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HIV Persistence during Therapy

Fifth International Workshop

St. Maarten, West Indies • December 6-9, 2011

Final Program

This program is jointly sponsored by the University of Massachusetts Medical School
Office of Continuing Medical Education and Informed Horizons.



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Fifth International Workshop on HIV Persistence during Therapy

Scientific Program

Tuesday, December 6, 2011

Abstract

15:00 Satellite Symposium: Unique Challenges and Opportunities for Eradication of Brain HIV-1 Reservoirs
Sponsored by the National Institute of Mental Health

19:00 Welcome Dinner

Wednesday, December 7, 2011

MORNING SESSIONS

| | | |
|--------------|--|---|
| 8:00 | Opening Remarks Mario Stevenson | <i>University of Miami Leonard M. Miller School of Medicine, Miami, FL, USA</i> |
| 8:10 | SESSION I: MODELS OF HIV PERSISTENCE | |
| Chairs: | José Alcami Monsef Benkirane | <i>Instituto de Salud Carlos III, Madrid, Spain</i> <i>Laboratory of Molecular Biology, CNRS UPR 1142, Montpellier, France</i> |
| 8:10 | Viral Activators Evaluated for Treatment of Viral Persistence in a Nonhuman Primate Model for AIDS Therapy Paul Luciw | 01 <i>University of California Davis, Davis, USA</i> |
| 8:30 | Simian Models of Viral Persistence Jeff Lifson | <i>NCI-Frederick, Frederick, USA</i> |
| 8:50 | Eradication Trials in SIVmac251-infected Macaques Andrea Savarino | 02 <i>Istituto Superiore di Sanità, Rome, Italy</i> |
| 9:10 | HIV-1 Latency in <i>in-vitro</i> Differentiated Central Memory Cells Vicente Planelles | 03 <i>University of Utah School of Medicine, Salt Lake City, USA</i> |
| 9:25 | Generation of HIV Latency in BLT Humanized Mice J. Victor Garcia | 04 <i>University of North Carolina at Chapel Hill, Chapel Hill, USA</i> |
| 9:40 | The Contribution of Splenic Macrophages to SIV Infection and Changes in this Population Following Antiretroviral Treatment Julia Russell | 05 <i>Johns Hopkins University School of Medicine, Baltimore, USA</i> |
| 9:55 | Mega-ART Induces Viral Suppression and Restriction of the Viral Reservoir in a Simian AIDS Model Iart Shytaj | 06 <i>Istituto Superiore di Sanità, Rome, Italy</i> |
| 10:10 | SIV/Macaque Model of Highly Active Antiretroviral Therapy: Viral Persistence and Ongoing CNS Inflammation M. Christine Zink | 07 <i>Johns Hopkins University School of Medicine, Baltimore, USA</i> |
| 10:25 | Break | |

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| 11:00 | SESSION II: BASIC SCIENCE OF HIV PERSISTENCE | <u>Abstract</u> |
| Chairs: | Mario Stevenson Alain Lefeuvre | <i>University of Miami Leonard M. Miller School of Medicine, Miami, USA General Hospital, Toulon, France</i> |
| 11:00 | Control of HIV Latency by the “Two Peas in a Pod:” Polycomb and P-TEFb Jonathan Karn | 08 <i>Case Western Reserve University, Cleveland, USA</i> |
| 11:20 | New Mechanisms of HIV Transcriptional Latency Monsef Benkiran | 09 <i>Laboratory of Molecular Biology, CNRS UPR 1142, Montpellier, France</i> |
| 11:40 | Intracellular Tat Expression Modifies the Environment of Infected Lymphocytes José Alcami | 10 <i>Instituto de Salud Carlos III, Madrid, Spain</i> |
| 12:00 | Thoughts on Elimination of Latent HIV Reservoirs Jerome Zack | 11 <i>University of California, Los Angeles, USA</i> |
| 12:15 | Lunch | |
| AFTERNOON SESSIONS | | |
| 14:00-16:00 | Poster Viewing Session | |
| 16:00 | SESSION III: VIROLOGICAL ASPECTS OF HIV PERSISTENCE | |
| Chairs: | John Coffin Christine Rouzioux | <i>Tufts University, Boston, USA CHU Necker-Enfants Malades, Paris, France</i> |
| 16:00 | Characterizing Latent HIV Reservoirs Sarah Palmer | 12 <i>Swedish Institute for Infectious Disease Control and Karolinska Institute, Stockholm, Sweden</i> |
| 16:20 | Perspectives on Therapeutic Intervention and Eradication in HIV Infection Tae-Wook Chun | 13 <i>NIH, Bethesda, USA</i> |
| 16:40 | Residual HIV Replication on ART Javier Martinez-Picado | 14 <i>AIDS Research Institute (IrsiCaixa) and ICREA, Barcelona, Spain</i> |
| 17:00 | Epigenetic Modifications that Control Latency in T-Cells and Macrophages: Effect Of Chromatin Remodeling Complexes and Tat Modifications. Fatah Kashanchi | 15 <i>GMU, Manassas, USA</i> |
| 17:15 | Exosomes from HIV-1 Infected Cells: Trojan Horses that Contain TAR miRNA and Proteins that Effect Latency Fatah Kashanchi | 16 <i>GMU, Manassas, USA</i> |
| 17:30 | Targeted Activation of Viral Gene Expression by Exogenous Tat During Infection Inhibits the Establishment of HIV-1 Latency Daniel Donahue | 17 <i>McGill University AIDS Centre, Jewish General Hospital, Montreal, Canada</i> |
| 17:45 | M1 Polarization of Human Monocyte-derived Macrophages (MDM) Restricts Pre- and Post-integration Steps of the HIV-1 Life Cycle. A Potential Role of APOBEC3A Guido Poli | 18 <i>San Raffaele Scientific Institute & Vita-Salute San Raffaele University, Milano, Italy</i> |
| 18:00 | Hematopoietic Progenitor Cells (HPCs) are Preferentially Infected by CXCR4- and Dual-tropic HIV, and HIV from Latently Infected HPCs can be Transferred to CD4+ T Cells <i>in vitro</i> Adebowumi Onafuwa-Nuga | 19 <i>University of Michigan, Ann Arbor, USA</i> |
| 18:15 | TRIM22 Inhibits Sp1-dependent HIV-1 Transcription Elisa Vicenzi | 20 <i>San Raffaele, Milan, Italy</i> |
| 19:30 | Dinner | |

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| 8:00 | SESSION IV: INNATE IMMUNITY AND HIV PERSISTENCE | |
| Chairs: | Monsef Benkirane Marie-Lise Gougeon | <i>Laboratory of Molecular Biology, CNRS UPR 1142, Montpellier, France</i> <i>Institut Pasteur, Paris, France</i> |
| 8:00 | The Cytosolic Exonuclease TREX1 Digests HIV Reverse Transcripts to Avoid Triggering an Antiviral Interferon Response in T Cells and Macrophages Judy Lieberman | 21 <i>Harvard Medical School, Boston, USA</i> |
| 8:20 | Innate Immunity & Establishment of HIV Reservoirs Nicolas Manel | 22 <i>Institut Curie, Paris, France</i> |
| 8:40 | How Samhd1 May Change Our View of Viral Restriction Nadine Laguette | 23 <i>Laboratory of Molecular Biology, CNRS UPR 1142, Montpellier, France</i> |
| 9:00 | microRNAs and the Innate Immune Response to SIV Infection Jeanne Sisk | 24 <i>Johns Hopkins University School of Medicine, Baltimore, USA</i> |
| 9:15 | Break | |
| 9:30 | Poster Viewing Session | |
| 10:00 | SESSION V: IMMUNE CONTROL OF HIV RESERVOIRS | |
| Chairs: | Nicolas Chomont Marie-Lise Gougeon | <i>VGTI-Florida, Port St. Lucie, USA</i> <i>Institut Pasteur, Paris, France</i> |
| 10:00 | Relevance of Monitoring HIV Viral DNA Intermediates <i>in vivo</i> Una O'Doherty | 25 <i>University of Pennsylvania, Philadelphia, USA</i> |
| 10:20 | The Impact of HIV-associated Inflammation on HIV Persistence Steven Deeks | 26 <i>San Francisco General Hospital, University of California, San Francisco, USA</i> |
| 10:40 | Immunological Mechanisms Involved in HIV Persistence: Keeping Memory, Keeping HIV Nicolas Chomont | 27 <i>Vaccine and Gene Therapy Institute of Florida, Port St. Lucie, USA</i> |
| 11:00 | Increased Susceptibility to CD8 T Cell Mediated Killing Limits the HIV-1 Reservoir in Naïve CD4 T Cells from Elite Controllers Mathias Lichterfeld | 28 <i>Massachusetts General Hospital, Boston, USA</i> |
| 11:15 | Differential Impact of IL-7 and IL-15 on HIV Reservoir Persistence Claire Vandergeeten | 29 <i>VGTI-Florida, Port St. Lucie, USA</i> |
| 11:30 | Modulation of Oxidative Stress Induces Apoptosis in Long-lived Phenotypes <i>ex vivo</i> Barbara Chirullo | 30 <i>Italian Institute of Health, Rome, Italy</i> |
| 11:45 | Lunch | |

AFTERNOON SESSIONS**Abstract****14:00-15:00 Poster Viewing Session II****15:00-15:30 SESSION VI A: LATE BREAKER ABSTRACTS**Chair: Alain Lafeuillade *General Hospital, Toulon, France***15:30-16:00 SESSION VI B: RESEARCH PRESENTATIONS FROM FIRMS SUPPORTING THE MEETING**Chair: Alain Lafeuillade *General Hospital, Toulon, France*15:30 Title TBA
On behalf of Gilead Sciences Inc.: Romas Gelezunas; *Foster City, USA*15:45 Title TBA
On behalf of Tibotec: Guenter Kraus; *Mechelen, Belgium***16:00 SESSION VII: ACUTE HIV INFECTION**Chairs: Mark Wainberg *McGill University AIDS Centre, Montreal, Canada*
Martin Markowitz *Aaron Diamond AIDS Research Center, New York, USA*16:00 A Randomized, Open-label Trial of 5-drug *versus* Standard 3-drug PI-based cART Initiated
During Acute and Early Infection: 96-week Results 31
Martin Markowitz *Aaron Diamond AIDS Research Center, New York, USA*16:20 The Effect of Mega-HAART and HAART Instituted During Fiebig I to IV Acute HIV Infection on
HIV Reservoir Size and Gut T cells 32
Jintanat Ananworanich *The Thai Red Cross AIDS Research Center, Bangkok, Thailand,
and the US Military HIV Research Program, Rockville, USA*16:40 Reduced HIV-1 Reservoir Size after 10 years of Suppressive Antiretroviral Therapy in
Patients Initiating Treatment during Primary Infection 33
Maria Buzon *Ragon Institute of MGH, MIT and Harvard, Charlestown, USA*16:55 Control of HIV-1 Replication in CD4⁺ T Lymphocytes by using PKC Theta Inhibitors as a Strategy to Reduce
the Size of Reservoirs during Primary Infection 34
Mayte Coiras *Instituto de Salud Carlos III, Madrid, Spain***17:00 SESSION VIII: ANATOMIC RESERVOIRS**Chairs: José Gatell *Hospital Clinic, Barcelona, Spain*
Alain Lafeuillade *General Hospital, Toulon, France*17:00 Tissue Analysis of Lymphatic Reservoirs of HIV Infection 35
Timothy Schacker *Department of Medicine, University of Minnesota, Minneapolis, USA*17:20 Virologic Analysis of Lymphatic Reservoirs of HIV Infection 35
Mario Stevenson *University of Miami Leonard M. Miller School of Medicine, Miami, FL, USA*17:40 Pharmacologic Analysis of Lymphatic Reservoirs of HIV Infection 35
Courtney Fletcher *University of Nebraska Medical Center, Omaha, USA*18:00 The Brain and Spleen are Reservoirs of SIV Infection in Macrophages 36
Janice Clements *Johns Hopkins University School of Medicine, Baltimore, USA***18:20 Poster Viewing Session****20:00 Gala Dinner**

| 8:00 | SESSION IX: NEW APPROACHES & ERADICATION TRIALS - PART I | |
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| Chairs: | Alain Lefeuillade Jean Michel Molina | <i>General Hospital, Toulon, France Hopital Saint Louis, Paris, France</i> |
| 8:00 | Designing Clinical Trials for HIV-1 Eradication Daniel Kuritzkes | 37 <i>Harvard Medical School, Cambridge, USA</i> |
| 8:20 | The Role of Chemokines in the Establishment of HIV Latency Sharon Lewin | 38 |
| 8:40 | The HIV-1 Eradication Pipeline: Challenges and Opportunities Daria Hazuda | 39 <i>Merck Research Laboratories, West Point, USA</i> |
| 9:00 | The Effect of Vorinostat on Latent HIV-1 Expression <i>in vivo</i> : Preliminary Findings from a Clinical Study in ART-suppressed HIV-1-infected Patients David Margolis | 40 <i>Institute for Global Health & Infectious Diseases, UNC Chapel Hill, Chapel Hill, USA</i> |
| 9:20 | Effect of Maraviroc Intensification on the Decay of HIV-1 DNA in PBMC of Recently Infected Patients Initiating Treatment with Raltegravir plus Tenofovir/Emtricitabine: a 48-week Randomized Study Maria Puertas | 41 <i>IrsiCaixa - AIDS Research Institute, Badalona, Spain</i> |
| 9:35 | Dynamics of Immune Activation and PD-1 Expression in Recently Infected HIV-1 Naïve Subjects Intensifying with Maraviroc a Raltegravir plus Tenofovir/Emtricitabine Regimen Marta Massanella | 42 <i>IrsiCaixa, Badalona, Spain</i> |
| 9:50 | Picomolar Dichotomous Activity of Gnidimacrin Against HIV-1 Latent Infection Chin Ho Chen | 43 <i>Duke University Medical Center, Durham, USA</i> |
| 10:05 | Poster Viewing Session | |
| 10:30 | SESSION X: NEW APPROACHES & ERADICATION TRIALS - PART 2 | |
| Chairs: | David Margolis José Gatell | <i>Institute for Global Health & Infectious Diseases, UNC Chapel Hill, Chapel Hill, USA Hospital Clinic, Barcelona, Spain</i> |
| 10:30 | CCR5 Knock-out in Hematopoietic Stem Cells Paula Cannon | 44 <i>USC Keck School of Medicine, Los Angeles, USA</i> |
| 10:50 | A Single Infusion of Zinc Finger Nuclease (ZFN) CCR5 Modified Autologous CD4 T-cells Correlates with Increases CD4 Counts and Effects on Viral Load in Aviremic HIV-infected Subjects Carl June | 45 <i>Abramson Cancer Center, University of Pennsylvania, Philadelphia, USA</i> |
| 11:10 | Targeted Disruption of CXCR4 in Human CD4 ⁺ T cells with Zinc-finger Nucleases Craig Wilen | 46 <i>University of Pennsylvania, Philadelphia, USA</i> |
| 11:30 | Excision of HIV Proviral DNA Using Tre-recombinase Jan van Lunzen | 47 <i>University Medical Center Hamburg-Eppendorf, Hamburg, Germany</i> |
| 11:45 | Direct Targeting of Integrated HIV Sequences Using Engineered Homing Endonucleases Keith Jerome | 48 <i>Fred Hutchinson Cancer Research Center, Seattle, USA</i> |
| WORKSHOP CONCLUSIONS | | |
| 12:00 | Alain Lafeuillade Françoise Barré-Sinoussi | <i>General Hospital, Toulon, France Institut Pasteur, Paris, France</i> |

Posters

| title and author | abstract |
|---|----------|
| An Animal Model to Evaluate the Eradication of Latent SIV Infection in Rhesus Macaques on ART <i>RM Dunham</i> | 01 |
| Plasma Biomarkers of Acute Retroviral Infection in the <i>Macaca nemestrina</i> Model of CNS Disease: CNS Disease, Latency, and Agings <i>KW Witwer</i> | 02 |
| A New Chimeric SIVmac251/SIVmac239 Virus for Vaccine Studies Requiring Moderate Sensitivity to Neutralization and Resistance to TRIM5a <i>PA Marx</i> | 03 |
| <i>Ex vivo</i> Modeling of Viral Reactivation Strategies in Virally Suppressed Subjects <i>R Fromentin</i> | 04 |
| Role of NFAT in Reactivation of HIV-1 Latency in Primary Memory CD4 ⁺ T Cells <i>A Bosque</i> | 05 |
| Latent HIV Infection Occurs in Multiple Hematopoietic Progenitor Cell Subsets and is Reversed by NF-κB Activation <i>LA McNamara</i> | 06 |
| Complete Transcriptome Analysis of Latently Infected CD4 ⁺ T Cells <i>F Romerio</i> | 07 |
| Unique Mechanisms of HIV-1 Transcriptional Regulation in the CNS <i>M Churchill</i> | 08 |
| Do Gene Expression Levels and Genetic Polymorphisms in HIV Integrase Cofactor LEDGF/p75 have an Impact on HIV-1 Disease Progression <i>WD Spiegelaelere</i> | 09 |
| Differential Role of p-TEFb during HIV-1 Productive <i>versus</i> Latent Infections <i>M Famiglietti</i> | 10 |
| CD4 ⁺ T Cells in HIV-1 Patient Blood Release Platelet-sized, Protoplasmic Bodies that Evade Immunologic Intervention and Transmit HIV-1 <i>CL Bristow</i> | 11 |
| Simian Immunodeficiency Virus in the Brain Leads to Altered Type I Interferon Signaling During Acute Infection <i>L Alammar</i> | 12 |
| Expansion of CD14 ^{high} CD16 ^{neg} CCR2 ^{low/neg} Monocytes During SIV and HIV Infection that Suppress CD8 ⁺ T Cell Proliferation <i>L Gama</i> | 13 |
| Negative Regulation of HIV-1 Transcription by a Heterodimeric Complex of NF-κB1 p50 and Naturally Occurring Truncated STAT5 (STAT5Δ) <i>G Poli</i> | 14 |
| A Human LEDGF/p75 Knockout Cell Line to Study the Mechanism of HIV-1 Integration Site Distribution <i>R Schrijvers</i> | 15 |

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| Endogenous CCL2 is a Negative Regulator of APOBEC3A Expression in Macrophages: Role in HIV-1 Infection <i>L Fantuzzi</i> | 16 |
| Erythrocytes Differentially Bind Infectious HIV-1 Virions and Serve as Efficient Carriers for <i>Trans</i> Infection of HIV-1 to CD4(+) Cells: Effects of Antibodies and Complement <i>Z Beck</i> | 17 |
| Modest Deviations from Optimal Adherence to Antiretroviral Therapy Promote Residual HIV-1 Replication in the Absence of Virological Rebound in Plasma <i>AO Pasternak</i> | 18 |
| Novel Action Mechanism of Macrophage-specific HIV-1 Reverse Transcriptase Inhibitors <i>B Kim</i> | 19 |
| Residual Viremia in Patients with a Nevirapine-including Antiretroviral Regimen is not Associated with HIV-specific Cellular Immune Response <i>D McIlroy</i> | 20 |
| Evolution of HIV-1 Quasispecies and Coreceptor Usage in Cell Reservoirs under Suppressive Antiretroviral Therapy <i>J Izopet</i> | 21 |
| Multidrug-resistant Variants of HIV-1 Existing in Cells as Defective Quasispecies Can Be Rescued by Superinfection by Other Defective HIV-1 Variants of Different Subtypes <i>MA Wainberg</i> | 22 |
| An Atlas of HIV-1 Reservoirs, Compartments and Drug Resistant Sanctuaries <i>R Fox</i> | 23 |
| Long Term Control of HIV-1 Infection Is Associated with Lack of Infection of CD4 T Cells in <i>Trans</i> and is Related to Alteration in Cholesterol Metabolism <i>G Rappoccio</i> | 24 |
| Rationalization of Physicochemical Properties of Coumarin Derivatives to Design Potent HIV-Integrase Inhibitors <i>VK Srivastav</i> | 25 |
| Discontinuation of Long-term ART Initiated at Seroconversion can be Associated with Prolonged High Viremia and Preservation of CD4 Cells <i>SI Kinloch-de Loes</i> | 26 |
| Viral and Lymphocyte Dynamics in Acute HIV-1 Infection: RV217-The Early Capture HIV Cohort Study (ECHO) <i>ML Robb</i> | 27 |
| Reduction of Transmitted Virus in Vaccinated Monkeys after Mucosal SIV Challenge. <i>J Whitney</i> | 28 |
| Defensins and RNases Show Potential Antiviral Effects During <i>in vivo</i> and <i>in vitro</i> Exposure to HIV-1 <i>W Zapata-Builes</i> | 29 |
| Zinc Finger Nucleases Disrupting SIV/HIV-pol-gene Action to Irreversibly Inactivate HIV Proivirus Within Latently Infected Cells <i>M Wayengera</i> | 30 |

| title and author | abstract |
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| Low-level Viremia and Blips During HAART are Preceded by Increased Levels of Viral Production <i>M Nijhuis</i> | 31 |
| Cellular Metabolism of Nucleoside Analogs Predicts Antiviral Potency in Activated Macrophages: Implications for Eradication of Viral Reservoirs <i>C Gavegnano</i> | 32 |
| Comparison of Histone Deacetylase (HDAC) Inhibitors in Clinical Use: Potential for Disrupting HIV-latency, Effect on T-cell Activation, and Toxicity <i>TA Rasmussen</i> | 33 |
| Reactivation of Latent HIV and Subsequent Killing of HIV-expressing Cells by Cytotoxic Anti-HIV Designer T Cells <i>GK Sahu</i> | 34 |
| Inhibition of HIV-induced Apoptosis in Primary CD4 T Cells is Similar Across ART Drug Classes <i>NW Cummins</i> | 35 |
| ART in Early Infection: Quantifying Effects on the CNS Viral Reservoir <i>CL Sammet</i> | 36 |
| The Pro-differentiating Agent All <i>Trans</i> Retinoic Acid (ATRA) is a Potent Enhancer of HIV-1 Escape from Quiescence Generated by the Combination of Oxidative Stress Modulator Auranofin and PKC Activating Compound Bryostatin 1 <i>S Norelli</i> | 37 |
| Single Mutations in HIV Integrase Produce High-Level Resistance to Raltegravir During Infection of Macrophages <i>MD Marsden</i> | 38 |
| Intensification of Antiretroviral Treatment with Maraviroc <i>G Chryssos</i> | 39 |
| HIV Cure-Related Clinical Research: Results of an International Community-Led Workshop <i>M Harrington</i> | 40 |