

# **Women's Research Initiative on HIV/AIDS**

**Sanctuary Resort on Camelback Mountain**

**Paradise Valley, AZ**

**April 23 – 26, 2009**

**2009 Meeting Summary**

# Women’s Research Initiative on HIV/AIDS

## 2009 Meeting Summary

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## Overview of the Women's Research Initiative on HIV/AIDS

Over the past decade, the global burden of the AIDS pandemic shifted to women in terms of new infections, total cases, and deaths. Unfortunately, research on HIV/AIDS in women has not kept pace and critical questions about HIV/AIDS in women remain unanswered. Until these questions are addressed, we are limited in our ability to design effective prevention and treatment strategies, resulting in further infections and deaths associated with HIV and AIDS. In 2003, the Women's Research Initiative on HIV/AIDS (WRI) was launched to respond to this shift and to help overcome a critical obstacle to progress in the AIDS pandemic – namely that research on women is inadequate, inefficient, and uncoordinated.

Since its inception, the Women's Research Initiative on HIV/AIDS has focused on **more, better and faster research** related to HIV disease in women. The WRI has worked to encourage, enable and coordinate efforts across disciplines and organizations to improve research related to HIV disease in women.

Over the years the WRI has drawn upon the knowledge and efforts of over 75 experts from many disciplines and perspectives related to women's health and HIV. These experts include academic, community and private practice clinicians, research scientists from academic, government, and pharmaceutical industry settings, HIV-positive women, and representatives of advocacy organizations.

In 2009, the WRI established a formal membership structure and invited 30 members from this diverse group to serve in a staggered 3-year term to enhance the focus and deliverables from this experience-rich think tank. The meeting design was also modified to include six invited presentations to enrich and expand the discussion. For a full list of WRI members and invited speakers for 2009, please see the Appendix.

### WRI 2009 Discussion Summary

The WRI 2009 meeting included experts from the WRI membership as well as invited guest speakers on emerging research topics. The purpose of the WRI 2009 meeting was to identify and then prioritize research questions in order to determine the area of focus that would most significantly impact our understanding of HIV disease in women.

In order to expand the scope of discussion, the invited presentations were specifically selected to encompass a wide range of topics such as vaginal ecology, inflammation, clinical trials enrollment, microbicides, immunology, and elite controllers of HIV infection. Each of these talks fueled rich discussion and often culminated in unique synthesis and perspective by the group.

In addition to the invited presentations and discussion, the WRI held small group breakout sessions to identify gaps and refine the lists of research questions. The gaps identified in the breakout sessions were primarily in the following areas (for a full list of identified gaps, please see Appendix B):

- Impact of hormones and other factors on transmission and immune protection
- Impact of sex-based differences on PK, immune responses, and pathogenesis
- Impact of sex and race on HIV care
- Improving and enhancing clinical care
- Prevention strategies
- Co-morbidities, toxicities, and aging
- Pregnancy
- Clinical trials

One of the primary challenges identified by the group each year is the inability to collect and search information on ongoing and completed research focused on HIV in women. This limitation means that the gaps identified specifically represent a lack of information in the public domain and may or may not represent a lack of research. The WRI has identified this issue as a major limitation in this field.

After two days of presentations and group discussions, the group identified a fundamental question that must be addressed in order to significantly move research on HIV in women forward:

***How do women become infected and how do they protect themselves from HIV infection?***

This seemingly basic and obvious question is in fact much more complicated and nuanced than expected at first glance. Breaking down this question generates a number of further questions about research priorities, research design and implementation, and communication or dissemination of research findings. The following section will summarize the WRI 2009 recommendations in these three areas.

## **WRI 2009 Research Recommendations**

### **Research Priorities**

Examining the question '*How do women become infected and how do they protect themselves from HIV infection?*' generated research priorities in three categories: biologic research, behavioral research, and social research. Further, the WRI agreed that there are significant opportunities for innovation in research design and in translating research learnings into practice.

## Biologic Research

Questions related to the biology of HIV disease in women. **Research funding should be directed to studies that:**

- Determine the impact of sex hormones, both endogenous and exogenous, on HIV infectivity. (Do endogenous and exogenous hormones have an affect on founder virus? Are there sex differences in founder virus strains?)
- Determine the impact of vaginal and rectal ecology on HIV infectivity.
- Determine the impact of semen on HIV infectivity. (Does semen inhibit or augment HIV infectivity? How does semen impact endogenous antimicrobials in the female genital tract? How does male age and/or treatment affect semen and infectivity?)
- Identify why some women, who are at high risk yet HIV-negative, are persistently more resilient against HIV infection/acquisition. (More work is needed to understand protective innate and adaptive immunity in women.)
- Identify natural protective factors for HIV, i.e. how do women's bodies naturally protect themselves from HIV. (e.g. mucosal immunity)
- Evaluate whether or not there is an association between sex hormones and measure of activation in "elite controllers"(longitudinal research is needed on the effect of menopause on female "elite controllers"). Also, do female "elite controllers" shed virus in the genital tract?
- Determine the role of inflammation in HIV transmission and disease progression.
- Identify the molecular mechanism responsible for differences in virologic control among men and women.
- Explore similarities and differences in HIV infection and dynamics between young women who were perinatally infected vs. horizontally infected.
- Intensify research efforts throughout the genital tract (especially upper genital tract) as well as genital pharmacology, immunology and correlates of protection.

## Behavioral Research

Questions related to the behavior of individuals (both women and men) that increase or decrease the likelihood of prevention and/or effective treatment. **Research funding should be directed to studies that:**

- Identify the psychosocial dynamics operating in interpersonal relationships that promote or impede engaging in protective practices and behaviors (particularly important by race, age, religious or cultural affiliation, and socio-economic status).
- Determine how current testing paradigms/availability affect HIV acquisition in women. What is the effect of the current testing policy on women? What is the impact outside of pregnancy? Do women know if/when they have been tested?

- Explore the potential of targeting behavioral intervention to the time of ovulation (exploiting the window of vulnerability for HIV infection based on the hormonal shifts over the course of a women’s cycle).
- Develop prevention modalities for women in various contexts (single partners vs. multiple partners, etc).
- Incorporate multiple modalities such as PREP, microbicides and behavioral interventions not just one or the other.

### Social Research

Questions related to the behavior of communities that increase or decrease the likelihood of prevention and/or effective treatment. **Research funding should be directed to studies that:**

- Identify the cultural and/or social factors operating in a community that promote or inhibit HIV infection, treatment, and care.
- Investigate fundamental mechanisms and context specificity of social drivers to HIV vulnerability in women and girls.
- Integrate sex and gender scholarship in HIV research. Social interventions to address gender inequality may help to reduce HIV infection rates.
- Devise and test interventions to help people stay HIV-negative who have tested HIV-negative previously.
- Identify effective adherence tools for use in HIV prevention trials.
- Define what’s known about stigma and how it affects HIV infection/acquisition. What are the gaps in stigma research? In the work being directed toward women at risk, what is being done to intervene at the provider/community level where the stigma is being derived? Particularly examine the impact of stigma on routine HIV testing.

### Research Design

While the major theme of “*How do women become infected and how do they protect themselves from HIV infection?*” can be segmented into biologic, behavioral, and social questions, it is essential that researchers integrate these questions into an inter-disciplinary approach to research design. **Research funding should be directed to studies that incorporate these innovative design considerations:**

- Novel use of both quantitative and qualitative research methods.
- Design models that move beyond exclusive reliance on randomized testing to consider other dimensions of efficacy.
- Recognizes that basic research occurs in a behavioral and social context -- so research design and methods to answer basic questions must consider these factors.

- Rigorously assess inclusion and exclusion criteria in studies and identify potential systemic barriers to women’s participation in HIV preventative and therapeutic research.
- Evaluate factors (including investigator bias) associated with enrollment and retention of women in studies in both industry and non-industry sponsored studies.
- Demonstrate a commitment to work with the community to identify high-risk populations for trial participation in the United States.

### Translating Findings into Practice

While many critical questions remain unanswered, the WRI agrees that there are significant gaps and time lags in translating new research findings into clinical practice. ***Funding should be directed to initiatives that quickly and effectively translate new research findings into clinical practice:***

- Broad dissemination of or access to information detailing ongoing or completed research projects through a universal database or compendium to reduce duplication of efforts and enhance knowledge sharing to improve future research design and development.
- Medical education initiatives that help care providers incorporate new knowledge into clinical practice.
- Professional development for researchers to help them integrate basic, behavioral, and social research methods in design of more effective interventions.

### Additional Recommendations

- More research and efforts need to be employed on the question of how to engage and maintain HIV-positive (and at risk) people in care (it appears that this is not so much to do with HIV, but the context of lives that are presenting barriers for people to get in and stay in care.)
- Develop a “best practices” document regarding the recruitment and retention of women in HIV research.
- The development of guidelines is needed with regard to pregnancy testing in studies, bearing in mind the context of the trials. Some noted the ethics and issues might be different in treatment and prevention studies. It’s not known how many false positive or chemical pregnancies lead to discontinuation of interventions, how it impacts study results, if testing less frequently would solve this problem or how to proceed with the best interests of both the trial participant and the trial results.

- Identify mechanisms to integrate and disseminate current knowledge on social, behavioral and clinical findings to clinical providers. A broader recommendation is dovetailed onto this that efforts be made to define the state of knowledge and disseminate information via women's health updates at major conferences. Moreover, information should be shared with fellows and young investigators to spur interest in the field and offer mentorship opportunities to engage the next generation of impassioned investigators interested in women and HIV issues.
- There needs to be the establishment of a mechanism to advance innovative and/or riskier research with seed funding.
- There needs to be a mechanism to reward science researchers who are doing a good job mentoring junior investigators.
- Increased funding is needed for effective treatments/programs for substance abuse.
- Examine and define mental health issues among women at risk for HIV.
- There is a need to better understand HIV transmission among women in incarcerated settings.
- Define barriers to access for new prevention modalities (such as PREP and microbicides) and how to roll out these new modalities.
- More needs to be done to educate providers (especially male providers) about provision of quality care for HIV-positive and at risk women, as well as how to talk to women clients about research.

## Appendix A – WRI 2009 Participant List

**Kathy Anastos, M.D.**

Professor of Medicine  
Montefiore Medical Center

**Judith D. Auerbach, Ph.D**

Vice President, Science & Public Policy  
San Francisco AIDS Foundation

**Gina Brown, M.D.**

Coordinator, Microbicides & Women & Girls  
Research  
NIH/OAR

**Terri Creagh, Ph.D.**

Director of Research  
Clinical and Epidemiologic Research

**Judith Feinberg, M.D.**

Professor of Medicine  
University of Cincinnati

**Debbie P. Hagins, M.D.**

Clinical Director  
Chatham County Health Dept.

**Sharon Lee, M.D.**

Director  
Family Health Care

**Joseph Mrus, M.D., M.Sc.**

Medical Director  
Tibotec Therapeutics

**Monica Ruiz, Ph.D., M.P.H.**

Director, HIV Prevention Research Program  
Forum for Collaborative HIV Research

**Linda Scruggs**

Director of Program  
AIDS Alliance for Children, Youth & Families

**Laura N. Armas-Kolostroubis, M.D.**

Clinical Director  
Tx / Ok AETC

**Dawn Averitt Bridge**

Founder  
The Well Project

**Elizabeth Connick, M.D.**

Associate Professor of Medicine  
University of Colorado Denver

**Judith Currier, M.D., M.Sc.**

Professor of Medicine, Associate Chief, Division of  
Infectious Diseases  
UCLA

**Monica Gandhi, M.D., M.P.H.**

Assistant Professor  
University of California, San Francisco

**Yasmin Halima**

Vice President  
AIDS Treatment Activist Coalition

**Patty Martin, Pharm.D.**

Associate Director, Medical Affairs  
Gilead Sciences, Inc.

**Tonia Poteat, M.M. Sc., M.P.H.**

Physician Assistant  
Chase Brexton Health Services

**Ellie Schoenbaum, M. D.**

Professor  
Albert Einstein College of Medicine

**Daniel Seekins, M.D.**

Group Director, HIV Medical Strategy  
Bristol-Myers Squibb

**Stephen P. Storfer, M.D.**

Senior Associate Director of Virology  
Boehringer Ingelheim Pharmaceuticals, Inc.

**Kimberly Struble, Pharm.D.**

Medical Team Leader  
Food and Drug Administration

**Carmen D. Zorrilla, M.D.**

Professor Ob-Gyn  
University of Puerto Rico

## Appendix B – WRI 2009 Speaker List

**Dawn Averitt Bridge**

Founder  
The Well Project

**Monica Gandhi, M.D., M.P.H.**

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**Monica Ruiz, Ph.D., M.P.H.**

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**Steven Deeks, M.D.**

Professor of Medicine  
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**Karen Newell-Rogers, Ph.D.**

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**Kimberly Struble, Pharm.D.**

Medical Team Leader  
Food and Drug Administration

**Charles Wira, Ph.D.**

Professor of Physiology  
Dartmouth Medical School

## Appendix C - Identified Gaps from Group Brainstorming Sessions

- IMPACT OF HORMONES AND OTHER FACTORS ON TRANSMISSION AND IMMUNE PROTECTION
  - Which endogenous microbicide(s) in secretions from the female reproductive tract are responsible for protection against HIV infection? How can this protection be enhanced to close the Window of Vulnerability?
  - What is the role(s) of commensals (pH, bacteriocins, etc.) in protection against HIV transmission?
  - What are the relative contributions of endogenous microbicides and IgG-specific anti-HIV antibodies for protection against mucosally-transmitted/founder viruses?
  - Are there exogenous microbicides that enhance endogenous immune protection?
  - What is the role of semen in HIV transmission?
  
- IMPACT OF SEX-BASED DIFFERENCES ON PK, IMMUNE RESPONSES, AND PATHOGENESIS
  - Pharmacokinetics and pharmacogenomics vis a vis sex (especially understanding impact of sex on treatment responses and toxicities related to antiretroviral therapy)
  - Understanding the impact of endogenous and exogenous sex hormones on the biology and treatment of HIV-1 infection;
  - How do sex hormones affect the immune system and how does this change with aging?
  - Improve understanding of sex-based differences in pathogenesis, disease progression, toxicity and response to HIV therapy.
  
- IMPACT OF SEX AND RACE ON HIV CARE
  - What causes the enormous racial disparities in both HIV prevalence and treatment outcomes, and what are the best ways to address these disparities?
  - Understanding the heightened morbidity of HIV infection in African American women in the US, and research on effective strategies to reverse this - specifically strategies aimed at prevention, earlier diagnosis, earlier treatment, and ensuring better health care in general.
  - How can adherence to care and treatment be improved for women?
  
- IMPROVING AND ENHANCING CLINICAL CARE
  - What is the best way to ensure that all clinicians have basic competency in HIV? (All clinicians are expected to have basic competency in diabetes, heart disease, and other chronic, life-threatening illnesses. However, often primary care providers and specialists who provide consultative care for HIV patients don't know the basics. This can lead to dangerous clinical interventions on one end or unwarranted withholding of care on the other.)
  - What motivates people with HIV to seek care and what helps them to remain in care?
  - What is the best way to prevent or manage medication fatigue - i.e. when patients who have been virologically suppressed for a long time stop taking their medications?

- PREVENTION STRATEGIES
  - Identifying effective combinations of prevention strategies.
  - Can women controlled prevention interventions be developed and implemented?
  - Development of biomedical prevention technologies for women including better understanding of genital tract pharmacology and immunology.
  
- CO-MORBIDITIES, TOXICITIES, AGING
  - Understanding the impact of HIV and its therapies on metabolic outcomes in women (especially cardiovascular disease, lipoaccumulation and lipoatrophy, diabetes);
  - Which complications of HIV disease are most common and how can they be prevented and managed in women (i.e. CV risk)?
  - Profile and address the issue of women, HIV and mental health co-morbidities.
  - Characterize PK of HIV in women including pharmacokinetics of pregnancy, menstrual cycle and menopause and impact of treatment; management of women in sero-discordant relationships who wish to conceive.
  
- PREGNANCY
  - How should management of HIV in pregnancy be integrated into longer term treatment strategies for women (what are the best regimens, safest during pregnancy and beyond)
  
- CLINICAL TRIALS
  - The challenge of recruitment, access and retention of women in clinical trials.