

8th
**COLORADO
ALPHAHERPESVIRUS
LATENCY SYMPOSIUM**

Vail, Colorado

May 16-19, 2018



*to convene researchers active in alphaherpesvirus latency
to discuss current advances in a relaxed venue*

Dear Colleagues,

Welcome to the 8th symposium of the Colorado Alphaherpesvirus Latency Society. Since 2011, we have assembled at this time to discuss current advances in alphaherpesvirus latency in this idyllic mountain setting of the Christiania Lodge. Our field is rapidly advancing as we embrace this era of big science with its massive data sets, amazing ability to microscopically study virus/cell interactions at the single-molecule level in real-time, application of hybridization with flow cytometry to investigate and collect rare virus/cell interactions, high-throughput providing single-cell analyses, ability to clone/mutate/select/characterize virus genes in the setting of the intact genome, virtually unlimited supplies of human induced neurons, and exciting advances in therapeutics including *in vivo* virus genome editing and novel vaccine developments – to name but a few. In the background of these rapid advances, it is nice to set aside our administrative duties, and for one brief moment, just talk science. Our goals are shared, to eradicating disease produced by alphaherpesvirus reactivation through understanding the molecular mechanisms underlying establishment, maintenance and reactivation from latency. Our approaches are different, but with free and open discussion, we all can learn. Quoting Karl Popper, “A rationalist is simply someone for whom it is more important to learn than to be proved right; ... by gladly allowing others to criticize his ideas and by gladly criticizing the ideas of others.” This is a difficult charge, but we are succeeding.

As the provers suggest, “If you want to go fast, go alone. If you want to go far, go together.” Individually, our 70 attendees have traveled an accumulated 116,701 miles from 3 continents, 6 countries and 21 states and together we have published over 3009 PubMed sited papers involving herpesviruses. We will hear 31 oral presentations by established investigators and 12 two-minute poster summaries by new investigators. I hope all will visit each poster during the meeting. Again this year we are hosting a select group of exceptional undergraduates whose interest in herpesvirology is just beginning. Please take time to encourage this future generation of alphaherpesvirologists.

Our Don Gilden Memorial Lectureship, a grassroots endeavor initiated and generously funded by fellow alphaherpesvirologists, is in its second year. We are extremely fortunate to have Dr. Ana Pombo from the Berlin Institute for Medical Systems Biology at the Max Delbrück Center for Molecular Medicine present this year’s lecture that highlights her studies to understand the interplay between gene regulation and genome architecture focusing on defining rules and principles of genome function. It is hoped that this highly technical lecture may provide new ideas concerning the mechanism by which transcription is controlled during establishment/maintenance and reactivation of latency.

Following Ana’s keynote presentation, Tamara Goldstein and Linda Wang will provide a brief musical tribute to close a significant chapter of our symposium; unless it snows as last year.

We have a few items to cover during the Business Meeting and a few votes to cast by the attending program committee members. CALS is a joint affair; if you wish to join the program committee you can do so at the Business Meeting.

The fourth definition of ‘symposium’ in the American College Dictionary reads: “among the ancient Greeks, a convivial meeting, usually following a dinner, for drinking, conversation and intellectual entertainment.” This describes our traditional informal Friday Night Fireside Chat which closes the meeting by providing a special time to relax while posing questions that may not have answers, *yet*; problems that have no solutions, *yet*; and experiments that cannot be done, *yet*.

Finally, I wish to thank our generous benefactors and our family of alphaherpesvirologists, both of whom are critical to the continued success of this annual symposium that is the Colorado Alphaherpesvirus Latency Society; an interactive meeting where established collaborations are strengthened and new collaborations are formed.

Enjoy CALS 2018

Colorado Alphaherpesvirus Latency Symposium

May 16-19, 2018

Christiania Lodge
Vail, Colorado

Wednesday, May 16

6:00 pm dinner; Christiania Lodge

Thursday, May 17

7:00 – 8:00 am breakfast & poster set up, Christiania Lodge

8:00 – 8:10 am welcome: Randy Cohrs

8:10 – 10:10 am Session I: Clinical

10:10 – 10:30 am break

10:30 – 12:30 pm Session II: Molecular I

12:30 – 3:00 pm lunch / free time

3:00 – 4:00 pm Session III: Molecular II

4:00 – 5:15 pm Don Gilden Memorial Lectureship presented by Ana Pombo
remembrance by Peter Kennedy and introduction by David Knipe

5:15 pm music by Tamara Goldstein and Linda Wang; Christiania Lodge

6:45 pm group photograph

7:00 pm dinner; La Tour

Friday, May 18

7:00 – 8:00 am breakfast; Christiania Lodge

8:00 – 8:10 am comments: Randy Cohrs

8:10 – 10:10 am Session IV: Herpesvirus-host interactions

10:10 – 10:30 am break

10:30 – 12:30 pm Session V: Neuronal latency models

12:30 – 2:30 pm lunch & business meeting; Christiania Lodge

2:30 – 3:30 pm Session VI: Reactivation

3:30 – 6:00 pm Session VII: Poster presentations

3:30 – 4:00 pm Oral overview

4:00 – 6:00 pm Poster viewing

7:00 pm dinner; Up The Creek

following dinner fireside chat; Christiania Lodge, fireplace room

Saturday, May 19

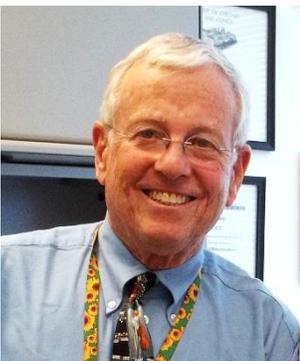
7:00 am breakfast; Christiania Lodge

Don Gilden Memorial Lectureship

2018 Lecturer Ana Pombo, Ph.D.



Ana Pombo investigates how the 3D folding of chromosomes influences gene expression in mammalian development and disease, and how poisoning of RNA polymerase II is regulated to prime genes for future activation. She received her DPhil from University of Oxford (1998, UK) where she pioneered high resolution imaging of transcription sites in mammalian nuclei. She was awarded the Royal Society Dorothy Hodgkin Fellowship (UK; 1998-2002), and started leading her research group in 2000 at the MRC Clinical Sciences Centre, Imperial College London (UK). Her laboratory showed that Polycomb repression is associated with RNA polymerase II poisoning, and developed high-resolution cryoFISH approaches to study spatial relationships between genomic regions and nuclear landmarks. She was awarded the Robert Feulgen Prize 2007 for her contributions to imaging nuclear architecture. Her laboratory moved to the Berlin Institute for Medical Systems Biology, at the Max Delbrück Center (Berlin, Germany) in 2013, and she was appointed Professor (W3) at Humboldt University of Berlin. Her laboratory has developed Genome Architecture Mapping, an orthogonal ligation-free approach to map chromatin contacts genome-wide.



Don Gilden, M.D. (1937 – 2016)

Don Gilden received his BA from Dartmouth College and his M.D. from the University of Maryland, completed Neurology residency at the University of Chicago and postdoctoral fellowship in neurovirology at Johns Hopkins. He was Professor of Neurology at the University of Pennsylvania and the Wistar Institute before moving to Colorado where he served as Professor of Neurology and Microbiology, as well as Chairman of the Department of Neurology at the University of Colorado School of Medicine for more than 24 years. Don published over 450 papers, reviews and chapters and had NIH funding continuously. He received many distinctions including the Alumni Award for Distinguished Service from the University of Chicago School of Medicine, the Pioneer Award of the International Society for NeuroVirology, the Honor Award and Gold Key for outstanding contributions to medicine and distinguished service to mankind from the University of Maryland School of Medicine, and the Drexel University College of Medicine Hilary Koprowski Prize in Neurovirology. He was elected to the Association of American Physicians, the Fellowship in the American Association for the Advancement of Science, and the Johns Hopkins Society of Scholars. Don was a superb clinician, outstanding teacher and effective administrator. Don's passion for science and medicine was second only to his love for his wife, Audrey, and family. Don will always be remembered as a supportive mentor, friend to all and the "heart of CALS."

Founding lectureship supporters

Ann Arvin	Nicholas Baird	Marius Birlea	John Blaho
David Bloom	Edouard Cantin	Donald Coen	Elisabeth Cohen
Randall Cohrs	Leonardo D'Aiuto	Stacey Efstathiou	Lynn Enquist
Anne & Mike Gershon	Thomas Kristie	Todd Margolis	Satish Mehta
Duane Pierson	Rozanne Sandri-Goldin	Nancy Sawtell	Luis Schang
Deepak Shukla	Padma Srikanth	Vaibhav Tiwari	Hua Zhu

Continuing lectureship supporters

Nicholas Baird	Marius Birlea	Randall Cohrs	Ian Mohr
Scott Schmid	Abel Viejo-Borbolla		

Thursday morning, May 17

7:00 breakfast & poster setup; Christiania Lodge

8:00 welcome: Randy Cohrs

Session I: Clinical

Moderator: Todd Margolis

8:10 Vishwajit L. Nimgaonkar
HSV-1 exposure and age related cognitive impairment: Relevance for latent infections?

8:30 Barry T. Rouse
Pathogenesis of herpes encephalitis-perhaps!

8:50 Anne A. Gershon
Enteric zoster, diagnosis with saliva, and use of a guinea pig model to study the role of innate immunity in protection against VZV infection

9:10 Padma Srikanth
Manifold manifestations of versatile varicella zoster virus (VZV)

9:30 Keith R. Jerome
Efficient *in vivo* gene editing of latent herpes simplex virus via adeno-associated virus (AAV)-mediated delivery of meganucleases or CRISPR/Cas9

9:50 Anna Wald
Genital and oral mucosal shedding and cellular immune response after first episode genital herpes simplex virus type 1 infection

10:10 coffee break

Session II: Molecular I

Moderator: John Blaho

10:30 Moriah Szpara
Genomic analysis of HSV-1 in the niche of genital infection

10:50 Joshua Schiffer
Bottlenecks to intra-host evolution of herpes simplex virus-2

11:10 Matt Taylor
Quantifying HSV-1 recombination through differential fluorescent protein expression

11:30 Erin Buckingham
Limited effect of the neurovirulence protein ICP34.5 on reassortment of the LC3 autophagy protein with purified HSV1 when compared with PRV and VZV

11:50 Richard Thompson
HSV-2 VP16 regulation and viral pathogenesis

12:10 Ian Mohr
Neuronal DNA damage response (DDR) pathway regulates the maintenance of HSV-1 latency

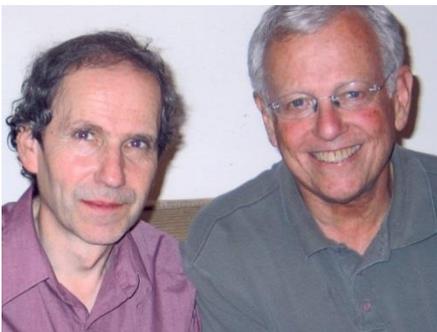
Thursday afternoon, May 17

12:30 lunch / free time

Session III: Molecular II

Moderator: Benedikt Kaufer

- 3:00 Anna Cliffe
Neuronal hyper-excitability triggers JNK-dependent reactivation of herpes simplex virus from latency
- 3:20 Patrick Lomonte
Chromatinization of promyelocytic leukemia nuclear bodies (PML NBs)-associated latent HSV-1 genomes requires functional PML NBs and histone H3.3 chaperones
- 3:40 David M. Knipe
Herpes simplex viral functions promote a poised latent infection
- 4:00 **Don Gilden Memorial Lectureship presented by Ana Pombo**
RNA polymerase II: at the crossroads of gene regulation and genome architecture
remembrance by Peter Kennedy and introduction by David Knipe
- 5:15 music by Tamara Goldstein and Linda Wang; Christiania Lodge
- 6:45 group photograph
- 7:00 dinner; La Tour



Don Gilden was one of the most complete, personally warm and accomplished people I have ever known. He was one of the most gifted clinician-scientists of his generation who made many seminal discoveries in Varicella Zoster (VZV) virus latency and reactivation as well as in the field of Multiple Sclerosis. He was never afraid of challenging accepted scientific dogma and made many important contributions to Neurovirology, including the first identification of latent VZV DNA in human peripheral ganglia, the molecular proof of *zoster sine herpette*, the recognition of zoster vasculitis and the protean neurological manifestations of VZV reactivation, many contributions to latent VZV gene expression in ganglia, and much else besides. As well as his scientific accomplishments Don was also a wonderful, affectionate, and engaging human being. As a testament to this I am thinking particularly of his great love for his family, his remarkable gift for making friends which he seemed to raise almost to an art form, his widespread popularity, his unflinching loyalty to his friends and medical and scientific colleagues, his great generosity both in the material sense and also in terms of his giving so much of his time to others, his passionate love of music as evidenced by his ability and enthusiasm as a highly accomplished amateur violinist, and his sheer zest for life with the rather rare ability to enjoy just about every aspect of living. These included such pursuits as skiing in the Colorado mountains, dining with friends and family at fine restaurants, enjoying summer barbecues in his beautiful Colorado home, swimming in his local pool, playing sports with his sons and friends, and exploring the interesting sights of foreign lands. And, of course, he also greatly enjoyed his professional work as a neurologist and scientist which he kept up virtually until the day he passed away. In many ways the fact that he was taken away from us so quickly and while he was still at the top of his game both personally and professionally makes his passing and absence from all our lives particularly painful. Yet it is because of these very human qualities that we all remember him with such fondness and vivid memories. Some people leave a legacy of scientific discoveries while others are remembered primarily for their humanity. In Don's case he leaves a wonderful legacy that embraces both professional excellence and great personal qualities, and I know for certain that I shall never meet such an extraordinarily gifted and rounded person again in my lifetime. -Peter Kennedy, MD, PhD

Friday morning, May 18

7:00 breakfast; Christiania Lodge

8:00 comments: Randy Cohrs

Session IV: Herpesvirus-host interactions

Moderator: David Davido

8:10 Werner Ouwendijk

A nonhuman primate model of varicellovirus infection of the enteric nervous system

8:30 David Koelle

CD4 T-cell responses to VZV: Is gE special?

8:50 Homayon Ghiasi

Role of IFN- γ over-expression in HSV-1 latency-reactivation

9:10 Tao Peng

IL-17c, peripheral nervous system and herpes infection

9:30 Edouard Cantin

A role for gut commensal bacteria in herpes stromal keratitis

9:50 Nancy M. Sawtell

Herpes simplex virus reactivation and the mechanism of neuronal destruction

10:10 coffee break

Session V: Neuronal latency models

Moderator: Ravi Mahalingam

10:30 Victor Hsia

Electrophysiology of HSV-1 infection of DRG neurons during acute and quiescent phases

10:50 Ian Hogue

Alpha herpesvirus egress and spread uses constitutive secretory mechanisms and does not depend on action potential firing in neurons

11:10 Andrea Bertke

A novel RET agonist maintains HSV latency

11:30 Dave Bloom

Lund human mesencephalic neuronal cell line supports HSV-1 latency *in vitro*

11:50 Abel Viejo-Borbolla

Attempts to establish latency models for varicella zoster virus using human peripheral neurons

12:10 Leonardo D'Aiuto

Human brain organoids to model HSV1-CNS interactions

12:30 lunch & business meeting; Christiania Lodge

Friday afternoon, May 18

Session VI: Reactivation

Moderator: Scott Schmid

- 2:30 Angus C. Wilson
Towards a generalized model of HSV-1 reactivation, one step at a time
- 2:50 Clinton Jones
Regulation of reactivation from latency by stress-induced factors
- 3:10 Phil Krause
Is ICP27 the key to HSV latency?

Session VII: Poster presentations

Moderators: Caroline Kulesza & Seth Fietze

- 3:30 Oral overviews
- Poster 1 Andrew Bubak
Varicella zoster virus induces nuclear translocation of neurokinin-1 receptor, promoting lamellipodia formation and viral spread in spinal astrocytes
- Poster 2 Daniel P. Depledge
Revisiting HSV-1 latency at single cell resolution
- Poster 3 Chiharu Graybill
Whole genome sequencing and GC-skew plot reveal potential origins of DNA replication in varicella-zoster virus (VZV)
- Poster 4 Alex Greninger
Ultrasensitive capture of human herpes simplex virus genomes directly from clinical samples reveals extraordinarily limited evolution in cell culture
- Poster 5 Hui-Lan Hu
Neuronal non-homologous end-joining (NHEJ) pathway regulates the HSV-1 latent-lytic switch
- Poster 6 Dallas Jones
VZV productively infects human PBMCs to modulate expression of immunoinhibitory proteins and blocking PD-L1 enhances virus-specific CD8⁺ T cell effector function
- Poster 7 Srinivas KP
Defining the stepwise nature of HSV-1 reactivation
- Poster 8 Orkide Koyuncu
The alpha herpesvirus switch: escape from silencing
- Poster 9 Mackenzie Shipley
Genome-wide surveillance of genital HSV-1 from multiple anatomic sites over time
- Poster 10 Emilia Vanni
The latency-associated transcript locus of herpes simplex virus 1 is a virulence determinant in human skin
- Poster 11 Benjamin E. Warner
Essential gene mutations in varicella-zoster virus without need for complementation
- Poster 12 Qiaojuan Zhang
Regulation of T-type Ca²⁺ channel expression by interleukin-6 in ND7/23 sensory-like neurons post HSV infection
- 4:00 Poster viewing
- 7:00 dinner; Up The Creek
- following dinner – fireside chat; Christiania Lodge, fireplace room

Saturday morning, May 19

7:00 breakfast; Christiania Lodge

departure

What's with the card at the end of the program?

Please use the note card at the end of the program to jot down any questions you may have that were not addressed during the meeting; these will be read at the Friday Night Fireside Chat for open discussion. Anytime during the meeting or after the poster session, please deposit the notecard (unsigned) in the box located by the door.

Discussants

Peter Baci
Nicholas Baird
John Blaho
Sara Bustos
Randy Cohrs
Jane Dantine
David Davido
Rachel Dawson
Seth Fietze
Michael D. Gershon
Charles Grose
Zeb Hawkins
William Jacobs
Ken Jones
Benedikt Kaufer
Peter Kennedy
Caroline Kulesza
Ravi Mahalingam
Todd Margolis
Satish Mehta
Maria Nagel
Faith Osinaga
Brent Palmer
Aaron Prattis
Joel Rovnak
Scott Schmid
Hannah Tsingine
Georges Verjans

8th
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POSTER SESSION

