ISAR News
Newsletter of the International Society for Antiviral Research

Editors Anthony Vere Hodge and Luis M Schang Guest editor Joana Rocha-Pereira

Report on the 31st ICAR, Porto, Portugal

IN THIS ISSUE

ISAR President's message
(Johan Neyts)

It is my great pleasure and honor to address you as the new president of ISAR. ISAR/ICAR has always been close to my heart. I attended my first ICAR (here in Brussels, Belgium) as a young Ph.D. student in 1990. This was at the time when the HIV pandemic was growing to dramatic proportions and when many academic labs and companies were involved in the race against time to develop potent and safe drugs to treat infections with this dreadful virus. In subsequent years and decades, the hard work and dedication of so many resulted in the drugs which are available today. Since then, AIDS-drugs have saved millions of lives. An enormous achievement! Yet, another, more recent revolution - that I was also lucky enough to witness - was the development of drugs that enable us to cure chronic infections with the HCV. Also these drugs are saving the lives of so many. There are several other very important evolutions which I have witnessed in the past 30 years during which I have been active in this field, such as on the development of treatments for infections with HBV, herpesviruses and influenza.

ICAR and ISAR have always been at the forefront in the field of antivirals. The society played a prominent role in bringing scientist and clinicians

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together and to help disseminate data. The work is not done. The world badly needs a cure for HIV and it would be also of great importance to have therapies that can cure chronic HBV infections. There are still many other viral infections for which we do not have (potent) drugs at hand, despite the fact that they have a huge impact on human health. Just think for example of RSV, rhinoviruses (that cause exacerbations of asthma and COPD), adeno-, polyoma- and noroviruses. There is also an urgent need for better influenza drugs. Likewise, there are no (good) drugs to treat infections with neglected and emerging viruses (such as for example Ebola, Lassa, dengue and Chikungunya). The world is not prepared for the next epidemic/pandemic. The successes of the past, such as on HIV and HCV, have shown how efficient highly potent antivirals can be. Within ISAR, we all share the same mission to aid in the battle against viruses.

ISAR/ICAR is (and has always been) unique in bringing together medicinal chemists, virologists, pharmacologists and clinicians. This results in a unique and important blend of expertise leading to an uncountable number of important collaborations and interactions. Collaborating is nice and important, but it is even nicer if this can happen in an atmosphere of friendship. I am very grateful to so many ISAR-friends and colleagues for the pleasant interactions and the friendship. ISAR is a warm society of dedicated people.

We live in a globalized world, which has changed a lot when compared to 30 years ago. It will hence be important to make sure that ISAR/ICAR also recruits in those parts of the world that have in the past been somewhat under-represented in our society. We were convinced that a more concerted action in communication and outreach of ISAR is needed. I am therefore pleased to announce that we are, to that end, implementing a Communication and Outreach Committee that will be chaired by Kara Carter. The aim is to have the following workgroups to act in concert (i) the website & social media workgroup (co-chairs Andrea Brancale and Angela Stoyanovitch), (ii) the Webinars workgroup (chair Raj Kalkeri); the (iii) the publication workgroup (co-chairs Anthony Vere-Hodge and Luis Schang) and (iv) the Ambassadors program (co-chairs Subhash Vasudevan, Raj Kalkeri, Luis Schang & Pei-Yong Shi). I am really glad that we have a team of dedicated ISAR ambassadors that will make sure that ISAR/ICAR generates sufficient exposure all over the globe. Also the very successful Webinars have and will (further) contribute to such exposure. Obviously, social media play nowadays a very important role in outreach; hence we plan to make more intensive use of this technology. Angela Stoyanovitch kindly accepted to take the lead on this. I am also pleased to announce that ISAR will soon have a brand new attractive and easy to navigate website. A big thank to Andrea Brancale for all his efforts in this.

The 31st ICAR in the beautiful city of Porto is already a couple of months behind us. I believe that we can proudly conclude that this ICAR, also, was a great success. I want to wholeheartedly thank all of you, who contributed to that success, for your dedication and efforts. I want to express a special word of appreciation to José Esté, who has worked tirelessly during his term as president to make the society thrive and the meeting grow. A big thank as well to Rhonda Cardin and Roger Ptak, who have come to the end of their terms on the board, as well as to another tirelessly working former president, namely Bob Buckheit, who has now come to the end of his term as Past-President. On this occasion, I would also like to congratulate the newly elected board members, Pei Yong Shi and Joana Rocha Pereira. We are very much looking forward to working with you. Thank you Joana for having been "kind-of-a-local-organizer" for ICAR-Porto. A big congratulation to Kara Carter for being elected as the incoming President; I am very much looking forward to working with you Kara.

Thank you also Rhonda for all your effort in running the WIS-committee and Roger for making sure that we receive sufficient sponsoring to keep the Society financially healthy. Also, the hard work of the Board members, Jennifer Moffat, Mike Bray and Kathie Seley-Radtke, is very much appreciated. A very special word of thanks to our Treasurer, Brian Gowen, for his meticulous follow-up of the financials. Much appreciation as well for all the efforts of Mark Prichard and Justin Julander to put the program together, to organize the abstract reviewing, and for so much more. A very special word of thanks to Graciela Andrei for all your hard work as Secretary during the past 6 years, as well as for your tremendous effort on the travel grants. As mentioned above, Raj Kalkeri did an outstanding job in organizing the webinars and Andrea Brancale on updating the (at that time still old) website with the information for the Porto meeting. Thank you as well Anthony Vere-Hodge, for your continued effort to make sure that we have each year several issues of ISAR news. Jennifer Moffat and Brian Gentry did a much appreciated job in running the poster award committee and Kathie the Chu-award Committee. Maaike Everts organized an excellent career development session in Porto and Brian Gentry is doing a wonderful job on archiving the documents and pictures of ISAR. Thanks as well to Rich Whitley for running the Scientific Excellence Award Committee. Finally, it has been truly

wonderful to work with Regina and Kelly of Caliber Meetings.

Besides the people named above, many others contributed a lot of their time and energy to the Society and the Conference. I would like to personally thank all of them, but I am afraid that I may forget some. Finally, if you do have ideas and suggestions, to improve the Society, the conference or our international visibility, please let me or the other members of the board know. Thank you for your continued support,

Very best regards, Johan Neyts

I. HIGHLIGHTS OF THE 31ST ICAR, PORTO, PORTUGAL
(R. Anthony Vere Hodge)

INTRODUCTION

The 31st ICAR was held in Porto, Portugal from June 11 to 15, 2018, the meeting being at the Alfândega Conference Center. This was the first ICAR to be hosted by Portugal. We thank Joana Rocha-Pereira for being our local host.

The 31st ICAR was held at the Alfândega Conference Center.

On behalf of ISAR, twelve volunteer rapporteurs (Mike Bray, Graciela Andrei, Ester Ballana, Kara Carter, David Durantel, Brian Gentry, Zlatko Janeba, Jennifer Moffat, Clasien J. Oomen, Bart Tarbet, Eva Riveira-Muñoz and José A. Esté) have prepared an official report entitled **Meeting report of the 31st International Conference on Antiviral Research** (Bray et al. Antiviral Res. 2018 Aug 4;158:88-102.doi: 10.1016/j.antiviral.2018.08.002).

The volunteers have provided their views on the highlights of the 31st ICAR, aiming to convey the speakers' goals, results and conclusions. It is hoped that this report illustrates the success of the 31st ICAR in promoting new discoveries in antiviral drug research and development.

Meeting report contents.

The 32nd ICAR will be held in Baltimore, Maryland, USA, May 12-15, 2019. Please see below the next ICAR meeting flyer.

32nd ICAR, May 12-15 , Baltimore.

WOMEN IN SCIENCE
(Rhonda Cardin)

The 31st ICAR meeting in Porto, Portugal, was another great year for the Women In Science (WIS) Roundtable and our second presentation of the ISAR WIS Speaker Award at ICAR! This year marks the 6th year of the WIS Roundtable event, which first occurred in 2013, the same year that the WIS Committee was formed. The moderator for the WIS Roundtable in Porto was Kara Carter, our new ISAR President-Elect and WIS Committee member. We congratulate Kara on her election and highlight that Kara will be the second WIS Committee member to lead the society, with the first being Amy Patick, former President of ISAR and first Chair of the WIS Committee. Other WIS Committee members that have served in ISAR leadership roles include Graciela Andrei, Kathie Seley-Radtke, Jennifer Moffat, Heather Greenstone, Maaike Everts, and

Rhonda Cardin. Their roles include ISAR Secretary (Graciela), ISAR Committee Chairs (Kathie, Jennifer, Maaike, Rhonda), and ISAR Board members (Kathie, Jennifer, Heather, Rhonda). We also want to warmly congratulate and thank our Porto native and fellow WIS Committee member, Joana Rocha-Pereira, for introducing us all to such a wonderful and beautiful city!

On behalf of the WIS Committee, and as Chair, I would like to express our many thanks for the strong support of the WIS Roundtable by ISAR, ISAR Board members, and especially, to our ISAR Presidents that saw the value and impact for the society and continue to support this program (Amy Patick, Bob Buckheit, José Esté, and our new President, Johan Neyts)! All ISAR members, both male and female, should be very proud of the ISAR WIS Committee's progress towards their goal to provide a forum that focuses on the challenges and opportunities encountered by women scientists and the need for networking and mentoring. Evidence that we are doing something right is what we saw at the ICAR meeting in Porto: impressive numbers of our young women scientists as speakers and poster award recipients…Thanks, ISAR, for your support!

2018 WIS SPEAKER AWARD
(Rhonda Cardin)

Rhonda Cardin, the WIS speaker, A. Desiree LaBeaud, and José Esté

This year, ISAR was pleased to present the 2nd WIS Speaker Award of Excellence to Angelle Desiree LaBeaud, Stanford University School of Medicine, for her research in emerging infectious diseases, including Dengue, Zika, and West Nile virus. She is recognized as a woman scientist who has made outstanding contributions to the field of antiviral research and has shown leadership in mentoring young women scientists.

Desiree LaBeaud's presentation of her studies in Kenya were impressive and kept the audience captivated on her efforts to monitor virus population dynamics and to educate mothers and children at the 'grassroots level' in order to intervene in virus infection and to decrease standing water mosquito habitats. Needless to say, her research was inspiring to a number of attendees!

WIS ROUNDTABLE
(Kara Carter)

The 6th Women in Science Roundtable was the first event on day one of ICAR and was held on Monday, June 11, from 12:00 – 1:45 PM. The WIS Roundtable participants included both women and men and centered on discussions concerning the challenges and opportunities encountered by women scientists while navigating the twists and turns of career progression in today's research environment.

A goal of the Roundtable is to provide an environment for networking with fellow women scientists in industry, government, and academia who conduct all aspects of antiviral research. This Roundtable provided an opportunity to participate in a panel discussion with our 2018 WIS Speaker Award recipient, Angelle Desiree LaBeaud, Stanford University School of Medicine; Joana Rocha-Pereira, Rega Institute KU Leuven; and

Kara Carter and the 3 panellists during the WIS roundtable

Heather Greenstone, NIAID, NIH, as well as other antiviral research scientists in the audience. The panellists answered a variety of questions from the audience and provided insights into their own career

experiences. Hot topics included advocating for yourself, how and when to seek promotion or opportunities, and how to deal with challenging situations in the work place. It was extremely interesting to hear their very diverse answers and funny stories in response to the questions

WIS Mentoring Program
(Rhonda Cardin)

The Mentoring Program was launched at the 2014 ICAR in Raleigh, NC, when Roundtable participants were asked if they would like to be mentored or serve as mentors. From the start, the Mentoring Program has had a positive impact, bringing together women scientists from all aspects of antiviral research and at different stages of career development. Mentors have provided career advice and scientific expertise in academia, government, and the pharmaceutical industry and are in contact with mentees throughout the year by email, phone, or skype.

In the coming year, we will undergo a 're-structuring' of the Mentoring Program, so please stay tuned for announcements and an upcoming ISAR News issue that will highlight changes which will expand mentoring opportunities for the ISAR Society!

POSTER AWARDS
(Jennifer Moffat and Brian Gentry)

This year's ICAR poster award competition in Porto was highly competitive (as always)! The international team of judges included Andrea Brancale, Jinhong Chang, Leen Delang, MaaikeEverts, Cybele Garcia, Brian Gentry (co-chair), Zlatko Janeba, Dirk Jochmans, Chris Meier, Jennifer Moffat (co-chair), Joana Rocha-Pereira, Kathie Seley-Radtke, Bart Tarbet, Enzo Tramontano, Subhash Vasudevan, and Zhengqiang Wang. One hundred and twelve posters registered to be judged in the three categories (undergraduate/graduate student, postdoctoral researcher and young investigator) and each category had many excellent posters in the running for both poster prizes and the chance to give a shotgun talk at Friday's opening session, which was co-chaired by Kylie Markovich and Megan Lloyd. The results were announced at the banquet.

Jennifer Moffat and Brian Gentry presenting the Poster Awards during the Banquet hosted at Casa Ferreirinha.

The shotgun winners were Poster #36 "Computer-Aided Discovery and Characterization of Novel Ebola Virus Inhibitors" by Stephen Capuzzi, Poster #39 "Understanding flavivirus pathogenesis: hijacking of human proteins by non-coding viral RNA" by Sander Jansen, Poster #104 "Inhibition of cytosolic phospholipase A2alpha impairs coronavirus replication by interfering with virus-induced replicative organelle formation" by Christin Muller, Poster #119 "N-acylhydrazones as RNase H selective inhibitors active against replication of HIV-1 NNRTIs resistant variants" by Angela Corona, and Poster #129 "Dual Effect of the Multi-Kinase Inhibitor Midostaurin on Acute and Latent HIV-1 Infection" by Edurne Garcia-Vidal.

The winner of the Young Investigator category was Poster #128 "The Ebolavirus VP35 Oligomerization Domain: Crystal Structures and Biophysical Characterization of a New Potential Antiviral Target" by Luca Zinzula (who received 800 Euros and a publication fees waiver from Antiviral Chemistry and Chemotherapy for a manuscript submitted to the journal). The two 2nd place winners in this category were Poster #2 "Susceptibility of paramyxoviruses and filoviruses to inhibition by 2′-monofluoro- and 2′-difluoro-4′-azidocytidine analogs" by Michael Lo and Poster #167 "A Drug Repurposing Approach Identifies different Approved Compounds that Specifically Inhibit Human Cytomegalovirus (HCMV) Replication with Mechanisms different from that of the Current Anti-HCMV Drugs" by Beatrice Mercorelli (both received prizes of 300 Euros).

The Young Investigator category, Beatrice Mercorelli (2nd prize) and Luca Zinzula (1st prize)

The Post-Doctoral category saw a four-way tie for first: Poster #73 "Broad Spectrum Virucidal Non Toxic Strategies" by Valeria Cagno, Poster #94 "Targeting Cyclophilin A to Block Viral Immune Responses" by Che Colpitts, Poster #103 "A New System for a Silent Virus: Developing a Skin Tissue Model for Human Cytomegalovirus" by Megan Lloyd, and Poster #119 "N-acylhydrazones as RNase H selective inhibitors active against replication of HIV-1 NNRTIs resistant variants" by Angela Corona (each received 400 Euros).

Three of the Post-Doctoral category winners: Angela Corona, Megan Lloyd and Valeria Cagno

Finally, in the graduate student category, first place went to Poster #102 "Combination of enterovirus inhibitors delay or prevent the development of enterovirus-A71 resistant variants" by Kristina Lanko (received 800 Euros). The second place winners were Poster #16 "Heteroarylpyrimidine (HAP) and novel non-HAP capsid assembly modifiers show differences in their mode of action in vitro" by Angelica Corcuera, Poster #37 "The novel nucleoside analogue LJ-4269 inhibits coronavirus replication" by Natacha Ogando, Poster #78 "Molecular mechanism of highly potent NS5A

The winners of the Graduate student category

inhibitors" by Melissa Navarro, Poster #197 "Treatment of an EV-D68 Infection with Human Intravenous Immunoglobulin (hIVIG) in a Respiratory and Neurological Model in AG129 Mice" by Brett Hurst, Poster #209 "Gamma-Non-Symmetrically-Modified d4T Triphosphates as Anti-HIV Prodrugs" by Chenglong Zhao, and Poster #216 "In vivo replication of human norovirus in zebrafish larvae" by Jana Van Dycke (each received 300 Euros).

THE CHU FAMILY FOUNDATION (TCFF) SCHOLARSHIPS FOR EARLY CAREER WOMEN 2018

(Kathie Seley-Radtke)

This year we had fourteen outstanding applicants for the TCFF Scholarships and the TCFF committee had a very tough decision due to the quality of the applicants. Ultimately the committee selected three winners for the $3000 scholarships - Ms. Alba Torrents de la Peña (the Netherlands), Dr. Crystall Swabrick (Duke-NUS, Singapore) and Ms. María Laura Morell (Argentina). Crystall will spend time in Dr. Daniel Luque's laboratory at the Centro Nacional de Microbiologia/ISCIII in Spain to learn some new techniques related to her project, Alba will be taking a course on "advanced vaccinology" as well as a second course on leadership and management training, while Maria will spend time with Dr. Anna Överby in the Laboratory for Molecular Infection Medicine at Umea University in Sweden. Congratulations to our winners and we look forward to seeing them again at future ICARs.

The Chu Family Foundation Scholarships were initiated by The Chu Family Foundation (TCFF) together with both the International Society for Antiviral Research (ISAR) or the International Society of Nucleosides, Nucleotides and Nucleic Acids (IS3NA). The TCFF support the professional development of early career level women who have

shown the potential for significant contribution in the field of antiviral research (ISAR) or nucleoside/tide and/or nucleic acid research (IS3NA). The scholarships provide funds to attend specialized workshops, visit or work in another laboratory to obtain new skills, take courses, or acquire specialized training in any other way. Just a reminder, but the competition for next year's Chu Scholarships will open later this fall. So watch for an announcement or contact Kathie Seley-Radtke (kseley@umbc.edu) for more information.

ICAR'S FIRST ANNUAL PECHAKUCHA CONTEST

(Kathie Seley-Radtke)

This year in Porto, ICAR experienced its first PechaKucha presentation contest. If you weren't there, you may be asking "What is PechaKucha?" So PechaKucha is a presentation format where the presenter has 20 slides, each on the screen for only 20 seconds. The slides advance automatically so the presenter has to carefully time themselves to keep up with the slides, since they cannot control the speed. Also important, a good PechaKucha presentation incorporates humor, something about themselves in addition to their research, and maybe a surprise or something that is unexpected. Bottom line, the goal is to entertain the team of judges (and the audience) while still informing! Our brave contestants were a mix of graduate students and postdocs and I'm sure those that attended would agree that they exceeded our expectations!

The winner of the $200 first prize was Ryan O'Hanlon, Icahn School of Medicine at Mount Sinai, "Combination of Oseltamivir and a Novel Kinase Inhibitor has Synergistic Antiviral Activity against Influenza Viruses" (Abstract #161). Ryan not only dressed as James Bond (see below), but tailored his entire presentation in a spy thriller format!! Needless to say, we were thrilled he agreed to redo his presentation the next morning for those still attending ICAR. The two second place winners each received $100 - Christin Muller, Justus Liebig University Giess, "Inhibition of cytosolic phospholipase A2alpha impairs coronavirus replication by interfering with virus-induced replicative organelle formation" (Abstract #154) and Valeria Cagno, University of Geneva, "Broad Spectrum Viricidal Non-toxic Strategies" (Abstract #111). All three were deemed to have done an outstanding job at the PechaKucha timing as well as the rules to include humor and something personal about themselves in addition to detailing their research! And a big thanks goes out to our outgoing President José Esté, who agreed to give us an extra $100 this year which allowed us to give out 3 prizes instead of 2.

Kathie Seley-Radtke and the three winners Ryan O'Hanlon, Valeria Cagno and Christin Muller

The other six contestants were Stephen Capuzzi, University of North Carolina, "Computer -Aided Discovery and Characterization of Novel Ebola Virus Inhibitors" (Abstract #58); Anna Koromyslova, German Cancer Research Center "Nanobodies Reveal Functional Epitopes and Potential Mechanisms of Norovirus Neutralization" (Abstract #241); Megan Gribble Lloyd, SUNY Upstate Medical University, "A New System for a Silent Virus: Developing a Skin Tissue Model for Human Cytomegalovirus" (Abstract #149); Natacha Ogando, Leiden University, "The Novel Nucleoside Analogue LJ-4269 Inhibits Coronavirus Replication" (Abstract #59); and Clara van Hoey, University of Vienna "First Steps Towards Developing Novel Inhibitors of Enterovirus Polymerases (Abstract #132). All of our brave contestants did an excellent job – so much so that our new President, Johan Neyts, has agreed to continue this exciting event for the next ICAR in Baltimore; so we hope to see you all there where we will get to experience more fun and creative PechaKucha talks!

PECHAKUCHA, COMMUNICATING SCIENCE WITH STYLE

(Ryan O'Hanlon)

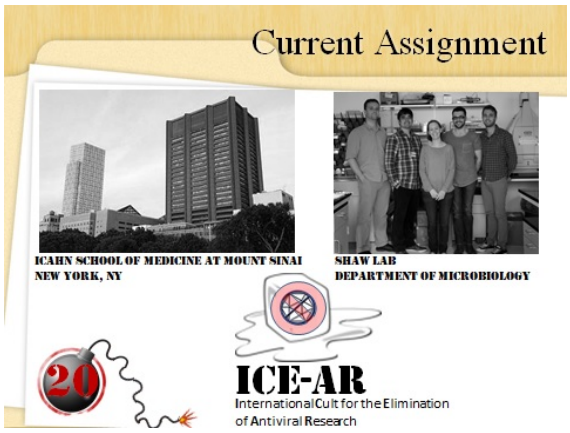
Before attending this last ICAR or reading this article, you probably have never heard of a PechaKucha, and you would not be alone. Until ISAR asked me to participate in a PechaKucha competition, I had no idea of its existence. In fact, no one that I knew was familiar with this presentation style. Some of my colleagues still cannot remember its name to this day and recall that I recently gave a "Pikachu". Aside from the unusual name, presenting 20 second slides, with no control in their progression, would seem like an odd way of communicating scientific work. Can

Ryan O'Hanlon during his PechaKucha presentation

figures from complicated experiments be digested this quickly? It could take 20 seconds just to describe the experiment behind the results, then poof, onto the next topic. This introduces the risk of the dialog falling out of sync with the presentation, creating more opportunities for stumbling and awkward moments where the presenter must reorient. Most would consider this torture, especially given that shotgun poster talks are an acceptable and effective alternative. In comparison, PechaKucha looks like one of those silly challenges from a Japanese game show.

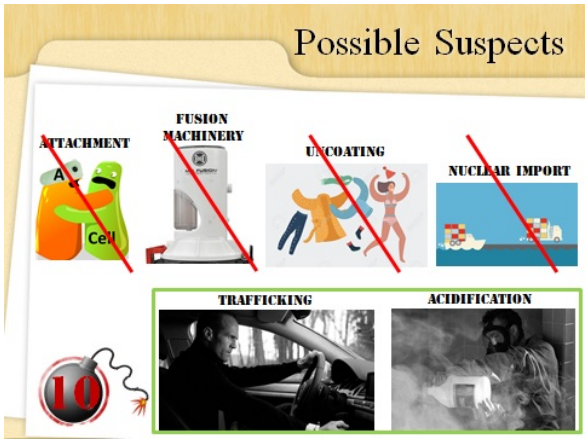
At least, this is how it would appear if one was expecting a PechaKucha to be like a traditional science talk. However, if one uses this format to share a simpler story, rather than a data dump with conclusions, a PechaKucha becomes a versatile platform for science communication. Its original architects designed it to keep out the lengthy explanations and focus on the headlines. Its simplicity is likely what led other groups adopting the format as a way to introduce ideas to a broader audience across related fields or even the lay public. Furthermore, the emphasis on the addition of humor, unpredictability, and entertaining elements into the presentation makes them more approachable and fun. Among the PechaKuchas from competitions that are posted online, many give the impression that they were given at a happy hour or some other informal and leisurely event. Keeping this in mind, is there a reason why a talk on an antiviral topic could not be presented this way? What would be the appropriate setting and audience for a science-based PechaKucha?

These important questions were challenging to answer as I crafted a PechaKucha the weeks before the 31st ICAR. For the contest, I was instructed to present the research from my abstract, include a story about myself, and entertain the audience in a span of 6 minutes and 40 seconds. At 20 seconds per slide, I could manage to say around 60 words. In other words, if I was going to show experimental data, I had about 3 sentences to summarize why it was done, how it was done, and my interpretation of



The first slide of Ryan's presentation

the results. If I cut out the details and just presented the headlines, this was manageable. On the other hand, where could I fit in a story about myself? I went to YouTube and PechaKucha.org to look for examples that could help, but none of these were presentations of scientific data from an abstract. It turns out that most PechaKuchas have a single large image per slide, usually as a device to echo an idea of the speaker, and not as a figure to interpret. With no appropriate model on how to blend my story with experimental data, I was going to have to create a new style constructed on untested ideas.



Slide 10 of Ryan's presentation

I found the best way to cram my research, my story, and entertaining elements in a short presentation was to create a theme tying in all three. Inspired by action spy movies, I presented my research as a top secret briefing to fellow ISAR "agents". By incorporating items in my presentation in context to this theme, the ideas could become an analogy to

which the audience could relate. Instead of presenting data on binding kinetics, I, in spy attire could describe the assignment and show a picture of the drug targets under the title "Known Associates", that was sufficient to convey the message. Most tables and figures could be simplified into fun pictures, humorous bits and details my personal life could be inserted seamlessly, and I could blame my experimental woes on a fictional nefarious organization while keeping the audience engaged. It took a lot of extra work to put this theme into my PechaKucha, but it simplified my message and made it easier for the audience to digest. On the other hand, I was betting that the audience would be receptive to such an unorthodox style. Regardless, winning the competition was not my priority. I was more interested in using it as a creative outlet to share my story and hopefully meet others with common interests.

Luckily, upon arriving at the ICAR, I discovered that the competition was to take place during a networking session. The session itself seemed like the appropriate environment for a PechaKucha, a relaxed and more informal setting with an audience needing a break from the standard lecture. After delivering my talk, the positive response from strangers in the audience was slightly overwhelming. I had more conversations with different people in the couple hours after the competition than at any other part in the conference. As I had hoped, my talk made me more approachable to others, breaking the ice enough to start a conversation about science and my personal life. Overall, the experience was a delightful way to network. In addition, I was asked to present it again after the shotgun poster session, which was recorded and can be viewed here:

https://youtu.be/AYRHKWg3U0I.

In the near future, I hope the PechaKucha competition could be expanded to allow more people to share their science and their personal lives. This format has a special way of engaging the audience and encouraging dialog that is missing from talks and poster sessions. Perhaps giving a PechaKucha will broadly be accepted as the new way for scientists to network.

ANTIVIRALS CONSORTIUM AT THE 31ST ICAR

(ESR, Anna Plaszczyca)

ANTIVIRALS is an EU-funded consortium aiming to train 15 Early Stage Researchers (ESRs) in the field of antiviral drug development. All ESRs pursue their Ph.Ds. in one of the 7 academic or 5 industrial partners and participate in regular meetings. The program started in 2015 and this year's ICAR was also the final assembly of our network.

Mysteriously, during recruitment process only one man and 14 women were selected for our program! Therefore, the "Women in Science" roundtable that opened the meeting definitely felt relevant. The panelists shared inspiring stories about their own careers and underlined the importance of having

Some of the ESRs during the WIS roundtable

supporting mentors. It was heartening to see women with very diverse personalities and backgrounds succeeding in high level scientific positions. Throughout the meeting we could see that ICAR organizers put a lot of emphasis on support of female researchers, which was very encouraging.

The ANTIVIRALS session was met with a lot of interest from ICAR attendees. After network introduction by its scientific coordinator Frank van Kuppeveld all ESRs held short (90 seconds!) pitch presentations aimed to attract audience to their talks or posters. This was a great way to think a bit outside of the box to extract key aspects of our projects and spark the interest of the crowd. Five ESRs were also selected for oral presentations during the main program. I think all of us appreciated this recognition and opportunity to share our work with such a great audience. The atmosphere in the lecture hall was very friendly, and many of us got interesting questions and even collaboration offers.

Most ESRs also presented their research during poster sessions. Here again the audience was highly engaged, resulting in many fruitful discussions. The exchange of exciting ideas is probably the best part of every conference and during ICAR everyone seemed really happy to share their research and engage in the conversation. Work of ANTIVIRALS fellows was appreciated by organizers – four out of seven poster prizes in graduate students' category

went to ESRs, including 1st prize for Kristina Lanko - congratulations!

ESR Kristina Lanko, 1st prize in the Poster competition, Graduate students category

Two ESRs, Natacha Ogando and Clara Van Hoey, bravely participated in the first ever Pecha Kucha competition giving an audience-friendly 'small talk' presentation about their Ph.D. projects. The new format was entertaining and it would be really interesting to see more talks showing research in this unusual and creative way.

The general feeling during the meeting was very relaxed and almost family-like, with many regular long-time attendees. This for sure facilitated interactions. There were many opportunities for networking, both with our peers and well-established researchers. We felt like there was almost no barrier between renowned group leaders and Ph.D. students. Also the schedule of conference left plenty of time for networking – during satellite sessions, but also less formally during the breaks and free afternoon on Wednesday, which we spent exploring the city with new colleagues.

What stood out to us was the ICAR's support for young researchers at the beginning of their careers. Many selected speakers were Ph.D. students or postdocs, which is not always the case in other conferences. Also the number of travel grants (three of which went to ANTIVIRALS' ESRs), scholarships and awards was impressive. Financial support enabling participation in the meetings or undertaking an additional training is extremely important and it was great to see that ICAR organizers created a lot of opportunities for early stage researchers.

Antiviral drug development is an extremely multidisciplinary field and this was well reflected by the range of topics discussed during ICAR. From epidemiology, basic virology research to antiviral drug screening and medicinal chemistry, all of us could not only find something relevant to our own work, but also get insight into novel findings in related areas. Also the background of the attendees

The ANTIVIRALS scientific coordinator Frank van Kuppeveld

was really diverse, including scientists from both academia and pharmaceutical companies. This felt very close to the main idea of our network, which was bringing together universities and industrial partners working in both basic and applied research to train a new generation of scientists in all aspects of drug development.

Last but not least, the city of Porto was a wonderful place to host a conference and we all enjoyed steep cobblestone streets and famous wine cellars. For the majority of ANTIVIRALS' ESRs this was the first time at ICAR, but I am sure many of us hope to be back next year!

ISAR BUSINESS MEETING REPORT

(Brian Gowen/ Graciela Andrei)

The ISAR held its annual business meeting at the Alfândega Congress Centre, Archive Hall I, during the 31st ICAR on Thursday, June 14. Brian Gowen (Treasurer) presented a summary of the ISAR finances. Net assets at the end of the 2017 fiscal year totaled $648,996 held in several banking and investment accounts.

The net assets total is up from $633,398 at the end of the 2016 fiscal year and the increase is due in part to the $12,198 surplus after paying all of the bills associated with the 30th ICAR held in Atlanta, GA. While we won't know the final numbers for the Porto ICAR until late July or August when all revenue support has been received and meeting expenses paid, estimates suggest that we should be very close to having a balanced budget. The outcome will be presented at next year's ICAR to

Fiscal year 2017 net assets

Assets	
Bank Accounts	$170 017,94
Cetera Investments	$295 228,58
Fidelity Investments	$183 749,90
TOTAL	$648 996,42

Liabilities	
Accounts Payable	$0
TOTAL	$0

be held in Baltimore, MD. Also presented during the business meeting was the year-end financial statement reflecting ISAR's revenue sources and expenses for 2017. As reflected in the table next page, the principal sources of revenue in support of the meeting are the many generous sponsors and the conference registration fees. Notably, investments performed well with gains surpassing $30,000 in 2017, compared to $13,000 in 2016.

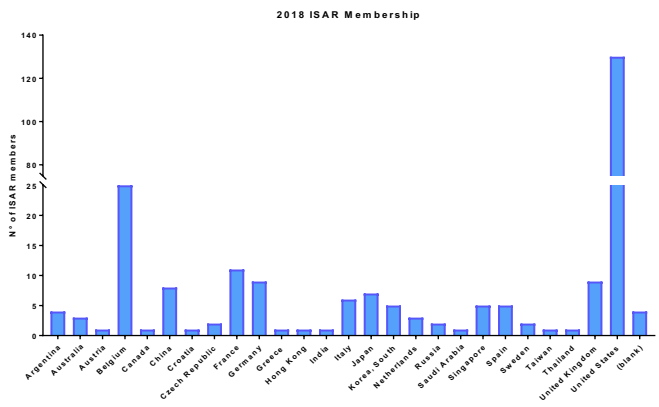
Graciela Andrei (Secretary) provided a report on the 2018 ISAR Membership and on attendance at the 31st ICAR in Porto. Twenty-six countries are represented in the Society, with a total of 246 members through June 2018 (130 from USA). A total of 280 attendees as of June 10, 2018 from 38 different countries were registered for the 31st ICAR.

This year, the Society received 74 applications for a travel grant award. Because of the restricted amount of available budget, some of the grant applications could not be funded. Based on the scientific review of the submitted abstracts, a ranking was established based on the scores provided by four independent reviewers. The Society awarded a total of 43 Travel Merit Grants (16 from North America and Asia and 27 from Europe who received an award of $800, and $400, respectively) to help these members defray the costs of attending the conference. The Society also awarded 13 Travel Merit Assistance Awards to participants coming from low/middle-income countries to support their attendance to the meeting.

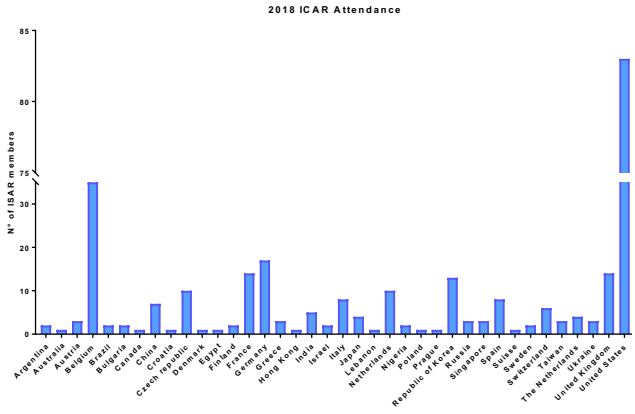
For recipients of this award, besides a $1000 stipend, the registration fee was waived. The Society invested a total of $40,100 in Travel Awards, which highlights the considerable funds made available by the Society during the past years to increase the attendance of young investigators at the meetings

2017 Income		
Membership Dues		$9 641,00
Sponsorship Support		$154 811,60
TCFF		$ 15 000,00
WIS		$ -
President's Fund		$ 3 400,00
Registrations for ICAR		$133 090,00
Gain/Loss Investments		$31 080,46
	Total	$ 347 023,06
2017 Expenditures		
Administrative		$ 20 912,21
TCFF Awards		$ 9 517,96
WIS Expenses		$ 2 121,66
President's Fund		$ 1 506,76
ICAR 2017		$ 288 859,14
ISAR Management		$ 3 607,00
	Total	$ 326 524,73
Net Income		$ 20 498,33

Year-end financial statement for 2017.



2018 ISAR membership



31st ICAR attendance

CURRENT RESEARCH

Can microorganisms be evolved to function with a synthetic genome?

(Piet Herdwijn, Rega Institute for Medical Research, Leuven, Belgium)

Editorial comment (R. Anthony Vere Hodge):

In 2014, Piet Herdewijn (Rega Institute for Medical Research, KU Leuven, Belgium) gave the inaugural Antonín Holý memorial award lecture entitled *From modified nucleoside to a chemically modified genome*. When I met Piet again in Porto, I congratulated him on his memorable Holý award lecture and that I was interested to know how the modified organism had survived since that time. He kindly agreed to prepare an update for this issue of the ISAR News.

For those ISAR News readers who missed this excellent lecture, please see the summary in my 27th ICAR meeting report [Antiviral Research 111 (2014) 143–153] – Piet gives a brief summary here.

Piet's update

Genomic DNA composed of three canonical bases, adenine, cytosine and guanine, and the artificial base, chlorouracil, were used in a culture of an *E.coli* strain which was set out to evolve. Selection over 25 weeks in a cultivation device that automatically adjusts the lowest tolerable thymine concentration yielded descendants that grew with only chlorouracil. Mutations accumulated massively during adaptation. This genome scale evolution of the chemical constitution of a microorganism demonstrates that the chemical barrier of natural biodiversity can be overcome, even at the level of nucleic acids and their building blocks. Continuous evolution experiments have shown a point of no return, when thymine became toxic for the organism (Marliere Ph, personal communication). These experiments of accelerated evolution, might warrant for similar processes to occur with viruses.

In a follow up of the replacement of thymine by chlorouracil in a full genome context by automated selection techniques, we have investigated the possibility to change all 4 canonical bases by unnatural bases to serve as genetic templates *in vivo* at the level of one gene. This study is a prelude to start *in vivo* evolution to obtain a bacterial organism with a fully artificial genome. This has been carried out successfully with two sets of non-canonical bases: ClU/FC/c7A/c7G and ClU/BrC/c7A/Hx. With both cassettes, a fully morphed gene encoding a dihydrofolate reductase was generated by PCR and was shown to transfer and confer trimethoprim resistance in *E. coli*. These are the first examples of fully modified DNA molecules being functional *in vivo*.

Marliere et al., Angew Chem, 2011, 50, 7109 – 7114.
Eremeeva et al., Angew Chem, 2016, 55, 7515 – 7519.
Eremeeva et al., Chemistry Eur J, 2017, 23, 9560 – 9576.

Novel concepts in enteric virus infection open avenues for the development of broad spectrum therapeutics.

(Carmen Mirabelli, University of Michigan Medical School, Ann Arbor, US)

Enteric viruses naturally infect the gastrointestinal (GI) tract and are transmitted by the fecal-oral route. These viruses belong to several viral families (e.g., *Caliciviridae, Picornaviridae, Reoviridae, Astroviridae, Adenoviridae*) and cause a significant number of illnesses worldwide ranging from diarrhea to neurological diseases. Epidemiological evidence indicates that enteric viruses, in particular human norovirus (NoVs) and hepatitis A virus, are the leading causes of foodborne illnesses in developed countries (*1*). In addition, NoVs are the cause of one fifth of all acute gastroenteritis illnesses worldwide with an economic burden estimated at ~$60 billion globally (*2*). Human enteroviruses (EV) are traditionally enteric viruses although their pathophysiology affects other tissues and organs. EVs are indeed associated with a broad range of diseases: febrile illnesses, common cold, asthma exacerbations, myocarditis, pancreatitis, neurological syndromes and acute flaccid paralysis (namely poliomyelitis when poliovirus-associated). With the exception of worldwide-available, safe vaccines for poliovirus, hepatitis A and rotavirus, no therapeutics or prophylactic regimens are available for the other enteric virus infections. As those viruses are tremendously diverse, the development

of pan-active antiviral strategies is a great challenge. To complicate the picture, the last decade has seen an upsurge of studies challenging the standing paradigm of the **single infection unit** where a single enteric virus particle infects one target cell. This concept was and is supported by *in vitro* studies of enteric virus infection, even at the single cell levels, where one viral particle is sufficient to elicit the infection in cell lines (*3*). Based on this, the preferred strategy for the discovery of novel compounds with antiviral activity against enteric virus infection includes cell-based screening with standard cell lines (when available) and relatively low multiplicity of infection (MOI). However, it is striking to observe that the vast majority of compounds, endowed with *in vitro* antiviral activity in cell-based assay, are devoid of any activity when tested *in vivo* in animal model, or in clinical trials, in the context of infection in a complex organism.

The scenario of enteric virus infection *in vivo* must be more complex. Part of the complexity may be explained by taking into account the physiology of the GI tract, the first (or unique) site of replication for enteric viruses. This compartment integrates different systems for its correct functioning (nervous system, circulatory system, immune system) and its structure includes an exposed layer of different professional intestinal epithelial cells, a thick coating of mucus and millions of microbes collectively referred as the microbiome (e.g., bacteria, bacteriophages, helminths). The surface area of the GI tract corresponds to half a badminton field (*4*); therefore, the GI tract also represents the largest exposed surface of our body to the external environment. If the model of single infection union was valid *in vivo*, successful infections would be a rare event. Recent studies suggest instead that **enteric viruses travel in groups** (*5*). In particular, they cluster i) in vesicles with inverted phosphatidil-serine (PS) topology (*6*, *7*), and ii) at the surface of selected bacterial species (*8*, *9*). Both mechanisms promote the concentration of viral particles at the surface of the epithelial monolayer of the GI tract, in turn increasing locally the multiplicity of infection and the chances of a successful infection. In addition, a recent report suggests that virus-cloaked vesicles are also found in stools and those confer an advantage also in viral transmission (*7*).

As for the bacteria, this component was traditionally believed to offer protection against the invasion of pathogens (i.e., colonization resistance), in addition to shaping the intestinal immune system and metabolizing complex nutrients. However, a more complex interplay is emerging for enteric viruses, whereby the bacterial component can modulate viral infections by promoting or inhibiting them (*10*). Collectively, the interactions of commensal bacteria with enteric viruses have been classified for their direct or indirect effects on viral infection. Exemplifying the former, poliovirus, a member of the enterovirus family and etiological agent of poliomyelitis, interacts with the N-acetyl glucosamine containing polysaccharides of bacteria. This in turn increases its resistance to heat-inactivation (i.e., virus is more stable) and promotes systemic pathogenesis (i.e., virus is more neurovirulent) (*9*). In addition, the concentration of multiple poliovirus particles at the site of infection, with the bacteria working as a scaffold, multiplies the chances of successful infection by facilitating viral recombination (*11*). Human norovirus also binds to several bacterial species present in the gut as observed by electron microscopy (*8*). In addition, the commensal bacteria *Enterobacter cloacae* enhances virus infection in an *in vitro* B cell model by promoting cell binding (*12*). Indirect interactions generally involve host immune components and require animal models to dissect their mechanisms. Mouse mammary tumor virus (MMTV) represents an example of indirect interaction. By binding bacterial LPS, the virus promotes a Toll-like receptor 4 (TLR4) response that helps the virus evade the host immune system (*13*). Another example is murine norovirus (MNV), whose interaction with commensal microbes determines persistence of the virus via IFN-λ induction (*14*).

Altogether, these findings have clear implication for the design of successful treatments for enteric virus infection and may explain why previous attempts failed. As an example, WIN-like enterovirus capsid binders are highly potent entry inhibitors with *in vitro* activity in the low micromolar range. However, their activity *in vivo* has been associated with rapid drug-resistance emergence and their development was hence halted (*15*). If the dosing of a compound is based on its *in vitro* EC_{50} activity in a single infection unit model, the regimens *in vivo* will be likely sub-optimal (if virus is instead concentrated at the site of infection) and drug-resistant variants will quickly emerge. In addition, viruses, in vesicles or bound at the surface of commensal bacteria, may be protected from the action of entry inhibitors especially if those complexes could bypass receptor-mediated entry, as it has been proposed for enteroviruses (*6*).

There are still gaps of knowledge on these emerging concepts, but once filled, the resulting findings will open avenues for the development of new strategies to counteract enteric virus infections. Interesting examples could be the development of small molecules able to specifically destroy virus-cloaked vesicles and in turn decrease the transmission and the infectivity of enteric viruses, and/or the use of antibiotics to reduce/treat enteric virus infection by

targeting the bacterial "scaffold". Notably, these novel concepts have been studied in the context of selected member of picornaviruses, caliciviruses and reoviruses families. It will be of utmost interest to understand how conserved those infection pathways are and if shared across enteric viruses, the design of novel therapeutics will hold the promise for broad-spectrum activities.

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ISAR News is an official publication of the International Society for Antiviral Research. It is published four times a year as a free article in *Antiviral Research* (http://www.journals.elsevier.com/antiviral-research) and is posted on the ISAR website (http://www.isar-icar.com).

ISAR News is prepared by the ISAR Publications Committee: Anthony Vere Hodge and Luis Schang (co-chairs), Andrea Brancale, Mike Bray, Rhonda Cardin, Kara Carter, José Esté, Brian Gowen, Justin Julander, Jason Peng, Joana Rocha-Pereira, Aruna Sampath, Ashoke Sharon, Sietske Speerstra, Bart Tarbet and Simon Tucker.