Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
With the conclusion of an excellent meeting in Rome, Italy, my term as President officially hits the halfway point. After two years as President Elect working with Phil Furman and an upcoming two years as Past President assisting our next President José Esteé, it seems to be a great time to reflect on everything that has been accomplished and where I hope to leave things at the conclusion of my stint as President. The President’s Message in this issue of the ISAR News typically focuses on a long list of thanks for a job well done for our gathering in Rome – and I do plan on doing that – but let me start with a state of the Society message this year.

The Society is in a fantastic position financially and the Board and Officers are considering many objectives that will enhance your membership as well as attract new investigators to our Society and Conference. Among these are our initiatives with Women in Science, which just completed a very successful first round of WIS Awards to five very qualified women. It is my hope that we can continue to invest in young investigators of both genders to provide greater levels of financial and career development support during these times of decreased travel budgets and difficult funding availability. One of the primary goals during my Presidency is to find ways to ensure that the next generation of ISAR leaders become involved in the Society. It is imperative that ISAR identify and train our future leaders to assure that the Society will be in good hands when the current leadership moves into
retirement. As part of these efforts, I congratulate all the poster awardees and hope to enhance travel grants and to establish further award programs for young investigators. Hopefully we can assist more young investigators to attend the meetings and become regular participants with opportunities for training that will enhance scientific careers. The Women in Science initiative is pioneering these types of award and mentorship programs and I hope we can adapt them to further our educational mission and attract new sponsorships to the Society. This year’s Young Investigator/New Member reception was very well attended and it was great to see all the bright and energetic faces in the crowd and to have the opportunity to meet most of the attendees. Now I want to be sure our young members can return and take on important roles within the Society. If you are one of those young investigators who enjoyed the meeting and felt that the Society’s networking and career development opportunities were useful, please get in touch with me and let me know that you’d like to get more involved.

Formal networking at the reception for new ICAR attendees.

During the past year, with the leadership of Raj Kalkeri, we have also put emphasis on diversifying the attendees of the meeting. The bulk of our meeting attendees are from North America and Europe, but every year we get a small number of attendees from various other corners of the globe. I firmly believe that these attendees add greatly to the diversity of the Society and provide a significantly different viewpoint on viruses and antivirals that are important for our understanding of the needs for future antiviral drug development. The Ambassador Program has been established to identify leaders in these corners of the globe that can reach out to the scientific community within their regions or countries and provide ISAR/ICAR information and encourage new scientists to attend our meeting. We have identified Ambassadors from Africa, South America, India, Korea, China and are now embarking on the process of identifying what we need to do in order to bring new attendees from these areas to our meeting. After seeing the large turnout of Europeans to our meeting this year in Rome, it is obvious that we still have work to do even in Europe. We need more representatives of ISAR (Ambassadors) in all regions that are willing to assist with this important effort. We will be attempting to connect with attendees from many of these areas (including North America and the various regions of Europe) to continue the process of establishing a sub-committee that will assist our current membership committee with generating interest in ISAR. Like to help? Please let me know!
Informal networking in the Rome sunshine.

Last but not least, our efforts to generate a scientifically robust and information filled ISAR News continues. Last year we published four issues of the ISAR News and Antiviral Research graciously published the newsletter and the ICAR Scientific Report in the journal to ensure a wide distribution beyond meeting attendees. Our intent was to change the ISAR News to make the publication more relevant to our mission of education and our desire to make the News a valuable piece of your membership. I believe our first year of increasing the ISAR News to 4 issues was a success and plans are already in place to roll out four issues over the next year. We are missing one key ingredient from the current platform which we will endeavor to work on this year – we’d like to increase coverage and focus on activities among our members, such as new publications in the field, what our young members are doing, and interviews with Society members on a variety of topics. Our hope is that the ISAR News will become an important component of your membership in the Society and will have content that will make you look forward to receiving it and read it from cover to cover. I, and all members of the Publication Committee, welcome your suggestions for how to enhance the content of ISAR News. Anthony Vere Hodge and Mike Bray have taken leadership of the four issues of the ISAR News and members of the Publication Committee have taken on roles of guest editing different issues – for this current issue we have Justin Julander to thank while Rhonda Cardin and Luis Schang assisted with two of last year’s info-packed issues. Joana Rocha-Pereira will be the guest editor for issue 25.3 (target date for publication is January 2016).

And now on to the all-important thanks. There are so many people to thank for all the effort that goes into the planning and execution of an ICAR meeting and I don’t have room to even begin that effort. It’s also a worrisome exercise for me since inadvertently someone gets forgotten. I hope that I did an adequate job of recognizing everyone at our banquet, including our Board members, Committee chairs, speakers, audiovisual team, and Lauren Deaton and Elizabeth Haxton from Courtesy Associates. I continue to lean on Past Presidents Phil Furman, Joe Colacino and Amy Patick for advice and input and now have the privilege of working with our President Elect José Este who will take over the reins of the Society at the conclusion of the La Jolla meeting next year. Once again, Mark Prichard, working closely with Romano Silvestri, organized an excellent program for the Rome meeting. Having spent many years as Program Chair, I fully understand the level of effort, which goes into putting our programs and speakers together. The superb efforts of Roger Ptak to raise sponsorship money for the Society continue to keep our Society finances in fine order and enable us to hold our annual meeting. Graciela Andrei worked diligently to provide so many deserving young investigators travel grants to be sure they were able to attend and contribute to our meeting. ISAR’s Women in Science program welcomed sponsorship from David and Jane Chu as they establish the Chu Family Foundation Scholarship for the WIS program – application for the first awards from that sponsorship will be announced shortly. Andrea Brancale continues to improve the utility of our website and Ilane Hernana has enhanced our social media presence on LinkedIn and Facebook. I would also like to thank Karen Buckheit for stepping into the role of our official Society photographer during this year’s meeting. One last thanks is also in order – to all those young folks who welcomed me...
warmly at the Young Investigators Reception and the President’s Reception – your energy and enthusiasm for your science is contagious and I now have a new toast that I can utilize at all of my company events! There are many more people to thank individually than I have room for here but I would be remiss if I did not emphasize that your efforts are very much appreciated.

Scientific report: Highlights of 28th ICAR, 11–15 May 2015, Rome, Italy
(Anthony Vere Hodge)

I. Introduction

This summary has abridged reports on the lectures by the recipients of the Society’s three major awards, Phil Furman, Dennis Liotta and Erica Ollmann Saphire. Please see the Scientific Report (published in Antiviral Research) for the full reports on the awardee lectures, an account of the keynote presentations and three mini-symposia (RNA viruses, Antiviral Chemistry and Emerging viruses).

As this is a research conference, any references to clinical results should not be taken as a recommendation for clinical use. I wish to thank the three awardees who have kindly provided me with copies of their presentations and for giving me valuable comments.

II. Gertrude Elion Memorial Award Lecture: Sofosbuvir: A search for a cure.

Phillip (Phil) Furman, Furman Biotech Consulting, St Augustine, FL, USA

Bob Buckheit congratulates Phil Furman on receiving the Elion award.

Having joined Burroughs Wellcome in 1975, Phil 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 understanding its mechanism of action.

Fig. 1. Structure of PSI-6130, 2′-α-F, 2′-C-Methylcytidine.

Phil’s account started with the cytidine analog, PSI-6130 (Fig. 1). This was one of the more active compounds in development at the time but an important factor was that it lacked detectable cytotoxicity (CC₅₀ > 100 μM) in a panel of 5 cell lines (CloneA, Huh7, HepG2, CEM and PBM). In contrast to many reported cytotoxicity values, these are derived from assays in which the cells are replicating. It is important to compare the effect of a compound against both replicating virus and replicating cells in order to obtain valid therapeutic ratios.

PSI-6130 is metabolised in cells to the corresponding triphosphate (PSI-6130-TP), which is a good inhibitor of the HCV polymerase NS5B (Inhibition constant, $K_i = 0.06 \mu M$). However, the triphosphate had a short half-life ($T_{1/2} = 5$ h). It was considered highly desirable to have a triphosphate analog with a sufficiently long half-life to enable once-a-day dosing.

While studying the metabolism of PSI-6130 in cells, investigators at Roche, Pharmasset’s co-development partner, noted that some of the monophosphate, PSI-6130-MP, was converted to the corresponding uridine-MP (PSI-6206-TP) in primary human hepatocytes and was further metabolised to the uridine–TP (PSI-6206-TP). Phil and his team identified the enzymes that converted PSI-6130-MP to PSI-6206-MP and the enzymes that completed the metabolism to PSI-6206-TP. This uridine–TP analog was a less active inhibitor of the HCV polymerase than the cytidine–TP analog ($K_i = 0.42 \mu M$ and $0.06 \mu M$ respectively) but had a much longer half-life ($T_{1/2} = 38$ h and 5 h respectively). The long half-life of 38 h stimulated the interest of the research team. Because the uridine analog (PSI-6206) was inactive due to lack of metabolism to PSI-6206-MP, it was decided to use the phosphoramidate prodrug strategy to deliver the PSI-6206-MP into cells. [Phosphoramidate prodrugs were first introduced by Chris McGuigan, a former President of ISAR.] Although the approach is well known, there are side
chains that can influence the properties of the prodrug. Over 140 phosphoramidate prodrugs of PSI-6206 were synthesised. These were evaluated in a cascade of tests, which I find particularly interesting.

Every successful compound has to have two basic properties, a useful efficacy and a good safety profile. The cascade started with an assay comparing the compound in an HCV replicon system vs. a ribosomal-RNA (r-RNA) cytotoxicity test. The next steps were cytotoxicity evaluations in an extensive panel of cell lines, mitochondrial toxicity and bone marrow toxicity. In my experience, it is rare to find a compound-screening strategy giving so much emphasis to the safety profile. Only then, the compounds were tested for triphosphate levels, pharmacokinetic studies in rats and dogs and in vivo rat toxicity tests. The compound, PSI-7851, was the best compound in these tests.

The activity of PSI-7851 was confirmed against various HCV genotypes (1a, 1b and 2a in replicon cells, 1a and 1b in an infectious virus assay). Recombinant NS5B polymerases from HCV genotypes 1b, 2a, 3a and 4a were all inhibited by PSI-6206-TP (PSI-7409) (IC_{50} values 1.6 µM, 2.8 µM, 0.7 µM and 2.6 M, respectively). This suggested that PSI-7851 could be active against genotypes 3 and 4 (for which replicon assays were not available). In combination with interferon or ribavirin (RBV), PSI-7851 showed additive activity. Hence, PSI-7851 was selected as a suitable candidate for development.

PSI-7851 is a mixture of two diastereomers. In anticipation of questions from the FDA, the group decided to separate the isomers. The Rp isomer (PSI-7976) was then found to be less active than the Sp isomer (PSI-7977) (EC_{50} = 1.1 µM and 0.092 µM respectively). PSI-7977 (Fig. 2) was chosen as the lead candidate and given the name sofosbuvir.

Sofosbuvir was approved by the FDA in December 2013 and by the EU in January 2014. Later in 2014, Harvoni, the first once a day fixed-dose combination therapy for chronic hepatitis C, was approved. This is a combination of sofosbuvir with ledipasvir, a HCV NS5A inhibitor. As of September 2014, it has been estimated that, in the USA, more than 100,000 patients have received sofosbuvir as part of their treatment and have been cured of their HCV infection. For patients with chronic hepatitis C, sofosbuvir has been a “game-changer”.

III. The Antonín Holy´ Memorial Award Lecture: Novel therapeutics for treating viral diseases, cancers and inflammatory disorders.

Dennis C Liotta, Emory University, Atlanta, GA, USA
compounds, several cell-based assays were established, including a 2-day attachment assay (CXCR4 HIV-1 MAGI), and a 6-day infection assay (peripheral blood mononuclear cells [PBMC] with T-tropic HIV). To initiate the signalling pathway via CXCR4 receptor, CXCL12 binds to the receptor. To characterise the activity of any compound found to be active in the above assays, a radio-ligand displacement assay (125I labelled SDF-1 in CEM cells) was devised.

A further aim became apparent – the potential to target both CXCR4 and CCR5. There is considerable sequence homology (65% similar of which 33% is identical). The crystal structures have similar binding pockets. In the literature, AMD3451 had dual activity. Starting with the Aldrich database (5 million compounds) and using virtual screening for binding to both CCR5 and CXCR4, the top 300 compounds were identified. Of these, 38 compounds were purchased and tested (MAGI) to yield 13 compounds with activity at 100 μM of which 3 were active at < 10 μM. One of these, “compound 2”, had good activity in the MAGI-CCR5 and MAGI-CXCR4 assays (IC50 = 3.8 μM and 0.8 μM, respectively). It was a surprise to find that compound 2 was also active as a non-nucleoside reverse transcriptase inhibitor (NNRTI) of HIV. The general synthetic route to similar compounds was shown. In three weeks, more than 50 compounds were synthesised. Starting with three parameters (binding to receptors CCR5 and CXCR4 and activity as a NNRTI) would make structure-activity relationships (SAR) studies challenging. It was decided to focus on the binding to the two receptors. From these, “compound 3” (Fig. 3) was selected (IC50 = 0.21 μM and 0.18 μM, respectively). As an NNRTI, it was active at 10 μM. Interestingly, in the 125I-SDF-1 displacement assay, there was no effect even at 1 mM. May it be an advantage to have a compound that is able to inhibit the binding of HIV to the receptor, but unable to displace SDF-1?

![Fig. 3. Structure of “compound 3.”](image)

Another research approach has been to synthesise compounds containing the linking part of AMD-3100. This work led to Q-122 (MSX-122) with several major advantages. It does displace another compound (TN-14003) bound to CXCR4 but does not displace 125I SDF-1. The crystal structure of TN-14003 bound to CXCR4 is known. Q-122 (MSX0122) showed activity in two mouse models of cancer.

In pre-clinical toxicity testing, no toxicity was seen with doses up to 600 mg/kg in dogs or monkeys. Two Phase Ia trials have been completed; a single ascending dose study (up to 400 mg) in healthy volunteers and 56 daily doses in late-stage solid tumour patients. No toxicity was noted in these trials. In the latter trial, a woman who had fallopian tube cancer had a complete remission of her hot flashes during the dosing period. Therefore, a Phase Ib study was conducted for women with breast cancer taking tamoxifen. Such patients can be on a treatment regimen for 10 years and most (up to 80%) are subject to abnormal hot flashes, but approved products for post-menopausal hot flashes are contra-indicated in cancer patients. In both dose groups (100 and 200 mg), Q-122 showed reductions in hot flashes. Encouragingly, some subjects had a complete response to treatment (going from >50 hot flashes/week to zero). Alongside the response in the primary endpoint, there were positive improvements in various secondary end-points. The drug showed a good safety profile in this study. Interestingly, the mechanism for the reduction of hot flashes is unknown.

It seems surprising that an antiviral research program can be the source of the first potential therapy to treat hot flashes in the large number of women taking tamoxifen. Who could have predicted that this would be an outcome?

**IV. 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

Erica started her lecture with a photograph of William (Bill) Prusoff, noting that he has been called the “Father of antiviral chemotherapy”. She felt honoured to give a lecture in his name.
**Introduction**

Erica described how she was intrigued by viruses – they encode so few proteins yet get so much function from them. For example, filoviruses like Ebola encode 8 proteins and arenaviruses such as Lassa encode just 4 proteins. Yet these few proteins perform about 60 functions within the life cycle of the virus. How is this done? Erica suggests that one answer is that the proteins, which these viruses encode, are able to remodel, repurpose and rearrange themselves to extend their functional complexity.

**Remodel**

Erica showed us the structures of the GP of Ebola and Marburg viruses, first just the protein and then the fully glycosylated form as it exists on the viral surface. The extensive coating of sugar residues hides part of the protein from immune surveillance. This complete, fully glycosylated form does not bind to the receptor. The sugar-linked residues are cleaved off to leave a “naked” protein and the receptor binding site becomes exposed.

Human antibody (KZ52) was obtained from an Ebola survivor (1995). This antibody works in the test tube, in mice and in guinea pigs, but does not protect monkeys. Up to 2007, KZ52 was the best antibody against Ebola; was there still a way forward? During 2011–2012, several groups showed that combinations of antibodies are protective in monkeys. For example MB-003 from United States Army Medical Research Institute of Infectious Diseases (USAMRIID) is a cocktail of three antibodies, two binding to sites on the mucin domain, the third to the GP “glycan cap” which is cleaved off in the endosome. Although this cocktail does not work well in vitro, it does protect monkeys. There are many unanswered questions; how many antibodies? Which are best? What assay? Can there be synergy? To resolve such a complex set of unknowns, a large sample set is required.

The Viral Hemorrhagic Fever Immunotherapeutic Consortium (VHFIC) is a global collaboration to evaluate all available monoclonal antibodies (mAbs) to Ebola. Erica credited John Dye as the major player in bringing all the interested parties together to form the VHFIC. Initially, the “tortoise” path was set up. Samples of all the antibodies were sent to Erica’s laboratory for coding and then sent to all the collaborators to test in their various assays and to determine the antibody binding sites.

In parallel with the “tortoise” track, a “hare” track was initiated using 6 antibodies from two current combinations. As it turned out, this approach was fortuitous because the case zero of the current Ebola outbreak was in December 2013 and ZMapp, which emerged from the “hare” track, was discovered about February 2014. In August 2014, ZMapp was being used on a compassionate basis to treat health care workers who had become infected and were repatriated to the USA. ZMapp consists of three antibodies, 13C6 (binds to the top of the GP and recruits the immune system), 2G4 (binds to the base of GP) and 4G7 (also binds to base of GP). As the latter two antibodies are similar to KZ52, they enable the combination to be active in the neutralization test but also they contribute to the protection which is given by the 13C6 antibody.

After the first 7 months of the “tortoise” approach (and 81 mAbs), much has been learnt. There are mAbs which bind to various parts of the Ebola GP (number of mAbs): GP1 core (15), fusion loop (2), base of GP2 (8), glycan cap (17), mucin (16) and 23 mAbs are still undefined. USAMRIID carried out the protection test in mice, ranking mAbs on percentage survival of 10 infected mice. Those mAbs binding to the base of GP2 gave the better protection (50–100%). These are similar to KZ52 and to 2 of 3 mAbs in ZMapp. There were other mAbs, giving about 50% protection in mice, which could be considered for inclusion in a combination. Those mAbs, which bound to the base of GP, gave both protection and neutralization but there was only a rough correlation. Those mAbs, which bound to the GP1 top, GP1 core, glycan cap or mucin, gave protection but no strong neutralization. The explanation is that, when the GP is remodelled, the mucin and glycan cap are removed and therefore the core protein is not neutralized.

**Repurpose**

As an example of an arenavirus nucleoprotein (NP), Erica chose Lassa virus. Erica compared the NP to a multifunctional penknife – having roles in nucleocapsid assembly, immunosuppression, virion incorporation and regulation of the polymerase. The N-terminal and C-terminal domains open up to reveal a new site predicted to be the RNA-binding site. But the RNA gate, on the newly revealed surface of the N-terminal domain, has to open before ssRNA can bind. In addition, the C-terminal domain has a role in immunosuppression. It is folded so that it becomes an exonuclease able to digest dsRNA. How these functions are balanced is still unknown.

**Rearrange**

In Ebola and Marburg viruses, the VP40 protein alone can self-assemble to form virus-like particles. It also controls transcription. In 2000, the structure of the monomer was determined. In 2003, an octameric ring structure was discovered. In 2013, VP40 was shown to exist as a butterfly-shaped dimer, which was later found to be important in cellular trafficking. The dimers can further assemble and rearrange to form zigzag-shaped hexamers which lead to virus assembly. However, although octameric rings are not essential for virus assembly, mutants which prevent octameric ring formation are nonetheless lethal for
virus replication. The ring structure controls transcription. In conclusion, the multifunctional nature of VP40 can be explained by the formation of octameric rings to control transcription, dimers for trafficking about the cell and hexamers for virion assembly.

**Our understanding of molecular biology is evolving**

The traditional view is that a gene encodes a protein that folds so that the protein is able to perform one specific function. Working with Ebola virus has taught us that nature uses one protein folded in different ways to perform different functions. One gene encodes one protein (VP40) that folds and assembles into three distinct forms, each able to perform its own specific function. Erica likened VP40 to a “Transformer”, a child’s toy, which can be a robot or refolded to become a truck – one form can make RNA, while the other transports the virion to the cell surface.

Looking to the future, one can anticipate that the conformational alterations that underlie multifunctionality of other proteins from a diverse range of viruses will be identified. Will some patterns emerge? Will we be able to give computer programs new rules? Looking beyond viruses, what may we find? May there be some human proteins, which can fold into multiple forms? May that have implications in disease and/or drug therapy?

**V. Conclusion**

Our three awardees have each had remarkable careers. The Elion Award was presented to Phil Furman who, in his early days, worked on acyclovir with Trudy Elion. To my mind, acyclovir is the most important “game-changing” antiviral. It may not have the biggest sales but it is the first antiviral drug to combine good clinical efficacy with a truly remarkable safety profile. After some three decades, it still stands as a benchmark for safety. Today, acyclovir, and its prodrug valacyclovir, are used worldwide to treat herpesvirus infections. In the generally healthy population, the proportion of resistant virus remains below 1%. Prior to acyclovir, I do not recall anyone predicting that an antiviral could be used clinically for three decades with less clinical problems than the best antibiotics. However, Phil hardly mentioned acyclovir but focused on the research that led to sofosbuvir, another “game-changer”, this time for patients with HCV infections.

The Holý award was presented to Dennis Liotta. Like Phil, Dennis did not describe his work that led to the invention of important antivirals for HIV therapy (it has been estimated that more than 90% of HIV-positive patients in the USA have taken a drug invented or developed by Dennis) but he chose to describe his recent research. It is a remarkable journey in which the chemistry led him into new, unexpected territory.

The Prusoff award is for a young investigator who has already made an impact in the antiviral field and is set to continue to do so. Erica Ollmann Saphire is a highly qualified recipient. In her award lecture, she described how viral proteins are able to rearrange into different forms and so fulfill different functions. I have been lucky to listen to many fine lectures at ICAR meetings over the years but Erica’s lecture sailed straight into my top-ten.

I hope that my summaries of these three lectures will reflect some of the enthusiasm that the awardees had for their subjects and that, even if the topics are not in one’s own area of research, there is much of interest to be appreciated. Further information on other presentations at this ICAR will be found in the full Scientific Report to be published in *Antiviral Research*.

**Poster Award Recipients at the 2015 ICAR (Katherine Saley-Radtk)**

ICAR’s 2015 poster competition was, as usual, highly competitive and one of the highlights of the Banquet. Professor Saley-Radtk and her team of outstanding judges had a tough time this year due to the large numbers submitted – in total, 80 posters were competing – 40 in the graduate student category, and 20 each in the postdoc and young investigator categories. There were so many posters in fact, that extra judges had to be recruited on site! It is also notable that the young investigator category numbers were WAY up from previous years, so word must be spreading that the prize money is worth the effort. In the graduate student category, there were six winners of $500 each and in the postdoc category, there was a 1st prize of $750, a 2nd place prize of $500, and a tie for 3rd place, with two winners receiving $250 each. In the young investigator category we had a 1st place winner of $750 and a 2nd place winner who received $500.

The winners were:

Graduate student category (in alphabetical order):

- **Poster #167**: Namn Cheung – Identification of A Broad-Spectrum Inhibitor of Common RNA Respiratory Viruses by High-Throughout Screening
- **Poster #120**: Ilane Hernandez-Morales – Repositioning A Hepatitis C Virus Antiviral Small Molecule to Treat Dengue Infection
- **Poster #182**: Obaiaara Ihenacho – Effect of Nucleic Acid Sequence on DNA Polymerization And NNRTI Inhibitory Mechanisms of HIV-1 Reverse Transcriptase
- **Poster #213**: Michael Norris – Targeting intracellular potassium for the control of respiratory syncytial virus
- Poster #86: Hannah Peters – Design, Synthesis And Anti-Coronavirus Activity of A Series of Acyclic Fleximers
- Poster #107: Matthias Winkler – Efficient Synthesis of Ribavirin-Phosphoramidites For Biochemical Applications.

Postdoc category:
- First place – Poster #134: Roger Badia – Evaluation of the Histone deacetylase inhibitor ST7612A1 as an HIV-1 Latency Reactivation Agent;
- Second place – Poster #219: St. Patrick Reid – The Lipid Kinase Sphingosine Kinase 2 Is An Essential Host Factor Recruited By Chikungunya Virus During Infection
- Third place (tie) – Poster #138: Evelien Vanderlinden – T-705 And Ribvirin Induce Lethal Mutagenesis Of Influenza Virus, and
- Poster #136: Leen Delang – A Novel Class Of Chikungunya Virus Inhibitors Targets The Enzymatic Activity Of The Viral Capping Enzyme NSP1

Young Investigator category:
- First place – Poster #21: Dimitrios Topalis – Resistance To Nucleotide Analogues In HPV-Positive And HPV-Negative Cells Emerges Through A Multifactorial Process
- Second place – Poster #99: Cristina Tintori – Targeting Protein-Protein Interactions As A Successful Therapeutic Strategy Against Viral Infectious Diseases.

In addition to the poster awards, the judges selected five posters for shotgun talks. The winners were:
- Poster #200 – Beatrice Mercerelli – Early Inhibition of Human Cytomegalovirus Replication as a Therapeutic Option: Design, Identification, and Characterization of a New Anti-HCMV Candidate Drug with a Novel Mechanism of Action.
- Poster #212 – Tatiane Cristina Nogueira – Regulation of HPV16/18 E6, P52 and ATM in Parental and CDV-Resistant Cells after Cidofovir Treatment
- Poster #87 – Katharina Pfaff – Synthesis and in vitro Assay of Deoxyhypusine Synthase Inhibitors as Potential Anti-HIV Agents
• Poster #110 – Grigoris Zoidis - Novel Flutimide Analogues Targeting the Influenza Virus PA Endonuclease
• Poster #219 – St. Patrick Reid – The Lipid Kinase Sphingosine Kinase 2 Is An Essential Host Factor Recruited By Chikungunya Virus During Infection

This year’s judges included poster committee Chair Kathie Seley-Radtke and poster committee members Graciella Andrei, Andrea Brancale, José Este, Justin Julander, Brian Gentry, Gilles Gosselin, Chris Meier, Jennifer Moffat, Luis Schang and Eric Stavale. In addition, Kathie twisted the arms of a few new judges to help out since there were so many posters this year – so thanks also to Jinhong Chang, Sandra Liekens, Roger Ptak, and Enzo Tramontano!

The poster committee would also like to thank Graciella Andrei for constructing the new scoring sheet as well as Andrea Brancale for the new online poster submission system, which allowed the judges to look at the posters ahead of time and helped Kathie streamline the assignments. One major change to the poster judging system next year will see all posters being up both days, with an odd/even system for the presenters. For the first hour of the poster session, the even poster numbers will stand by their posters, while during the second hour, the odd poster numbers will stand by their posters. The order will reverse the second day.

That’s all for this year’s poster committee report - good work everyone – and we hope to see you all again next year in La Jolla!

ISAR Women in Science (Amy Patick)

Some good discussions at the 3rd annual WIS Roundtable.

At the recent 28th ICAR, ISAR-WIS hosted the 3rd Annual Women in Science Roundtable, which was a great success with all 80 seats reserved in advance. This session was open to all ICAR attendees, both women and men, and featured prominent women scientists who talked about the challenges they faced and the lessons they learned while navigating the twists and turns of their personal career progression. The featured speakers included: Gabriella Andrei, Jennifer Moffat, Katherine Seley-Radtke, and Kara Carter.

In addition, the WIS committee announced the awardees for the first annual ISAR-WIS Career Development Awards. These awards support the professional development of women with potential for significant contribution in the field of Antiviral Research by providing funds to attend a conference,
visit another laboratory, take a course, or acquire specialized training. Each award consisted of a $1500 stipend, a 2-year ISAR membership and a commemorative certificate. The 2015 awardees were Carol-Ann Eberle, Ph.D., Cecilia Martin-Gandul, Anastasia Hyrina, Ph.D., Lydia Meador, and Kristina Prachanronarong. The impact of these awards is best summarized by one awardee: “When I become a mentor to future students, I hope that I am able to inspire and encourage women in science just as you have inspired me”. ISAR-WIS is very pleased to announce that the Career Development Awards will continue in 2016 with a generous contribution by David and Jane Chu. The new career development awards will be formally known as the “Chu Family Foundation Scholarship for Women Scientists”. Please look on the ISAR website for more details!

Business meeting (Graciela Andrei and Brian Gowen)

The ISAR held its annual business meeting during the 28th ICAR on Wednesday, May 14. This year, the meeting consisted of reports by the Treasurer and the Secretary of the society.

Brian Gowen (Treasurer) presented a summary of ISAR finances. The net assets report (Table 1) showed total assets exceeded $800,000 just prior to the meeting, and the financial assets data accumulated of the past 6 years reflects the stability in terms of the recent overall health and financial standing of the society (see “Pre-ICAR Net Assets”) Also presented was the 2015 financial statement showing the year-to-date income and expenditures (Table 2) and the final outcome of the revenue and costs associated with the 27th ICAR

Table 1. ISAR net assets statement.

| Assets                      |                  |
|-----------------------------|------------------|
| Bank Accounts               | $661,478.12      |
| CDs                         | $106,335.36      |
| Investments                 | $230,029.30      |
| Euro Account                | ($6,657.76)      |
| **Total**                   | **$804,729.08**  |

Table 2. ISAR 2015 year-to-date financial standing.

| 2015 Income                 |                  |
|------------------------------|------------------|
| Membership Dues              | $4,665           |
| Corporate Support            | $116,600         |
| ICAR Registrations           | $130,554         |
| Interest                     | $436             |
| **Total Income**             | **$251,655**     |

| 2015 Expenditures            |                  |
|------------------------------|------------------|
| Administrative               | $4,102           |
| ICAR                         | $142,129         |
| **Total Expenses**           | **$146,231**     |

 Balance                  | $105,424
held in Raleigh, North Carolina in 2014 (see ISAR News Vol. 24.3). Thanks in large part to the fundraising efforts of Roger Ptak and good attendance numbers, our revenue in support of the meeting nearly matched the total expenses.

Finally, the estimated budget (Table 3, blue column) for the 28th ICAR in Rome, Italy, was presented along with the revenue and expenses that had been accounted for just prior to the meeting (Table 3, black column). We are hopeful that our conservative estimation of expenses and solid attendance will have us close to breaking even once all the revenue is received and the bills are paid.

Graciela Andrei (Secretary) provided a report on the 2015 ISAR Membership and on attendance at the 28th ICAR in Rome (see “2015 ISAR membership”). Thirty-seven countries are represented in the Society, with a total of 401 members up to May 1, 2015 versus 216 members for 2014. A total of 293 attendees from 41 different countries were registered for the 28th ICAR through May 1, 2015, compared to 255 total registrations from 23 countries for the previous ICAR meeting in Raleigh.

This year, the Society awarded a total of 52 Travel Grants (29 for PhD students, 13 for postdoctoral fellows and 13 for investigators) to help these members defray the costs of attending the conference. Depending on the distance to be travelled, awardees received a grant in the range of $120 to $1600. The total amount awarded was $34,045. A worldwide distribution [Africa (2), North America (8), South America (3), Asia (14) and Europe (25)] of the Travel Grants was

| Table 3. Estimated budget for 28th ICAR, Rome, Italy, 2015. |
|-----------------|-----------------|
| **Revenue**     | **Estimated**   | **Actual (May 5)** |
| Registration    | $132,150        | $130,554           |
| NIH Grant       | $0              | $0                 |
| Sponsorship/Exhibitors | $182,500    | $127,000           |
| **Total Revenue** | **$314,650**   | **$257,554**       |

| **Expenses**                           | **Estimated**  | **Actual (May 5)**  |
|----------------------------------------|---------------|---------------------|
| Advertising                            | $3,100        | $0                  |
| Venue, Events, Food and Beverages      | $141,534      | $106,796            |
| Audio Visual Equipment and Services    | $45,500       | $13,563             |
| Courtesy Associates                    | $74,680       | $22,172             |
| Sponsored Speakers (Travel, Lodging, Expenses) | $49,660    | $7,609              |
| Awards (Elion, Prusoff, Holy, Poster, Travel) | $64,500    | $0                  |
| Posterboards                           | $6,959        | $0                  |
| Conference Bags                        | $1,375        | $1,281              |
| Credit Card Fees                       | $10,000       | $4,000              |
| Cancellation Insurance                 | $1,300        | $1,642              |
| Abstract Submission Site               | $2,000        | $0                  |
| Registration and Other Supplies/Fees   | $1,975        | $155                |
| **Total Expenses**                     | **$402,583**  | **$156,948**        |

| Table 4. Evolution of the ICAR Travel Awards. |
|-----------------------------------------------|
| **2012** (Sapporo) | **2013** (San Francisco) | **2014** (Raleigh) | **2015** (Rome) |
| Number of awards  | 16                     | 44                  | 30               | 52               |
| Total amount awarded | $32,940            | $44,815             | $34,910           | $34,045          |

![Net Assets](chart.png)
reported. As shown in Table 4, increased travel funds have been made available by the Society during the past few years to increase the attendance of young investigators at the meeting. Applicants are encouraged to apply and to read the instructions for travel grant applications on the website.

Ebola Outbreak: May-June 2015
(Anthony Vere Hodge)

As a postscript to my previous summary (ISAR News 24.4), I was pleased to report that Liberia had been declared free of Ebola. With the number of new cases/week reducing to 9 each in Guinea and Sierra Leone (week ending 3rd May), I was hoping that this would have been my last Ebola report. This report covers the period from 27th April to 14th June. Much of the data and the quotations are from the WHO situation reports (www.who.int/en) but the comments are my personal opinions.

In Table 5, I have included the number of new cases/week and also the number of cases who had not been known contacts. To end this Ebola outbreak, the aim has been to bring the patients to an Ebola center within two days of symptom onset, before they become highly infectious. All known contacts are quarantined for 21 days and monitored closely. This seems to be the most effective way to successfully end lines of transmission.

Both previously and during this period, Guinea has organised huge educational campaigns but achieving full community cooperation is proving challenging. The number of new cases/week shows little sign of any downward trend. Each week, there are cases arising from unknown chains of transmission. I wonder if the active use of favipiravir and vaccine would help turn the tide but I can find no published information about this. I would value the WHO situation reports including a section on the use these antiviral approaches.

During May, Sierra Leone seemed so close to success. WHO report:

“In the week ending 10th May, Sierra Leone reported just two new cases, a mother and child, both known contacts and under quarantine. As at 12 May, Sierra Leone had reported zero cases for 8 consecutive days. ‘The Sierra Leonean district of Kambia, which has been the country’s main focus of transmission for over a month, reported zero cases in the week to 10 May.’”

But the following week, there were 8 new cases, and 4 from unknown contacts.

“Of these, three have a proven epidemiological link to a previous case. The remaining case, reported from Freetown, was identified after post-mortem testing of a community death. The source of infection is unknown, but the case was found in the Moa Wharf area.”

In week ending 24th May, Sierra Leone reported just 3 cases, two being known contacts. The WHO report highlights a difficulty:
expected. At the ICAR, Armand Sprecher of Médecins Sans Frontières (MSF) gave a Keynote presentation. In response to a question, he told me that, in Guinea, health workers came to be exposed to EVD. A total of 13 contacts are currently being monitored in Italy. On 14 May, the case is a Sierra Leone national who was working at an Ebola treatment centre near Freetown at the time of symptom onset. This is the same facility at which the recent Italian health worker case was stationed prior to their return to Italy. Investigations are ongoing into how both health workers came to be exposed to EVD. A total of 13 contacts are currently being monitored in Italy, none of whom are considered to have had a high-risk exposure. There have been a total of 869 confirmed health worker infections reported from Guinea, Liberia, and Sierra Leone since the start of the outbreak, with 507 reported deaths.”

The Italian health worker was taken to Rome for treatment and made a full recovery. This happened while we were in Rome for the ICAR, making our contact with Ebola a lot closer than any of us expected. At the ICAR, Armand Sprecher of Médecins Sans Frontières (MSF) gave a Keynote presentation. In response to a question, he told me that, in Guinea, MSF is vaccinating frontline health workers with the Merck vaccine (currently around 800 vaccinated) and that WHO has started doing ring vaccination, also with the Merck vaccine, in areas with reported cases. To my mind, the use of both the vaccine and favipiravir gives hope to Guinea and Sierra Leone that ending this Ebola outbreak is an achievable aim.

Postscript added 13th July.

New cases in Guinea and Sierra Leone have continued, there being about 20 to 30 cases/week. However, the WHO situation report (dated 8th July) notes:

“Although this [30] is the highest weekly total since mid-May, improvements to case investigation and contact tracing, together with enhanced incentives to encourage case reporting and compliance with quarantine measures have led to a better understanding of chains of transmission than was the case a month ago. This, in turn, has resulted in a decreasing proportion of cases arising from as-yet unknown sources of infection (5 of 30 cases in the week to 5 July). However, significant challenges remain.”

“Liberia was declared free of Ebola transmission on 9 May 2015, after reporting no new cases for 42 consecutive days. The country subsequently entered a 3-month period of heightened surveillance, during which approximately 30 blood samples and oral swabs are collected each day from potential cases and tested for EVD. On 29 June, this routine surveillance detected a confirmed case of EVD in Margibi County, Liberia.”

Liberia update: WHO Ebola Situation assessment (dated 10th July):

“Currently, 5 people have been confirmed with Ebola virus disease by laboratory testing. As part of the investigation into the source of this new cluster of infections, samples taken from the first person found to have Ebola were sent to the Liberian National Reference Laboratory for genetic sequencing. Tests on these samples have shown that the virus is genetically similar to viruses that infected many people in Margibi County more than 6 months ago, in late 2014.”

Invitation to 29th ICAR in La Jolla, CA, USA (Karl Hostetler and Doug Richman)

On behalf of ISAR, we welcome you to the 29th ICAR meeting to be held in La Jolla, California (near San Diego), on April 17–21, 2016. Here are a few fun facts about our area for history buffs:

- Historic home of the Kumeyaay people (they are still here and doing well, thank you), San Diego was first visited by Europeans in 1542 when Juan Cabrillo claimed the entire area for Spain, forming the basis for the settlement of Alta California 200 years later.
- The Mission San Diego de Alcala was founded in 1769 by Father Junipero Serra (now a
and was the first European settlement in California.

- In 1821, California became part of newly independent Mexico and in 1850 it was briefly the California Republic after the Mexican-American War.
- California joined the United States on September 9, 1850 when the state was admitted to the Union.
- San Diego is the eighth-largest city in the US and second largest in California.
- The presence of the University of California, San Diego (UCSD), the UCSD Medical Centers, the Scripps Research Institute, the Sanford-Burnham Institute, the Salk Institute and numerous biotech companies has made the area a center of biotechnology.

San Diego is known for its temperate climate. In April the average high temperatures range from 62 to 77°F (16.5 to 25°C), rainfall is not frequent and the ocean water temperature averages 60°F (16°C). This is too cold for me but OK for Canadian, Russian and Scandinavian visitors. When you are not attending the sessions, there are a number of interesting things to do including visits to the San Diego Zoo and Wild Animal Park, Balboa Park (home of the Museum of Natural History, Museum of Art and free Sunday concerts at the Organ Pavilion) or the USS Midway, a historic aircraft carrier. Attend plays in the evenings at the La Jolla Playhouse or the Old Globe Theater. The San Diego Padres major league baseball team may have games scheduled in the evenings during your stay. With over 90 breweries, San Diego is the craft beer capital of the U.S. and I’m sure the Hotel Hilton La Jolla/Torrey Pines will have samples in the bar (although not free samples).

Travel to San Diego is not difficult with non-stop flights from London, Tokyo, Mexico, Canada and East and West Coast gateways, including New York, Seattle, Chicago, Atlanta, Los Angeles, San Francisco etc. Looking forward to seeing you next year!