

**HEP DART 2007**  
**Frontiers in Drug Development for Viral Hepatitis**

**Scientific Program**

**Sunday, December 9, 2007**

**Abstract**

9:00 **Satellite Symposium: Toward Curative Therapies for Hepatitis C**

12:10 **Satellite Symposium Lunch**

**HEP DART 2007 Opening Session**

15:00 Opening Remarks  
Raymond F. Schinazi *Emory University/Veteran Affairs Medical Center, USA*

Chairs: Robert Murphy *Northwestern University, USA*  
Charles Rice *The Rockefeller University, USA*

15:15 **State of the Art Lecture**  
The Changing Global Epidemiology of HBV and HCV 01  
Kevin Fenton *Centers for Disease Control and Prevention, USA*

16:00 **State of the Art Lecture**  
New Insights into Hepatitis B Pathogenesis and Resistance 02  
Stephen Locarnini *Victorian Infectious Diseases Reference Laboratory, Australia*

18:00 **Welcome Reception**

**Monday, December 10, 2007**

Chairs: Raymond F. Schinazi *Emory University/Veteran Affairs Medical Center, USA*  
Robert Murphy *Northwestern University, USA*

8:00 Presentation of William H. Prusoff HEP DART Lifetime Achievement Award  
Raymond F. Schinazi *Emory University/Veteran Affairs Medical Center, USA*  
Robert Murphy *Northwestern University, USA*

8:10 **William H. Prusoff HEP DART Lifetime Achievement Award**  
A Pre-Mortem Lookback Investigation of One's Life in Research: 03  
The Payoffs of a Persistent Patient  
Harvey Alter *National Institutes of Health, USA*

8:50 **State of the Art Lecture**  
New Insights into the HCV Replication Cycle: Lessons Learned from Novel Culture Systems 04  
Ralf Bartenschlager *University of Heidelberg, Germany*

**Advances in New Models for HBV and HCV**

9:20 HCV Cell Culture Systems and the Development of Antiviral Therapeutics 05  
T. Jake Liang *National Institutes of Health, USA*

9:40 Role of Negative Regulatory Signals in the Pathogenesis of HCV 06  
Arash Grakoui *Emory Vaccine Center, USA*

10:00 A Model System for Hepatitis B and C Virus Co-infection 07  
Volker Brass *University of Freiburg, Germany*

10:20	<b>Special Lecture</b> Insights into the Impact of HBV and HCV Viral Dynamics on Antiviral Therapy Alan S. Perelson <i>Los Alamos National Laboratories, USA</i>	08
10:40	Panel Discussion	
11:05	<b>Break</b>	
	<b>Oral Abstract Presentations</b>	
	Chairs: Thierry Poynard Brent E. Korba <i>Groupe Hospitalier Pitié-Salpêtrière, France</i> <i>Georgetown University, USA</i>	
11:30	Interferon Modulation of Cellular microRNAs as a Novel Antiviral Mechanism Irene Pedersen <i>University of California, San Diego, USA</i>	09
11:40	DNA Microarray Analysis of the NS3 and NS5B Genes from Hepatitis C Genotype 1a Infected Patients Gustine Liu-Young <i>Yale University, USA</i>	10
11:50	Assessment of Both Virological Response at Week 4 and at Week 12 Optimizes Prediction of Treatment Outcome in Patients with Chronic Hepatitis C Treated with Peginterferon Alfa-2B plus Ribavirin Michelle Martinot-Peignoux <i>INSERM U-773-CRB3, France</i>	11
12:00	Week 24 is the Optimal Time Point for Predicting Outcomes at 2 Years with Telbivudine Rajender Reddy <i>University of Pennsylvania School of Medicine, USA</i>	12
12:10	<b>Lunch</b>	

**MONDAY EVENING SESSION**

**The Business of Hepatitis Antivirals**

	Chairs: Abel De La Rosa Patrick Higgins <i>Pharmasset, Inc., USA</i> <i>Pharmasset, Inc., USA</i>	
17:00	The Business of Hepatitis Antivirals: Bridging Diverse Interests Patrick Higgins <i>Pharmasset, Inc., USA</i>	
17:20	Panel Discussion Adam Cutler Sandra Lehrman Dennis Liotta Richard Smith Frank Zavrl <i>Canaccord Adams, USA</i> <i>Merck Research Laboratories, USA</i> <i>Emory University, USA</i> <i>JP Morgan Securities, Inc., USA</i> <i>Adage Capital, USA</i>	

**Tuesday, December 11, 2007**

**Diagnosis and New Treatments for HBV and HCV**

	Chairs: Ralf Bartenschlager Charles Rice <i>University of Heidelberg, Germany</i> <i>The Rockefeller University, USA</i>	
8:00	<b>State of the Art Lecture</b> HCV Replicons vs. Infectious Virus Systems in Drug Discovery Stanley M. Lemon <i>University of Texas Medical Branch at Galveston, USA</i>	18
8:30	<b>State of the Art Lecture</b> The Size of the Viral Inoculum Determines the Kinetics, Magnitude and Outcome of Hepatitis B Virus Infection Frank V. Chisari <i>Scripps Research Institute, USA</i>	19

	<b>Abstract</b>
9:00 Population Genetics of HBV and HCV Quasispecies: Implications for Drug Development and Drug-resistance Testing Robert W. Shafer <i>Stanford University, USA</i>	20
9:20 Nitazoxanide: A Potent Antiviral Agent against HCV and HBV Brent E. Korba <i>Georgetown University, USA</i>	21
9:40 Clinical Implications of Combined Intra-cellular and Cellular Evolution of HCV Resistance during Direct Anti-HCV Treatment Avidan U. Neumann <i>Bar-Ilan University, Israel</i>	22
10:00 Panel Discussion	
10:30 <b>Break</b>	
<b>Oral Abstract Presentations</b>	
Chairs: George Lau <i>Queen Mary Hospital, Hong Kong</i> Adrian DiBisceglie <i>Saint Louis University School of Medicine, USA</i>	
11:00 Phase 2 Studies with Albinterferon Alfa-2b (alb-IFN) Dosed q4wk Provide Insights into Dose Selection for Future Studies Ira Jacobson <i>Weill Medical College of Cornell University, USA</i>	23
11:10 Robust Antiviral Efficacy of a “Finger-loop” Allosteric Inhibitor of the HCV Polymerase in HCV Infected Chimpanzees Raffaele De Francesco <i>I.R.B.M. “P Angeletti,” Italy</i>	24
11:20 Preclinical Development of the Amphipathic DNA Polymer REP 9AC for the Treatment of HBV Infection Andrew Vaillant <i>REPLICor Inc., Canada</i>	25
11:30 Inhibition of Hepatitis C Virus Replication by Octadecyloxypropyl-(S)-HPMPA in Genotype 1B and 2A Replicons Karl Y. Hostetler <i>University of California, San Diego, USA</i>	26
11:40 FKBP8 Plays a Crucial Role in the Replication of Hepatitis C Virus Yoshiharu Matsuura <i>Osaka University, Japan</i>	27
11:50 Initial Recommendations for HCV Drug Resistance Analysis: A Consensus Statement from the HCV Drug Resistance Advisory Group Kai Lin <i>Novartis Institutes for Biomedical Research, Inc., USA</i>	28
12:00 <b>Lunch</b>	
<b>Hepatitis B Foundation Symposium: Early Detection and Management of Cirrhosis and Hepatocellular Carcinoma</b>	
Chairs: Timothy Block <i>Hepatitis B Foundation and Drexel University Medical College, USA</i> Harvey Alter <i>National Institutes of Health, USA</i>	
13:30 Introduction: Early Detection and Management of Cirrhosis and Hepatocellular Carcinoma Timothy Block <i>Hepatitis B Foundation and Drexel University Medical College, USA</i>	

	<b>Abstract</b>
13:40 Hepatocellular Carcinoma: Why Early Diagnosis is Needed Adrian M. DiBisceglie <i>Saint Louis University Liver Center, USA</i>	39
13:55 Assessment of Fibrosis: Non Biopsy Methods to Determine Hepatic Fibrosis Nezam H. Afdhal <i>Harvard Medical School, USA</i>	40
14:10 Screening Fibrosis: “La Révolution Française” Thierry Poynard <i>Groupe Hospitalier Pitié-Salpêtrière, France</i>	41
14:25 Treatment of HCC over the Past Decade: The Experience of over Four Thousand Patients in Japan Masao Omata <i>University of Tokyo, Japan</i>	42
14:40 Use of Pre-emptive Nucleoside Analogue Therapy for Hepatitis B Reactivation after Chemotherapy George K. K. Lau <i>Queen Mary Hospital, Hong Kong</i>	43

14:55 Panel Discussion

16:30 **Poster Session**

## **TUESDAY EVENING SESSION**

### **Immunology & Pathogenesis**

Chairs Lawrence M. Blatt *Alios BioPharma, Inc., USA*  
Michael Fried *University of North Carolina at Chapel Hill, USA*

#### 18:00 **State of the Art Lecture**

Cellular Immune Responses against Hepatitis C in Acute and Chronic Infection Margaret J. Koziel <i>Harvard Medical School, USA</i>	44
18:30 Broadly Neutralizing Antibodies to HCV: Definition of Epitopes and Antiviral Activity <i>In Vitro</i> and <i>In Vivo</i> Mansun Law <i>The Scripps Research Institute, USA</i>	45
18:50 Innate Immune Studies in Hepatitis B: Novel Studies in Pathogenesis and Treatment Kumar Visvanathan <i>Monash Institute of Medical Research, Australia</i>	46
19:10 Early Steps in the Replicative Cycle of Hepatitis B Virus Dieter Glebe <i>University of Giessen, Germany</i>	47
19:30 Panel Discussion	

## **Wednesday, December 12, 2007**

### **New Therapeutic Approaches I**

Chairs: Stanley M. Lemon *University of Texas Medical Branch at Galveston, USA*  
Karen Anderson *Yale University School of Medicine, USA*

#### 8:00 **State of the Art Lecture**

HCV Entry Pathways and Implications for the Development of Entry Inhibitors Matthew J. Evans <i>The Rockefeller University, USA</i>	53
8:30 The Role of CD81 and Scavenger Receptor Class B Member 1 in HCV Entry Peter Balfe <i>University of Birmingham, UK</i>	54
8:50 Lipid Droplet is an Important Organelle for Production of Infectious Hepatitis C Virus Kunitada Shimotohno <i>Keio University, Japan</i>	55

	<b>Abstract</b>
9:10 The Role of Cyclophilins and Cyclophilin Inhibitors in the Replication of HCV Rafael Crabbé <i>Debiopharm S.A., Switzerland</i>	56
<b>Oral Abstract Presentation</b>	
9:30 HCV Infection Increases Claudin-1 and Claudin-7 Expression by Inducing Cirrhosis Andras Kiss <i>Semmelweis Medical University, Hungary</i>	57
9:40 Panel Discussion	
10:05 <b>Break</b>	
<b>New Therapeutic Approaches II</b>	
Chairs: Yves Benhamou <i>Hôpital Pitié-Salpêtrière, France</i> Marion Peters <i>University of California, San Francisco, USA</i>	
<b>Oral Abstract Presentations</b>	
10:30 Development of Novel Hyperglycosylated Type 1 Interferons: A Strategy to Improve PK Performance without Loss of Biological Potency Lawrence M. Blatt <i>Alios BioPharma, Inc., USA</i>	58
10:40 Bioinformatics Resources Supporting the Analysis of Hepatitis C Virus Elliot J. Lefkowitz <i>University of Alabama at Birmingham, USA</i>	59
<b>Invited Presentations</b>	
10:50 A Combination of Direct Antiviral Compounds can Achieve Sustained Viral Response in Hepatitis C Virus-infected Chimpanzees David B. Olsen <i>Merck Research Laboratories, USA</i>	60
11:10 Potent Antiviral Activity of the Nucleoside HCV Inhibitor, R7128, in Prior IFN Non-responders John G. McHutchison <i>Duke University, USA</i>	61
11:30 R1626 Demonstrates Synergistic Antiviral Effect in Combination with Peginterferon Alfa-2a [40 KD], with or without Ribavirin, and High Barrier to Resistance Development David Nelson <i>University of Florida, USA</i>	62
11:50 Tenofovir DF (TDF) Showed Superior Antiviral Efficacy to Adefovir Dipivoxil (ADV) at 48 Weeks in Two Pivotal, Randomized, Double-Blind, Studies for the Treatment of HBeAg-Negative (-) and HBeAg-Positive (+) Chronic Hepatitis B (CHB): Study 102 and Study 103 Patrick Marcellin <i>Hôpital Beaujon, France</i>	63
12:10 Panel Discussion	
12:35 <b>Lunch</b>	
<b>WEDNESDAY EVENING SESSION</b>	
<b>Resistance to Antiviral Agents</b>	
Chairs: Patrick Marcellin <i>Hôpital Beaujon, France</i> Michael P. Manns <i>Hannover Medical School, Germany</i>	
16:00 <b>State of the Art Lecture</b> Navigating Dangerous Complexities: Antiviral Strategies for Clinical Trials for Hepatitis C Yves Benhamou <i>Hôpital Pitié-Salpêtrière, France</i>	
16:30 Overcoming HCV Treatment-resistant Characteristics Michael W. Fried <i>University of North Carolina at Chapel Hill, USA</i>	77

	<b>Abstract</b>
16:50 Genetic and Structural Variability of the Hepatitis C Viral Polymerase, NS5B: Implications for Resistance to Inhibitors Philip C. Simister <i>CNRS, France</i>	78
17:10 Panel Discussion	
<b>Co-infection with HIV and Other Viruses</b>	
Chairs: Robert Gish <i>California Pacific Medical Center, USA</i> Masao Omata <i>University of Tokyo, Japan</i>	
17:30 Treatment of HBV/HIV Co-infections Marion Peters <i>University of California, San Francisco, USA</i>	88
17:50 Treatment of HCV in HIV-infected Individuals Zelalem Temesgen <i>Mayo Clinic, USA</i>	89
18:10 HCV/HIV Co-infections: Challenges from the Perspective of TAG Tracy Swan <i>Treatment Action Group (TAG), USA</i>	90
18:30 Panel Discussion	
20:00 <b>Gala Party</b>	

### **Thursday, December 13, 2007**

#### **Pharmacology and Drug Interactions of HBV and HCV Therapeutics**

Chairs: Dennis Liotta <i>Emory University, USA</i> Nezam H. Afdhal <i>Harvard Medical School, USA</i>	
8:00 <b>State of the Art Lecture</b> STAT-C: Role in HCV Treatment Algorithm in 2008 John G. McHutchison <i>Duke University, USA</i>	
8:30 Preclinical Drug Metabolism in Viral Hepatitis Drug Discovery Adrian S. Ray <i>Gilead Sciences, Inc., USA</i>	97
8:50 Frontiers of Clinical Pharmacology in Hepatitis Drug Development Charles W. Flexner <i>Johns Hopkins University, USA</i>	98
9:10 <b>Special Lecture</b> Current and Future: HCV Maintenance Therapy Karen L. Lindsay <i>University of Southern California, USA</i>	99
9:30 <b>Break</b>	
<b>Late Breaker Abstracts</b>	
Chairs: Margaret J. Koziel <i>Harvard Medical School, USA</i> Stephen Locarnini <i>Victorian Infectious Diseases Reference Laboratory, Australia</i>	
10:00 <b>State of the Art Lecture - Part I</b> Long Term Follow-up of HCV Patients Completing Peg-IFN Plus Ribavirin Treatment - Is There a Cure? Michael P. Manns <i>Hannover Medical School, Germany</i>	115

	<b><u>Abstract</u></b>
10:20 <b>State of the Art Lecture - Part II</b>	
Delta Hepatitis: Treatment Options for a Largely Neglected Disease	116
Michael P. Manns <i>Hannover Medical School, Germany</i>	
10:40 Biochemical Mechanism of Entecavir as an Antiviral Polymerase Inhibitor	117
Karen S. Anderson <i>Yale University School of Medicine, USA</i>	
11:00 Advancing RNAi-based Therapeutic from Discovery to Clinic	118
Robert Gish <i>California Pacific Medical Research Institute, USA</i>	
Catherine Pachuk <i>Nucleonics Inc., USA</i>	
11:20 Panel Discussion	
11:50 Reframing the Knowledge and Looking Beyond the Horizon	
Eugene Schiff <i>University of Miami, USA</i>	
12:10 Closing Remarks	
Raymond F. Schinazi <i>Emory University/Veteran Affairs Medical Center, USA</i>	