California, Los Angeles, University of Cincinnati, University of Pennsylvania, University of Texas Health Sciences Center/Houston, University of Texas Medical Branch/Galveston, University of Washington, Wake Forest University School of Medicine, and Wayne State University Detroit. In FY 99, eight Centers were added: Brigham and Women's Hospital, Case Western Reserve University, Columbia University, University of Alabama at Birmingham, University of California, San Diego, University of Colorado, University of Rochester, and University of Utah. In FY03 the first round of WRHRs ended. The overall goal of the program is to bridge clinical training with research independence through a mentored research experience leading to an independent scientific career addressing women's reproductive health concerns. The emphasis is on research relevant to obstetrics and gynecology and/or its subspecialties: maternal-fetal medicine, gynecologic oncology, and reproductive endocrinology and infertility. Related fields such as adolescent gynecology, urogynecology, and the reproductive health of women with disabilities are also included. Mentors with established research programs covering a broad range of basic and applied biomedical and biobehavioral science related to obstetrics and gynecology, together with collaborating departments, form the intellectual and technical base for mentoring junior faculty accepted into the program.

An RFA for a third round of WRHRs was developed (RFA HD 030-020) with funding starting in FY 2004. The recipients are:

Gautum Chaudhuri, MD, PhD

The overall goal of this outstanding competing continuation application is to provide junior faculty trained in obstetrics and gynecology with the necessary training and research skills that will allow them to embrace a career in academic medicine related to

women's reproductive health. The application is well thought-out and logically organized. Specific themes of investigation range from basic science to clinical research. Faculty identified as mentors are highly qualified and constitute a network of excellent to outstanding clinical and basic science research scientists that offers a wide variety of research opportunities. Candidate Scholars are expected to identify a mentor and submit a research proposal prior to submitting an application. A strength of the application is the considerable experience acquired in research career development culminating in the successful training of five scholars.

Charles J. Lockwood, MD

This outstanding new application proposes a two-tiered approach to education and training that involves progressive steps towards individualizing a scholar's training in collaboration with the mentor and drawing from extensive departmental and institutional resources. Dr. Lockwood identifies three research tracks: basic, translational and clinical. A strong feature of the plan is the initial practical training in basic laboratory techniques and methods in cellular and molecular biology. The Department of Obstetrics and Gynecology has a successful past record in training academic clinicians and scientists. Mentors are accomplished basic and clinical scientists with extensive experience in mentoring. A strength of the application is its comprehensive plan for developing a WRHR center that is likely to succeed in creating a center of excellence for training and developing a new generation of independent investigators in the field of women's reproductive health.

David A Eschenbach, MD

The overall goal of this outstanding competing continuation application is to provide junior faculty trained in obstetrics and gynecology with the necessary training and research skills that will allow them to embrace a career in academic medicine related to women's reproductive health. The application is well thought-out and logically organized. Specific themes of investigation range from basic science to clinical research. Faculty identified as mentors are highly qualified and constitute a network of excellent to outstanding clinical and basic science research scientists that offers a wide variety of research opportunities. Candidate Scholars are expected to identify a mentor and submit a research proposal prior to submitting an application. A strength of the application is the considerable experience acquired in research career development culminating in the successful training of five Scholars.

Joanna M Cain, MD

The goal of this outstanding competing continuation proposal is to provide a stimulating and nurturing environment for junior faculty with competitive credentials and a strong interest in research. Faculty mentors are an interactive and cohesive group of established scientists who represent comprehensive and complementary interests and expertise within the fields of reproductive health. The application encompasses preclinical research on models ranging from lower systems to nonhuman primates with cutting edge clinical investigations in women's reproductive health research. A unique aspect of the research plan is targeted to increase the competency of clinical investigators. Another attractive element is the broad application and adaptability that can be individually tailored to the

Scholar. A strength of the application is the high level of achievement of previously supported Scholars, which attests to the success of this program for training physician scientists.

Garland D Anderson, MD

This excellent competing continuation program has targeted a broad-based, basic research approach to women's reproductive health problems. The application proposes focused training in three well-defined areas: molecular biology, cell biology and physiology, and clinical sciences. Mentors have strong research credentials with a very solid record of accomplishments in training academic faculty in women's reproductive health research. The pool of candidates is ideal and plans for monitoring and evaluating a Scholar's progress are impressive. A strength of this proposal is the commitment to diversity as demonstrated by their successful recruitment of underrepresented minorities. Additional strengths include an application that is well conceived, thoroughly documented, and carefully presented. The applicant demonstrates the necessary infrastructure to successfully train young physicians to become independent investigators in areas that address important women's reproductive health concerns.

A Eugene Washington, MD

The principal mission of this strong competing continuation application is to promote health and prevent disease by expanding the pool of well-trained, productive investigators in women's reproductive health research. The applicant proposes a structured program of sufficient duration, relevant didactic education, and immersion into a vibrant, intellectually challenging, research community leading to academic independence. Scholars will be recruited to pursue two general arenas in reproductive science: biomedical research and clinical research. Strengths include the mentors who have considerable experience in training post-doctoral investigators. Program staff will obtain clarification concerning the BIRCWH and WRHR Scholar selection process to assure that the intent of both programs is met. All-in-all, this excellent application attests to an ongoing commitment to nurture a cadre of newly trained independent investigators who will improve the health status of women.

Mary L Polan, MD, PhD

This highly rated competitive continuation proposal capitalizes on career development and advanced training in basic and clinical research in women's reproductive health. Scholars will be exposed to structured research and didactic experiences having the scope and rigor of an advanced research degree with mentoring by highly trained and experienced faculty with proven records of excellence in research and career development. Each trainee will have two mentors: a primary mentor for research and a secondary mentor for clinical continuity. Scholars will be mentored in reproductive biology and endocrinology, a major strength at the institution, and clinical and epidemiologic research. The training experience of mentors and the broad array of research opportunities they provide for Scholars are considered strengths. Another strong point is that the program has been successful in launching a cadre of independent investigators in research relevant to women's reproductive health.

Michael T Mennuti, MD

The goal of this excellent competing continuation application is focused on cultivating a cadre of independent Scholars in women's health, emphasizing multidisciplinary approaches. The applicant plans to identify talented physicians who have demonstrated potential for successful careers in research, place them in an exciting and supportive research environment under the guidance of an experienced mentor, and advance their skill sets in research to the point that they can establish a productive, independent line of investigation. A main strength is the attention to the development of a program that is tailored individually to each Scholar's interest and talents. To avoid potential overlap with the BIRCWH Program, Program staff will query all sites at the time of their annual review.

John M Malone, MD

This strong competing continuation application will provide each Scholar with a mentored research experience relevant to his/her long-term research interest. The applicant plans to proactively network each Scholar with senior, well-established investigators prominent in the Scholar's field of research. The cadre of experienced, extramurally funded mentors available to train Scholars will provide a firm basic and clinical research base that spans the broad spectrum of contemporary research that is relevant to women's health. These investigators will be complemented by a wide range of sophisticated clinical and research resources. Observations regarding the mentors' research experiences are reflected in the score and will be examined carefully at the time Scholars are selected. Overall, this program is expected to continue to contribute substantially to the nation's capacity for women's health research.

Baha M Sibai, MD

This well proposed excellent competing continuation application will focus on enhancing the research skills and expertise in academic obstetrics and gynecology. The primary emphasis of the program is to enhance the basic research skills and expertise of the Scholars and familiarize them with modern scientific techniques and principles, which they can subsequently apply to clinical problems in obstetrics and gynecology. A particular strength of the program resides in its determination to provide Scholars with extensive training in basic research methods, coupled to a tight, mentor guided research project and strong graduate level coursework. Concerns expressed about the high clinical load of past scholars will be addressed with more in depth monitoring by Program staff. Notwithstanding those concerns, we anticipate that Scholars in this established program will gain the investigative expertise to become competitive and successful independent investigators.

**GRIP REENTRY PROGRAM      FOGARTY INTERNATIONAL CENTER**

**Title:** Antenatal Corticosteroids in Latin American Countries

**Grant Number:** 1 R01-TW006970 - \$25,000

**Awardee:** Alecia Aleman, M.D.

Anetenatal Corticosteroids therapy is still being used in decrease neonatal mortality/morbidity in women at risk for pre-term labor. Preterm birth occurs in 10% of all deliveries but accounts for 74% of neonatal mortality. In relation to this problem, one of the most effective practices, with a high impact in perinatal health, is the use of antenatal corticosteroids. The general objective is to evaluate the magnitude, characteristics, and barriers for the administration of antenatal corticosteroids to women delivering preterm in Latin American countries.

**Title:** Screening for STDs Using Home Sampling in Estonia

**Grant Number:** 1 R01-TW006990 - \$25,000

**Awardee:** Anneli Uuskula, M.D.

This study addressed a significant problem in Estonia, names the rising rates of STD's in the population. The goal was to assess the feasibility, response rate, and acceptability of using home sampling of rune as a population screening tool for Chlamydia and Neisseria gonorrhea identification. This included development of a stratified random sample, multiple contacts with potential participants to maximize participation rates, and voluntary feedback of screening results to participants.

**ORWH/OIR Graduate Partnerships Program**  
**\$50,000**  
**to be submitted.**

**OIR**

### **UNDERGRADUATE SCHOLARSHIP PROGRAM for INDIVIDUALS from DISADVANTAGED BACKGROUNDS**

The OIRS, Office of Intramural Research (OIR) is responsible for the development and management of the Undergraduate Scholarship Program for Individuals from Disadvantaged Backgrounds (UGSP). The UGSP provides scholarships to undergraduate students who have been competitively selected from a nation-wide pool of candidates. An average of 15 scholarships are awarded each year.

### **ORWH/NIH REENTRY PROGRAM**

The ORWH Reentry Program was developed in 1992 as a pilot program to help fully trained scientists (women and men) reestablish careers in biomedical or behavioral science after taking time off to care for children or parents, or to attend to other family responsibilities. This program was originally started as a pilot program to encourage fully trained women and men to reenter an active research career after taking time off to attend to family needs. The success of this pilot program was the impetus to expand the program across the NIH and is currently supported by all NIH ICs. The aim of these supplements is to encourage fully trained individuals to reenter research careers within the missions of all the program areas of NIH. This program provides administrative supplements to existing NIH research grants for the purpose of supporting full-time or



part-time research by these individuals in a program geared to bring their existing research skills and knowledge up to date. It is anticipated that at the completion of the supplement, the scientist will be in a position to apply for a career development (K) award or for a research award. ORWH currently provides funding of \$20,000 for each of 2 years. In FY 04, ORWH continued sponsorship of 2 reentry candidates through NIDA.

**Dr. Jamie Nekich**

**Grant #: R01DA12881**

**Dr. Elizabeth McKenzie**

**Grant #: 5R01DA12645**

**Fellows Award for Research Excellence Program (FARE) Office of Education/OIR  
\$60,750**

**The Fellows Award for Research Excellence**, began in 1995. FARE provided recognition for the outstanding scientific research performed by intramural postdoctoral fellows. The award is sponsored by the NIH Fellows Committee, the Scientific Directors, the Office of Research on Women's Health, and the NIH Office of Education, and is funded by the Scientific Directors and the Office of Research on Women's Health. Fellows submit an abstract of their research, which is peer reviewed in a blind study section competition. Winners of FARE awards will each receive a \$1,000 stipend to attend a scientific meeting at which they will present their abstract, either as a poster or a seminar. ORWH contributes 25% of the awards to the winners of the competition. In FY 2004 there were 243 winners.

**Association for Women in Science Bethesda Chapter**

**\$5,000**

The Association for Women in Science (AWIS) Bethesda Chapter was founded in 1994 to address the issues and concerns of women in science. The goals of the organization are:

To increase, at all levels, the number of women obtaining their degrees in science and technology,

- To increase the number of women participating in the scientific and technological workforce at all levels,
- To raise public awareness of the scientific and technological skills and contributions of women,
- To work with other scientific, educational, and women's organizations in developing national and community programs that meet the above goals, and
- To provide awards for the recognition of individual women scientists in order to advance the above goals.

With these goals in mind, the organization is continuing the successful year-long seminar series entitled, "Networking for Career Success." This tenth annual series consists of approximately five seminars held at the campus of the National Institutes of Health (NIH) bi-monthly. The topics covered in each series are very diverse, ranging from issues of particular interest to women.

## **WISH-NET @ NIH.gov website**

**\$24,899**

**PRIMR**

Public Responsibility in Medicine and Research (PRIM&R), a non-profit organization based in Boston, has been working for 30 years to improve the diversity of both person and opinions in the field of science and research. In the fall of 2000, pursuant to a contact with the Office for Research on Women's Health (ORWH) at the NIH, PRIM&R established the Women In Science and Healthcare Network (WISH-net) Website (<http://wish-net/od.nih.gov>), a portal and index for both new developed and already available resources associated with mentoring, inspiring, and encouraging girl and women as they consider, embark upon, or struggle with, careers in healthcare, science, or medicine. WISH-net strives to provide resources for such a community and opportunities for finding mentors, roles models, and of other ways to support and encourage girls and women who may otherwise be discouraged from pursuing a career in the sciences.

Building from the advances of previous years, PRIM&R continued to improve by focusing on three separate dimensions.

- 1) Review proposed new content
- 2) Add additional interactivity and networking opportunities
- 3) Increase awareness of the site through outreach and marketing

### ***Improved Website:***

In years past, WISH-net was divided into sections for Middle/High School, College/Graduate Students, and Professional Women, representing the changing needs of girls and women as they advance and develop into different stages of their lives and careers. Each section promoted education, resources, professional and personal development, inspiration, and mentoring.

- PRIM&R also conducted a focus group with seventh graders at a Boston middle school to learn what students liked and disliked about the site. The girls were very candid in their responses, and suggested, among other things, more color and interactivity on the site. The focus group also commented that the WISH-net website should not “talk down to them” but rather encouraged the girls to pursue engaging and interactive science activities. As a result of this focus group, PRIM&R re-designed the WISH-net website so that it would be more attractive to the middle school audience, while not losing the material that was already created for the older audience. In the past, the website information was not well organized by age, so that visitors viewing the site as a professional might find themselves reading information written more for someone of a much younger age. The new site better organizes the material so that the content is appropriate for each age group. developed a user-friendly portal to display WISH-net information on [www.WISHnet.org](http://www.WISHnet.org). The logo for wish-net was also updated.

## **INTRAMURAL PROGRAM IN WOMEN'S HEALTH RESEARCH**

ORWH initiated the development of an NIH Intramural Program on Research on Women's Health's (IPRWH), an innovative, interdisciplinary program in Women's Health Research in the Intramural Research Programs (IRP). ORWH formed a Steering Committee and assigned tasks to develop, implement, and bring this program to fruition.

The IPRWH was created to serve as the focal point for all women's health research, including sex and gender comparisons, within the IRP. The mission of the IPRWH is to: 1) Promote, stimulate, and support efforts to improve the health of women through biomedical and behavioral research within the NIH IRP; 2) Enhance communication among, and recruitment of, researchers on women's health among the Institutes and Centers; and 3) Enhance interdisciplinary research through the development of specific training programs and recruitment of new clinical and basic research trainees into the IPRWH at the NIH.

Achievement of these goals is well underway through the following initiatives. First, the Women's Health Special Interest Group (WHSIG) is a highly successful and well-attended scientific lecture series established to serve as a forum for researchers across the NIH to share research ideas and methodology, develop collaborations, and learn about sex-based differences beyond the effects of hormones that are relevant to molecular, cellular, genetic and developmental processes and affect organ systems, behavior and the organism as a whole. WHSIG lectures have been held monthly since November 2002 and have been presented by experts in women's health researcher from within the NIH intramural program as well as the outside scientific community. This lecture series has provided an important forum for scientific interchange and establishment of collaborations between NIH IRP researchers and with scientists around the world highlighting an interdisciplinary approach to sex and gender differences in biology and disease from the molecular level to therapeutic clinical trials.

Second, four intramural training programs in women's health have been developed, for which the FNIH is currently seeking funding: a) Clinical Fellowship in Women's Health, b) Shared Post-Doctoral Fellow Program, c) Research Career Re-Direction Program, and d) Research Re-entry Program. These training programs will enable excellent inter- and multidisciplinary research in the area of sex/gender factors that influence the expression of health and disease. It is anticipated that applications will be solicited, received, reviewed, ranked, and awarded sometime in 2004 by the IPRWH.

Third, the IPRWH is also developing proposals to provide intramural funding support across NIH ICs for cooperative, collaborative and interdisciplinary projects directly related to issues of women's health and sex and gender comparison. Projects may be basic, translational, population-based, or clinical in nature.

### **OFFICE OF RESEARCH ON WOMEN'S HEALTH/OFFICE OF SCIENCE EDUCATION - Joint Program Highlights**

For several years, the Office of Research on Women's Health (ORWH) and the Office of Science Education (OSE) have worked together to provided educational resources for pre-college students and others who are interested in science and health careers. In fiscal 2004, the partnership sponsored two programs and one special project. The popularity of the first two programs makes it evident that they are filling an important need for material on careers for women in science.

Women are Scientists Video and Poster Series: *Colorful, informative videos and posters for middle-school students that feature women scientists. The series is designed to stimulate the interest of girls in science at a time when they are making decisions about the course choices that may affect their career options later. In the middle-school years, many girls are discouraged from pursuing advanced levels of study in math and science. This series is intended to make them aware of the many interesting and rewarding careers in the medical sciences and the educational requirements necessary to pursue them.*

**Highlights:** The *Women are Scientists* video series has been extremely successful. Each of the four videos won two awards, including *Women in Dental Research*, scheduled for release to the public in October 2004.

Because of the volume of requests for these videos, the OSE is in the process of reprinting the *Women are Pathologists* and *Women are Researchers* video kits. The 5,000 reprints of the *Women are Surgeons* video kits were distributed within a few months (50 kits are being held for possible special needs). The quick distribution of the reprints was due, in large part, to the filling of back orders. All of the videos are in the process of being digitized and will be available on the OSE website. In addition, OSE staff is investigating alternatives to reprinting the complete kits.

The total number of videos distributed in fiscal 2004 was 6,772. Of that total, the breakdown was: 723 of *Women are Pathologists*; 1,153 of *Women are Researchers*; and 4,896 of *Women are Surgeons*. The reported usage was: 32% for middle school, 19% for high school, 28% for home school, 11% to libraries, 5% for outreach activities, 9% for career counseling, and 6 % for other.

Work was begun for the production of a fifth video, *Women in Dental Research*. The Department of Health and Human Services has approved the project, and the Statement of Work has been sent for advertisement.

Women in Science Poster Series: *A series of free posters, with a companion website, aimed primarily at middle-school girls. The series emphasizes that science and medical research offer many different career paths, all of which are excellent opportunities for women. They feature careers in neuroscience, heart disease, and cancer research.*

**Highlights:** Posters are distributed primarily at the science teacher conferences attended by the OSE, and by mail through a request form on the OSE website. The posters have been especially popular at teacher conferences, where there is a dearth of materials that focus on women in science. In fiscal 2004, over 2,400 copies of each poster were distributed to teachers, State departments of education, and local school systems. An average of 1,500 unique hits to the website are received each month. This fiscal year, 5,000 of each poster were reprinted which has refurbished the supply available to the education community.

**ORWH/OSE Bookmarks: This is a special project requested by the director, ORWH. The directors of ORWH and OSE have approved the bookmark design. They will be printed in early fiscal 2005.**

### **Office of Education (OIR) and ORWH Joint Programs**

The ORWH provided the Office of Education, now the Office of Intramural Training and Education, with \$117,950 in FY2004 to support a series of programs for both our postdoctoral fellows and postbaccalaureate trainees.

For **Postdoctoral Fellows**, these programs included (1) the Survival Skills Workshops, five half-day workshops that were presented by Dr. Michael Zigmond and Beth Fisher of the University of Pittsburgh and addressed the topics of resume writing, job interviewing, negotiating a job offer, grant writing, and establishing a laboratory; (2) a career series consisting of panels of experts in career fields for which a biomedical research background is essential, including biodefense, teaching, patents, and technology transfer. The speakers for the career series were all former NIH fellows, who are particularly effective with the fellows and can offer them up-to-date information and networking for the jobs; (3) courses on Speaking and Writing about Science, each a 4-5 week course offered three times per year; (4) an Advanced Course: Speaking about Science, offered twice last year, offered a forum for in-depth, individualized assistance to each participant; (5) the Job Fair 2004, held annually in conjunction with the NIH Research Festival, which brought in companies that have jobs available - more than 600 fellows participated; (6) Science's NextWave, an on-line career development resource for postdoctoral trainees who are seeking biomedical career opportunities as they complete their training at the NIH.

For **Postbaccalaureate trainees**, the programs offered included (1) Career Enhancement Seminars designed to assist postbaccalaureate trainees as they prepare for careers in research, which include sessions on speaking about science, tips on scientific poster presentations, preparation for the MCAT and GRE tests, and the Myers-Briggs personality inventory; (2) the fifth annual Poster Day for NIH postbaccalaureate trainees, held early in May, that showcased a record total of 216 trainees, representing a wide range of institutes and centers, who presented their research accomplishments to the NIH scientific community; (3) the Premed Advising Workshop for postbaccalaureate trainees who plan to apply for admission to medical school, given by Paula Ashby, Assistant Director of Academic Services, University of Maryland Baltimore County, and Dr. Lee Ann Michelson, Assistant Director, Office of Career Services, Harvard University. All of these programs were well attended and evaluations conducted at the end of each indicated that they were well received and accomplished their purposes.

**National Institutes of Health-  
Tel Aviv University/Sackler Faculty of Medicine:  
Scholars Program in Women Health Studies**

Illana Gozes, Ph.D.  
The Lily and Avraham Gildor Chair  
for the Investigation of Growth Factors  
Department of Clinical Biochemistry  
Sackler Faculty of Medicine  
Tel Aviv University, Israel

Joan P. Schwartz, Ph.D.  
Assistant Director  
Office of Intramural Research,  
OD, NIH  
Building 1 - Room 135  
Bethesda MD

## **Report: 2004**

During the academic year of 2003/2004 five students were enrolled in the program which encompasses two months studies at the NIH and 10 months studies in Israel per year over the course of three years. The chosen projects are ranging from complications during pregnancy associated with Down syndrome and autism to cancer and diabetes. These projects are directly associated with women health and are using the most advanced technologies in medical sciences. The following outlines the specific projects.

## **Project 1:**

1] **Title of the project:** The mechanisms of intrauterine development of leukemia in Down syndrome – role of the ERG gene

2] **Student name:** Liat Rainis

3] **NIH mentor + name of the lab/institute:** Peter D. Aplan MD Senior Investigator Genetics Branch Center for Cancer Research [aplanp@mail.nih.gov](mailto:aplanp@mail.nih.gov)

4] **Israeli (TAU) mentor - department/faculty:** Shai Izraeli MD, Senior Lecturer of Pediatrics, Genetics and Molecular Medicine, Department of Genetics Tel Aviv University and The Sheba Cancer Research Center, Tel-Hashomer, Israel.  
[sizraeli@post.tau.ac.il](mailto:sizraeli@post.tau.ac.il)

5] **Relevance to women health:** (keywords relevant to women health are underlined). Research in many laboratories has revealed that most cases of leukemia in children develop during embryogenesis. The leukemogenic events during pregnancy are unknown. As a model she studies the leukemia of Down Syndrome. 10% of children with Down Syndrome are born with transient congenital leukemia that developed during pregnancy.

## **Project 2:**

1] **Title of the project:** Identification of target genes of the SSDP-modulated Ldb-based transcription complex

2] **Student name:** Revital Bronstein

3] **NIH mentor + name of the lab/institute:** Heiner Westphal, M.D. (LMGD, NICHD)

4] **Israeli (TAU) mentor - department/faculty:** Daniel Segal, Ph.D. Dept. Molecular Microbiology & Biotechnology, Faculty of Life Sciences

5] **Relevance to women health:** See in text below

The Ldb-based transcription complex is conserved from flies to man and regulates key developmental processes including axis formation in the embryo, neuronal patterning, and hematopoiesis. When malfunctioning in the hematopoietic system it often causes leukemia, including breast cancer (hence relevance to women health).

SSDP is a modulator of the complex, which the TAU and NIH groups of Segal and Westphal, respectively have identified both in mammals and in *Drosophila*.

Unraveling the details of the function and mode of action of the complex requires identification of its target genes. We use *Drosophila* as a simple and genetically amenable model for identifying the target genes of the complex, and will transfer this knowledge to the mammalian system.

To that end Revital has used microarrays of *Drosophila* for expression profiling of wild type versus SSDP mutant flies that we have generated. She has completed the 'wet work' and is about to finish the statistical and bioinformatics analysis of the data. She is doing this with the aid of Brian Oliver (NIDDK) who is an expert in *Drosophila* microarrays. The quality of Revital's data is exceptionally high hence her microarray data is very informative. Although she still has to polish up the bioinformatic treatment of the data it is already clear that they it yields a set of putative target genes of the complex, whose expression is affected by the mutants used. These include some known genes and some novel ones. We are excited to note that several of the putative target genes have mammalian homologs.

Revital will soon begin a series of experiments aimed at validating the most promising putative target genes, using molecular, genetic and biochemical tools available for *Drosophila*. Once verified – a similar analysis of their mammalian counterparts will be initiated.



### Project 3:

- 1] **Title of the project:** Pathways of ADNP distribution, regulation and processing throughout the brain: Potential involvement in autism.
  
- 2] **Student's name:** Irit Spivak –Pohis.
  
- 3] **NIH mentor + name of the lab/institute:** Y. Peng Loh, Ph.D. NICHD, Laboratory of Developmental Neurobiology, Section on Cellular Neurobiology. E-mail : [lohpy@mail.nih.gov](mailto:lohpy@mail.nih.gov)  
Joanna M. Hill, Ph.D. NIMH, Laboratory of Behavioral Neuroscience. E-mail: [hilljoa@mail.nih.gov](mailto:hilljoa@mail.nih.gov) .
  
- 4] **Israeli (TAU) mentor - department/faculty:** Professor Illana Gozes, Illana Gozes, Clinical Biochemistry, The Lily and Avraham Gildor Chair for the Investigation of Growth Factors, Sackler Faculty of Medicine. E-mail: [igozes@post.tau.ac.il](mailto:igozes@post.tau.ac.il) .
  
- 5] **Relevance to women health:** See in text below

Vasoactive intestinal peptide (VIP) is a 28-amino acid neuropeptide that has shown fundamental importance in neurodevelopment. VIP induces the synthesis and secretion of neuroprotective and neurotrophic compounds from glial cells. Activity-dependent neuroprotective protein (ADNP) is a VIP-responsive gene that is essential for brain formation. Ongoing collaborative studies between the laboratories at the NIH and TAU are deciphering the functional pathways of VIP and ADNP. Both genes exhibit sexual dimorphism in their expression in the brain. Joanna Hill, Ph.D. at the NIH treated mice *in utero* with a VIP antagonist (co-developed by Illana Gozes, Ph.D.). These antagonist treated mice were found to exhibit autistic-like behavior. It is widely known that autism is more abundant in males than in females. The mechanism by which VIP antagonism *in utero* leads to autistic behavior in adults is unknown, and we are investigating the potential involvement of VIP and ADNP in autism. Studies encompass new behavioral paradigms aimed to characterize disorders of social behavior, immunocytochemistry and analysis of gene expression with emphasis on VIP receptors and ADNP. Further studies involve neuronal tissue cultures to assess mechanisms of ADNP secretion and processing using a battery of ADNP antibodies and pulse-chase experiments. Autism is still enigmatic and is associated with abnormal brain development. Studies assessing ADNP that is crucial for brain formation may shed light on some aspects of the devastating autism.

#### **Project 4:**

1] **Title of the project:** The Role of IGF1 and IGFR In Skin Proliferation And Differentiation

2] **Student name:** Marianna Sadagruski

3] **NIH mentor + name of the lab/institute:** Helman LJ. MD NCI, Pediatric Oncology Branch, NIH; LeRoith D, MD PhD, NIDDK, Diabetes Branch, NIH

4] **Israeli (TAU) mentor - department/faculty:** Wertheimer E. MD PhD, Sackler School of Medicine, Dept of Pathology, TAU

#### **5] Relevance to women health:**

Approximately 9.3 million or 8.7% of all women over the age of 20 in the United States have diabetes. However, about one-third of them do not know it. Because of the increasing lifespan of women and the rapid growth of minority populations, the number of women in the United States at high risk for diabetes and its complications is increasing. Furthermore, for women who do not currently have diabetes, pregnancy brings the risk of gestational diabetes. Gestational diabetes develops in 2% to 5% of all pregnancies but disappears when a pregnancy is over. Women who have had gestational diabetes are at an increased risk for developing type 2 diabetes later in life.

Diabetes is associated with the development of severe chronic complications. One of the most severe and devastating complications associated with the disease is skin pathology and impaired wound healing. Several decades of extensive research have elucidated various pathways to be implicated in the development of diabetic skin disease. These include metabolic factors beyond blood glucose, intracellular signaling molecule proteins, and growth factors/cytokines.

In our previous studies we have shown that both insulin and IGF-1 are playing central roles in normal skin physiology and in the wound healing process. Furthermore, we have found that it is important to maintain a strict balance between insulin and IGF-1 activities. Misbalance toward one direction might lead to impaired wound healing, while misbalance in the other direction might result in cellular transformation.

In the present study my goal is to elucidate the role of insulin and IGF1 signaling in skin and in skin pathologies such as in diabetic skin complications as well as in skin cell mitogenesis. For this purpose it is crucial to distinguish which of insulin and IGF1 effects are overlapping and which effects are unique to insulin or IGF1 signaling pathways.

## **Project 5:**

1] **Title of the project:** The Kruppel-like factor-6 (KLF6) is a novel downstream target for IGF-1 action

2] **Student:** Itay Bentov

3] **NIH Mentor:** Derek LeRoith Diabetes Branch, National Institute of Diabetes, Digestive, and Kidney Diseases, National Institutes of Health, Bethesda, Maryland

4] **TAU Mentor:** Haim Werner, Department of Clinical Biochemistry Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

5] **Relevance to women health:** See in text below

The insulin-like growth factors (IGFs) are a family of growth factors, binding proteins and receptors that are involved in normal growth and are also implicated in pathological states. Epidemiological studies have suggested that high circulating IGF-1 concentrations are associated with an increased risk for breast, prostate, lung, and colorectal cancer. Most molecular targets of IGF-1, however, remain largely unidentified. Kruppel-like factor-6 (KLF6) is a zinc-finger tumor suppressor inactivated in astrocytic gliomas, prostate and colon cancers. KLF6 is a potent transactivator of the IGF-1 receptor (IGF-1R) promoter.

The aim of the present study was to examine the potential regulation of KLF6 gene expression by IGF-1. The human colon cancer cell lines HCT116 +/+ and -/- (with normal and disrupted p53) were treated with IGF-1 for different periods of time. Western blots, qRT-PCR and transfection assays were used to evaluate the effect of IGF-1 on KLF-6 production. Results obtained showed that IGF-1 stimulated KLF-6 gene transcription in cells with normal, but not disrupted, p53.

In summary, our results suggest that KLF6 is a novel downstream target for IGF-1 action. The molecular mechanisms responsible for regulation of KLF6 expression are currently being investigated.

The role of insulin-like growth factor system in the development of breast carcinoma is being sought not only as a prospective marker but also as a possible therapeutic target.

## **Global Health research Initiative Program for New Foreign Investigators (GRIP)**

**PAR-03-118**

**Fogarty International Center**

**\$50,000**

This Program Announcement (PA) is intended to promote productive re-entry of NIH-trained foreign investigators from low-income countries into their home countries as part of a broader program to enhance the scientific research infrastructure in developing countries, to stimulate research on a wide variety of high priority health-related issues in these countries, and to advance NIH efforts to address health issues of global import. The specific goal of this

initiative is to provide funding opportunities for the increasing pool of foreign biomedical and behavioral scientists, clinical investigators, nurses, and other health professionals with state-of-the-art knowledge of research methods to advance critical issues in global health upon their return to their home countries. After their term of research training, developing country participants supported by this PA are expected to continue independent and productive scientific careers, including expert training and consultation and/or research of biomedical issues within their home institutions.

ORWH supported 2 applicants.

**Alicia Aleman**, M.D.: to study the problem of preterm births in Latin American countries by use of steroids to avoid preterm births.

**Anneli Uuskula**, M.D.: to study the prevalence and distribution of sexually transmitted disease in Estonia.