



Meeting Report

Meeting report: 28th International Conference on Antiviral Research in Rome, Italy



R. Anthony Vere Hodge

Vere Hodge Antivirals Ltd, Old Denshott, Leigh, Reigate, Surrey, UK

ARTICLE INFO

Article history:

Received 26 September 2015

Accepted 28 September 2015

Available online 24 October 2015

Keywords:

Sofosbuvir

Hepatitis C virus

Ebola virus

RNA viruses

Emerging viruses

Antiviral chemistry

ABSTRACT

The 28th International Conference on Antiviral Research (ICAR) was held in Rome, Italy from May 11 to 15, 2015. This article summarizes the principal invited lectures. Phillip Furman, the Elion award recipient, described the research leading to sofosbuvir. Dennis Liotta, who received the Holý award, described how an investigation into HIV entry inhibitors led to a new therapy for cancer patients. Erica Ollmann Saphire, winner of the Prusoff Young Investigator award, explored the world of viral proteins and how they remodel to perform different essential roles in viral replication. The keynote addresses, by Raffaele De Francesco and Michael Manns, reported on the remarkable progress made in the therapy of chronic HCV infections. A third keynote address, by Armand Sprecher, related the difficulties and successes of Médecins Sans Frontières in West Africa ravaged by the Ebola outbreak. There were three mini-symposia on *RNA Viruses*, *Antiviral Chemistry* and *Emerging Viruses*. There was a good collection of talks on RNA viruses (norovirus, rabies, dengue, HEV, HCV, and RSV). A highlight of the chemistry was the preparation of prodrugs for nucleotide triphosphates as this opens a door to new options. The third mini-symposium emphasized how research work in the antiviral area is continuing to expand and needs to do so with a sense of urgency. Although this meeting report covers only a few of the presentations, it aims to illustrate the great diversity of topics discussed at ICAR, bringing together knowledge and expertise from the whole spectrum of antiviral research.

© 2015 Published by Elsevier B.V.

Contents

1. Introduction	173
2. Gertrude Elion Memorial award lecture: sofosbuvir: a search for a cure. Phillip (Phil) Furman., Furman Biotech Consulting, St Augustine, FL, USA.	173
3. The Antonín Holý Memorial award lecture: novel therapeutics for treating viral diseases, cancers and inflammatory disorders. Dennis C Liotta, Emory University, Atlanta, GA, USA.	174
4. The William Prusoff Young Investigator award lecture: remodel, repurpose, rearrange; how viruses leverage the few proteins they encode. Erica Ollmann Saphire, The Scripps Research Institute, La Jolla, CA, USA.	175
Introduction.	175
Remodel.	176
Repurpose	176
Rearrange.	176
Our understanding of molecular biology is evolving	177
5. Keynote addresses	177
5.1. From the elucidation of the HCV life-cycle to the development of highly effective antivirals. Raffaele De Francesco, Istituto Nazionale di Genetica Molecolare "Romeo ed Enrica Invernizzi" (INGM), Milano, Italy.	177
5.2. The MSF response to the West African Ebola outbreak. Armand Sprecher, Médecins Sans Frontières, Operational Center of Brussels, Belgium.	177
5.3. Advances in HCV therapies. Michael Manns, Hanover Medical School, Hanover, Germany.	178
6. Mini-symposium: RNA viruses	179
6.1. Cruising with norovirus: progress and challenges in antiviral drug discovery. Joana Rocha-Pereira, Rega Institute for Medical Research, Leuven, Belgium.	179

E-mail address: ISAR@courtesyassoc.com<http://dx.doi.org/10.1016/j.antiviral.2015.09.015>

0166-3542/© 2015 Published by Elsevier B.V.

6.2.	Developments in antivirals to prevent rabies. Anthony Fooks, Animal and Plant Health Agency, Weybridge, UK.	180
6.3.	Dengue therapeutics: state of the art and future directions. James Whitehorn, London School of Hygiene & Tropical Medicine, London, UK and Oxford University Clinical Research Unit, Ho Chi Minh City, Viet Nam.	180
6.4.	Hepatitis E: need for new therapies. Heiner Wedemeyer, Hannover Medical School, Hannover, Germany.	180
6.5.	Hepatitis C virus entry inhibitors. Thomas Baumert, University of Strasbourg, Strasbourg, France.	181
6.6.	Development of antivirals against respiratory syncytial virus. John De Vincenzo, University of Tennessee, Memphis, TN, USA.	181
7.	Mini-symposium: antiviral chemistry.	182
7.1.	Design, synthesis and biological evaluation of human DDX3 inhibitors with multiple antiviral activities. Maurizio Botta, Università degli Studi di Siena, Siena, Italy.	182
7.2.	Triphosphate prodrugs (triPPPPro's) of biologically active nucleoside analogs. Chris Meier, University of Hamburg, Hamburg, Germany.	183
7.3.	Molecular modeling studies on the ternary complex of dengue virus polymerase. Cecilia M. Cima, Cardiff University, Cardiff, Wales, UK.	183
8.	Mini-symposium: emerging viruses (sponsored by <i>Antiviral Research</i>)	184
8.1.	Globalization of chikungunya: 10 years to invade the world. Remi Charrel, Aix-Marseille Université Marseille, Marseille France.	184
8.2.	Emerging viruses in the Balkans and the Mediterranean region. Anna Papa, Aristotle University of Thessaloniki, Thessaloniki, Greece.	184
	Crimean-Congo hemorrhagic fever virus (CCHFV)	184
	Tick-borne encephalitis virus (TBEV)	185
	West Nile virus (WNV) (outbreaks in Greece).	185
	Phleboviruses.	185
8.3.	Middle east respiratory syndrome (MERS). Bart Haagmans, Erasmus MC, Netherlands.	185
9.	Contributor presentations	185
9.1.	Discovery and characterization of MK-8876, a novel non-nucleoside inhibitor of HCV NS5B that possesses broad genotypic potency. Steve Ludmerer, Merck & Co., Kenilworth, NJ, USA.	185
9.2.	Pharmacodynamic investigation of a human rhinovirus inhibitor in a hollow fiber infection model. Qin Yu, AstraZeneca R&D, Waltham, MA, USA.	186
10.	Conclusion	186
	Acknowledgements	187
	References	187

1. Introduction

This article provides an overview of the invited lectures at the 28th International Conference on Antiviral Research (ICAR), sponsored by the International Society for Antiviral Research (ISAR), which was held in Rome, Italy, from May 11–15, 2015. It begins with reports of lectures by the recipients of ISAR's three major awards, held in memory of Gertrude (Trudy) Elion, Antonín (Tony) Holý and William (Bill) Prusoff. These are followed by summaries of the three keynote addresses and the main presentations within the three mini-symposia on “RNA Viruses”, “Antiviral Chemistry” and “Emerging Viruses”. Because this review article simply provides short accounts of oral presentations, it is not generally accompanied by references to the scientific literature. Any descriptions of favorable treatment outcomes should not be taken as a recommendation for clinical use. Generally, I have added my personal comments on the meeting within the conclusion. In a few instances, I have added my own comment within the main text, indicated either by the wording or by the use of square brackets. One of my aims has been to illustrate how the great diversity of topics can stimulate thinking in other areas of antiviral research, one of the strengths of ICAR.

2. Gertrude Elion Memorial award lecture: sofosbuvir: a search for a cure. Phillip (Phil) Furman., Furman Biotech Consulting, St Augustine, FL, USA.

Having joined Burroughs Wellcome in 1975, Phil (Fig. 1) worked with Trudy Elion for ten years. During this time, he was involved in the development of acyclovir (Zovirax®) and its prodrug, valacyclovir (Valtrex®). In 2004, Phil joined Pharmasset. The focus of this presentation was his research at Pharmasset, leading to the identification of the activity of sofosbuvir and to an understanding of its mechanism of action against hepatitis C virus (HCV).

Phil's account started with the cytidine analog, PSI-6130 (Fig. 2). This was one of the more active compounds in development at that time, better than the Roche and Idenix nucleosides but possibly a little less active than the Merck compound. An additional important



Fig. 1. Bob Buckheit congratulates Phil Furman on receiving the Elion award.

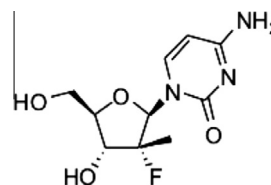


Fig. 2. Structure of PSI-6130, 2'- α -F, 2'-C-methylcytidine.

factor, PSI-6130 lacked detectable cytotoxicity ($CC_{50} > 100 \mu\text{M}$) in a panel of 5 cell lines (Clone A, Huh7, HepG2, CEM and PBM). Incidentally, the Merck compound showed no cytotoxicity in 3 cell lines but had a CC_{50} of $5 \mu\text{M}$ in CEM cells and therefore was rejected. In contrast to many reported cytotoxicity values, these are derived

Download English Version:

<https://daneshyari.com/en/article/2509778>

Download Persian Version:

<https://daneshyari.com/article/2509778>

[Daneshyari.com](https://daneshyari.com)