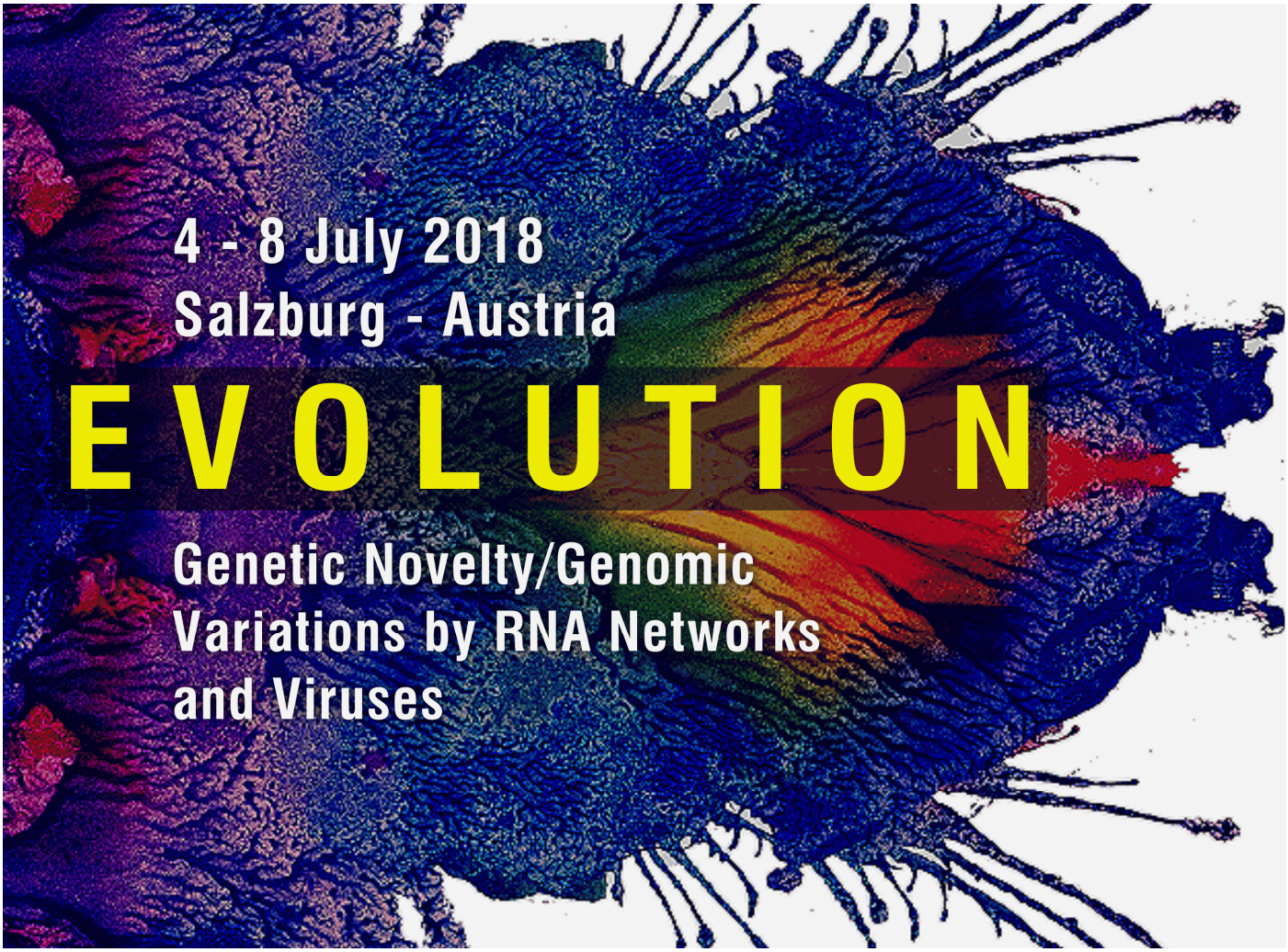

Programme
+
Abstracts

EVOLUTION –
Genetic Novelty/Genomic Variations by RNA-Networks and Viruses

4-8 July 2018, St. Virgil Conference Center, Salzburg

Registration: St. Virgil Conference Center

Programme
&
Abstracts

Talks
and
Poster-Presentations

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Programme & Abstracts

Wednesday, July 4, 2018

12:00 - 20.00 **Registration at St. Virgil**

19:45 **Welcome drink and warm reception by the organizer**

Thursday, 5th of July

8.45 Organization Affairs!

9.00 – 9.30 Guenther Witzany
Introduction: A New Concept of Life will lead to a New Theory of Evolution

9.30 – 10.00 Luis Villarreal
RNA virus opens the door from fittest type to RNA collectives: a personal account

10.00 – 10.30 Valerian V. Dolja
Origins and Evolution of the Global RNA Virome

Coffee Break – Tea Time (20 minutes)

11.00 – 11.30 Karin Moelling
What can viruses tell us about evolution?

11.30 – 12.00 Eugene V. Koonin
Inevitability of genetic parasites and their role in major evolutionary transitions

12.00 - 12.30 Mart Krupovic
Capsidocentric view on virus diversity, origins and evolution

12.30 – 13.00 Matti Jalasvuori
How genetically interconnected is the global microbiome?

Lunch

14.00 – 14.30 James A. Shapiro
No Genome is an Island: Developing a 21st Century Agenda for Experimental Evolution

14.30 – 15.00 Gustavo Caetano-Anollés
A 'double tale' of accretion in the structure of biological networks

15.00 – 15.30 Bryan R. Cullen
Viral epitranscriptomics

Coffee Break – Tea Time (20 minutes)

15.50 – 16.30 POSTER PRESENTATIONS

16.30 – 17.00 Felix Broecker
Did viruses build our immune systems?

17.00 – 17.30 Dušan Kordiš
The life history of domesticated genes illuminates the evolution of novel mammalian genes

17.30 – 18.00 Forest Rohwer
Piggybacking the Immune System and Pathogens

Friday 6th of July

8.45 Organization Affairs!

9.00 – 9.30 Erez Levanon
A-to-I RNA editing - immune protector and transcriptome diversifier

9.30 – 10.00 Corrado Spadafora
LINE-1 ORF2p-dependent chromatin remodeling, in response to stressing stimuli

10.00 – 10.30 Keizo Tomonaga
Roles of RNA transcripts from endogenous bornavirus-like elements in host evolution

Coffee Break – Tea Time (20 minutes)

11.00 – 11.30 Jeff Miller
Accelerated evolution by diversity generating retroelements in phage, microbes and microbiomes

11.30 – 12.00 Mariusz Nowacki
RNA-mediated trans-generational inheritance in ciliates

12.00 – 12.30 Irene Chen
Evolution and emergence of functional RNA: mapping the fitness landscape'

12.30 – 13.00 Sabine Müller
A small ribozyme as key mediator of diverse RNA processing pathways

Lunch

14.00 – 14.30 Norikazu Ichihashi
Experimental evolution of self-replicating RNAs with spontaneously-appeared parasites

14.30 – 15.00 Ulrich Müller
Lab Evolution of Group I Intron Spliceozymes in Cells

15.00 – 15.30 Julian Chen
Origin and Evolution of Telomerase

Coffee Break – Tea Time (20 minutes)

16.00 – 16.30 Jordi Gomez
mRNA Archaeaology

16.30 – 17.00 Andreas Werner
The many Faces of Antisense Transcripts

17.00 – 17.30 Reynald Gillet
Origins of tmRNA: the missing link in the birth of protein synthesis?

17.30 – 18.00 Tomohiro Mochizuki
New hyperthermophilic crenarchaeal virus with unusual genotype

19.30 – 21.00 **Music Performance, Conference Diner**

Saturday, 7th of July

8.45 Organization Affairs!

9.00 – 9.30 Eric Westhof
An evolutive and integrated view of the genetic code

9.30 – 10.00 Bojan Zagrovic
RNA-protein interactions and the structure of the genetic code

10.00 – 10.30 Steven Zimmerly
The evolutionary versatility of group II introns

Coffee Break – Tea Time (20 minutes)

11.00 – 11.30 Jan Attig
RNA-binding proteins limit and constrain the emergence of exons from Retrotransposons

11.30 – 12.00 Jonathan Stoye
The evolutionary journey of Fv1

12.00 – 12.30 David Prangishvili
How to package DNA: lessons from archaeal viruses

12.30 – 13.00 Lennart Randau
The small RNA landscape of hyperthermophilic archaea

Lunch

14.00 – 14.30 Chantal Abergel
Mimiviridae "Ménage à trois"

14.30 – 15.00 Matthias Fischer
Heterotrophic protists as a genomic hub for virophages and other mobile genetic elements

15.00 – 15.30 Hervé Seligmann
Giant viruses as protein-coated amoeban mitochondria?

Coffee Break – Tea Time (20 minutes)

15.50 – 16.30 POSTER PRESENTATIONS

16.30 – 17.00 Jean-Michel Claverie
Diversity and evolution of the emerging Pandoraviridae family

17.00 – 17.30 David Gilmer
Multipartite Phytovirus Long Distance Movement: Keep Connected or Die

17.30 – 18.00 Nobuto Takeuchi
The origin of the central dogma through conflicting multilevel evolution

Sunday, 8th of July

Sunday-Excursion half day (9.30 – 13.00) to an extraordinary place near Salzburg: **Salzburg Open-Air Museum**

(30 Euros including: transfer, guided tour and meals)

The **Salzburg Open-Air Museum** awaits you with 100 authentic and original historical buildings rebuilt on the museum grounds, telling tales of historic farming, trades, rural crafts and manufacturing. Take time to set off for a stroll through the past and dip deep into the rural history of Salzburg over the past six centuries.

Explore old farmhouses, marvel at the humble, yet multifaceted lifestyle of days long gone and enjoy the hospitality of the museum's cozy tavern. Take an unforgettable ride on the historic steam engine heritage railway through the scenic natural landscape of the museum grounds, which cover 50 hectares.

ABSTRACTS

Mimiviridae "Ménage à trois"

Sandra Jeudy[a], Lionel Bertaux[a], Jean-Marie Alempic[a], Audrey Lartigue[a], Matthieu Legendre[a], Nadège Philipp[a], Laure Beucher[b], Emanuele G. Biondi[a], Sissel Juul[c], Daniel J. Turner[c], Yohann Couté[b], Jean-Michel Claverie[a], **Chantal Abergel**[a]
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ABSTRACT
The discovery of Mimivirus in 2003 broadened the frontier of virology by revealing the existence of giant viruses with particle sizes and gene contents akin to that of cellular microbes. Among the growing list of giant viruses, the Mimiviridae stand out by their diversity (of size, gene content and host) and the fact that they can be parasitized by virophages. Moreover, Acanthamoeba-infecting Mimiviridae, present a uniquely complex mobilome. They encompass three clades each of which can be infected by different virophages and 7 kb-dsDNA transpovirons. Following our isolation of Megavirus vitis (clade C) with the Zamilon vitis virophage and the mvtv transpoviron, and of Moumouvirus australensis (clade B) associated to the matv transpoviron, we investigated the interaction network governing the differential propagation of the various mobilome components. We used Mass spectrometry-based analyses to characterize the proteomes of Z. vitis virophage particles produced in various host viruses replicating different transpovirons. The resulting virophage particles are composed of a surprisingly complex, albeit consistent, set of virophage, host virus and transpoviron-encoded proteins. Symmetrically, mobilome proteins were found in the host virus particles testifying to an intricate "ménage à trois". Our results indicate that transpovirons propagate both through virophage and host virus particles and exhibit clade selectivity.

A 'double tale' of accretion in the structure of biological networks

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ABSTRACT
The evolution of structure in biology is driven by accretion and change. Accretion brings together disparate parts to form bigger wholes. Change provides opportunities for growth and innovation. Networks can describe how parts associate in wholes. Here I review patterns and processes that are responsible for a 'double tale' of evolutionary accretion in the structure of biological networks. Parts are at first weakly linked and associate variously. As they diversify, they compete with each other and are selected for performance. The emerging interactions constrain their structure and associations. This causes parts to self-organize into modules with tight linkage. In a second phase, variants of the modules evolve and become new parts for a new generative cycle of higher-level organization. Evolutionary genomics and network biology support the 'double tale' of structural module creation and validate an evolutionary principle of maximum abundance that drives the gain and loss of modules. Examples of network evolution at various levels of complexity include the emergence of metabolic networks, the rise and diversification of the proteome, and the evolution of the ribosomal RNA scaffold that supports protein biosynthesis. Remarkably, the phylogenomic data-driven double tale of evolutionary accretion was already recounted in P. Strasb. Gr. Inv. 1665-6, a ~2,000-year-old papyrus roll from the ancient city of Panopolis in Upper Egypt archived at the University of Strasbourg national library.

RNA-binding proteins limit and constrain the emergence of exons from retrotransposons

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ABSTRACT
Retrotransposons are self-replicating genetic elements and pervasive in mammalian genomes. Most insertions are passive bystanders of genome function evolving by genomic drift, and are examples for a neutral model of sequence evolution. Yet, individual sequences have been adapted in diverse biological functions, from neurogenesis to placentation.
Adaptation is dependent upon presence or formation of exons, a pre-requisite for protein expression. I will present our transcriptome-wide analysis of the exonisation of Alu, LINE and LTR retrotransposons, the RNA-binding proteins (RBPs) that regulate this process, and the sequence constraints on exon emergence. I will argue that splice-repressive RBPs ensure a gradual emergence of exons from retrotransposons, and I will discuss possible implications for the evolution of retrotransposal sequences.

Did viruses build our immune systems?

Felix Broecker[1]
and Karin Moelling[2]
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ABSTRACT
Many pro- and eukaryotic antiviral immune systems share surprising similarities with replication machineries of viruses/transposons. For instance, Argonaute/PIWI enzymes at the core of RNA interference against viruses and transposons are structurally and functionally related to the retroviral reverse transcriptase (RT)-RNase H. RNase H-like enzymes are also involved in the eukaryotic interferon response, V(D)J recombination, the process generating antibody diversity, and in the prokaryotic CRISPR-Cas and bacteriophage exclusion (BREX) systems. Interestingly, the RNase H-like proteins mediating V(D)J recombination and CRISPR-Cas defense both evolutionarily originate from transposons. Endogenized retroviral envelope proteins, the syncytins, prevent maternal immunity against the fetus. Other endogenous viral elements from Borna- or Filoviruses may have rendered the host immune to the respective exogenous viruses. In this context, we have analyzed a previously poorly described HERV-K(HML-10) family of human endogenous retroviruses (HERVs) that has been suspected to modulate immunity by regulating expression of the complement component C4 gene. HML-10 invaded the ancestral genome about 35 million years ago and has been preferentially fixed in regions involved in immune defense. We show that many LTRs of HML-10 are functional promoters regulated by interferon and that retroviral transcripts can modulate gene expression and apoptosis *in vitro*. Although suppression of apoptosis and increased RT-RNase H activity originating from HERVs and other retroelements are hallmarks of cancer cells, a causal contribution of HERV expression during carcinogenesis is debated. We conclude that viruses/transposable elements have majorly contributed to the evolution of pro- and eukaryotic immune systems through various mechanisms, often involving RNase H-like enzymes.

Evolution and emergence of functional RNA: mapping the fitness landscape'.

Irene Chen
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ABSTRACT
Evolutionary outcomes are difficult, if not impossible, to predict, largely because the effect of any possible mutation is unknown. In other words, understanding evolution requires detailed knowledge of the relationship between sequence and activity, or the fitness landscape. Inspired by the RNA World of early life, in which RNA carried information and also performed catalytic functions, we study the emergence and evolution of functional RNAs. I will describe our experimental efforts to map complete fitness landscapes for ribozymes and the implications for optimizing ribozyme activity and replaying the 'tape of life'.

Origin and Evolution of Telomerase

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ABSTRACT
Telomerase is a eukaryote-specific reverse transcriptase that provides a solution to the end-replication problem of linear chromosomes by adding short DNA repeats to chromosome ends to maintain genomic integrity. Telomerase functions as a ribonucleoprotein (RNP) complex, containing minimally the catalytic telomerase reverse transcriptase and the essential telomerase RNA. Since its discovery in 1985, telomerase has been intensively studied in select model organisms which include ciliates, yeasts, plants, and vertebrates. This has led to the realization that the telomerase RNP is remarkably divergent in size, composition, biogenesis pathway and even the underlying mechanism for DNA repeat synthesis. In recent years, my lab has cloned and studied telomerase from a variety of diverse groups of eukaryotes, which has provided new insights into the essential core of the telomerase enzyme and its evolution along distinct phylogenetic lineages. In my talk, I will discuss our recent progress in understanding the structural diversity of telomerase RNA and the possible origin of the telomerase ribonucleoprotein.

Diversity and evolution of the emerging Pandoraviridae family

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ABSTRACT
With DNA genomes reaching 2.5 Mb packed in particles of bacterium-like shape and dimension, the first two Acanthamoeba-infecting pandoraviruses remained up to now the most complex viruses since their discovery in 2013. Our isolation of three new strains from distant locations and environments allowed us to perform the first comparative genomics analysis of the emerging worldwide-distributed Pandoraviridae family. Thorough annotation of the genomes combining transcriptomic, proteomic, and bioinformatic analyses, led to the discovery of many non-coding transcripts while significantly reducing the former set of predicted protein-coding genes. We found that the pandoraviruses exhibit an open pan genome, the enormous size of which is not adequately explained by gene duplications or horizontal transfers. As most of the strain specific genes have no extant homolog and exhibit statistical features comparable to intergenic regions, we suggest that de novo gene creation could contribute to the evolution of the giant pandoravirus genomes.

Viral epitranscriptomics

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ABSTRACT
While it has been known for almost 40 years that a wide range of virally encoded RNAs, including mRNAs, are extensively modified by addition of a methyl group to the N6 position of adenosine (m6A), the functional consequences of this epitranscriptomic modification had remained unclear. However, the prevalence of m6A across multiple different viral species, and the recently demonstrated conservation of m6A residues in several distinct isolates of HIV-1, clearly implies that m6A favors some aspect of the viral replication cycle. More recently, the identification of the factors that add m6A to mRNAs, especially the m6A "writer" METTL3, and the definition of factors that bind m6A on mRNAs, including the key m6A "reader" YTHDF2, have allowed the phenotypic consequences of m6A addition to be more fully characterized. Using overexpression and/or genetic ablation strategies, as well as by mapping and mutationally inactivating specific viral mRNA m6A addition sites, we have now examined the effect of m6A in the context of three distinct viral families: the lentivirus HIV-1, the paramyxovirus influenza A virus (IAV) and the polyomavirus SV40. In all three cases, we observe that addition of m6A strongly enhances viral mRNA and protein expression, and hence replication, and, in the case of IAV, increases pathogenicity in vivo. In this presentation, I will discuss our current understanding of the mechanistic basis for this phenomenon.

Origins and Evolution of the Global RNA Virome

Valerian V. Dolja[1], Yuri I. Wolf[2], Darius Kazlauskas[3,4], Jaime Iranzo[2], Adriana Lucia-Sanz[2,5], Jens H. Kuhn[6], Mart Krupovic[4], Eugene V. Koonin[2]
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ABSTRACT
The RNA viruses dominate the virome of eukaryotes reaching enormous diversity in animals and plants. The recent advances of metaviromics uncovered enormous diversity of the RNA viruses calling for a comprehensive phylogenomic analysis. We performed such analysis aiming at the reconstruction of the evolution of expanded global RNA virome. Because the only universal gene among RNA viruses is the RNA-dependent RNA polymerase (RdRp), we developed a computational pipeline that alternates the construction of RdRp phylogenetic trees with refinement of the underlying multiple sequence alignments. The representative tree derived from the thousands of viral RdRps consists of five major branches, two of which include +RNA viruses, one is a mix of +RNA and dsRNA viruses, and two consist of dsRNA viruses and -RNA viruses, respectively. This tree topology suggests that dsRNA viruses evolved from +RNA viruses on at least two independent occasions, whereas -RNA viruses might evolved from dsRNA viruses. Analysis of the gene gain/loss pattern along the tree branches that the last common ancestor of +RNA viruses encoded only the RdRp and a jelly-roll capsid protein with later acquisition of additional genes facilitating virus replication and virus-host interactions in distinct lineages. Phylogenomic analysis also reveals extensive gene module exchange among diverse viruses and pervasive horizontal virus transfer between distantly related hosts. Although the complex network of evolutionary relationships within RNA virome is bound to expand, our findings provide for a more complete reconstruction of the evolution of all three classes of RNA viruses.

Heterotrophic protists as a genomic hub for virophages and other mobile genetic elements

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ABSTRACT
Endogenous viral elements are frequently encountered in eukaryotic genomes and represent remnants of mostly ancient integration events of various RNA and DNA viruses. Whereas reverse transcribing viruses integrate as part of their infection cycles, genome integration of eukaryotic DNA viruses is thought to be rare. Although the virophage mavirus, a parasite of the giant Cafeteria roenbergensis virus (CroV), does not require a genome integration step as part of its replication cycle, it integrates very efficiently into the nuclear genome of its host, a marine heterotrophic flagellate. This is demonstrated by laboratory experiments as well as by genome surveys of natural flagellate populations. Mavirus integration is not a one-way route, as CroV infection is able to reactivate the endogenous mavirus. Indeed, mavirus-type virophages genetically resemble eukaryotic mobile genetic elements of the Maverick/Polinton family and may act as an adaptive immune system against giant viruses in certain protists. A closer look at the tripartite protist-virus-virophage interactions reveals aspects of mutualism and altruism that defy our traditional views of microbes and their viruses. Through their high genome mobility, mavirus-type virophages are likely to act as vehicles of lateral gene transfer and influence genome stability and recombination in their flagellate hosts. In addition, virophages may also contribute to the spread of other mobile genetic elements such as retrotransposons and transpovirons among protist and giant virus populations.

Origins of tmRNA: the missing link in the birth of protein synthesis?

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ABSTRACT
In bacteria, trans-translation is the primary quality control mechanism for rescuing ribosomes arrested during translation. This key process is universally conserved and plays a critical role in the viability and virulence of all bacteria. It is performed by the large and structured tmRNA and its protein partner small protein B (SmpB). I will first present some structural aspects of trans-translation from our recent cryo-electron microscopy studies, addressing the movements of tmRNA-SmpB through a stalled ribosome, and more particularly the conformational changes needed to transit from one ribosomal site to one another. From these modern data, I will then present a model in which proto-tmRNAs were the first molecules on earth to support non-random protein synthesis, explaining the emergence of early genetic code. In fact, an ancient tmRNA could be the missing link between the first mRNA and tRNA molecules and modern ribosome-mediated protein synthesis.

Multipartite Phytovirus Long Distance Movement: Keep Connected or Die

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ABSTRACT
All living organisms have to preserve their genome integrity to generate progeny. Positive stranded RNA multipartite viruses possess a genome split on two or more segments, each individually packaged. Initial entry of virions occurs via aphid, fungus or protozoa vectors with a high multiplicity of infection (MOI) that provides the delivery of at least one copy of each segment in a cell. After expression and amplification, the infection spreads to adjacent cells and reaches plant vascular tissues before dissemination to distant organs. While the journey of monopartite entities appears rather simple, those for multipartite viruses require the delivery of at least one of each segment in distant cells to reinitiate progeny generation. Current models consider stochastic dissemination of viral segments together with high MOI.
The biology and the journey of the Beet necrotic yellow vein virus, the most segmented positive stranded RNA phytovirus will be revisited focusing on the requirement for the formation of an RNA network between the 4 to 5 genomic segments. This network requires Watson-Crick interactions stabilized by viral proteins described essential for viral long distance movement. Segment coding capacity combined with interaction constraints may add evolutionary constraint.

mRNA Archaeology

Jordi Gómez[1,2] and Ascensión Ariza-Mateos[1]
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ABSTRACT
Different theories concerning the origin of mRNA point to the concatenation and expansion of proto- tRNA motifs or proto-tRNA-like structures bound to an amino-acid. We have used different biochemical and biophysical factors to search for motifs with a specific structure in the mRNA of the hepatitis C virus and other phylogenetically related viruses, as well as in the hepatic mRNA population. tRNA-like motifs are located in structurally or functionally relevant positions both in viral and in one of the liver mRNAs examined, the interferon alpha 5 (IFN5A) mRNA. Additionally in hepatic mRNAs population, the tRNA-like motifs are in an excess at molar ratio, indicating they could have participated in the formation of mRNAs in the distant past. Expanding on this finding, we have observed the repetition of a dsRNA motif next to the tRNA-like motif in both viral RNAs and IFN5A mRNA. The discovery of these motifs and patterns could suggest that the concatenation of the observed tRNA-like and dsRNA motifs was a biochemical activity from the remote past of the RNA consortia. This approach makes us believe that we are drawing the distant past close to the present through a non-phylogenetic method.

Experimental evolution of self-replicating RNAs with spontaneously-appeared parasites

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ABSTRACT
Parasitic entities, such as viruses, are ubiquitous and also play an important role in the evolution of host organisms. Here, I present an experimental evidence that parasitic entities appear spontaneously in a simple RNA-protein self-replication system and affect the population dynamics and evolution of the host RNA. We used a translation-coupled RNA replication system encapsulated in water-in-oil droplets we have previously constructed(1). This system includes an artificial genomic RNA that replicates using the own encoded replication enzyme. During replication, a parasitic RNA, which lost the replication enzyme gene, spontaneously appeared and co-replicated with the genomic "host" RNA, representing an oscillation in population dynamics(2). The presence of the parasitic RNA facilitated the evolution of the host RNA and produced diversity in the host RNA. These results suggest that the origin of parasitic entities dates back to the ages of RNA replicators and have been playing an important role in the long evolution of life.

References
1. Ichihashi, N., K. Usui, et al. (2013). Darwinian evolution in a translation-coupled RNA replication system within a cell-like compartment. Nat Commun 4: 2494.
2. Bansho, Y., T. Furubayashi, et al. (2016). Host-parasite oscillation dynamics and evolution in a compartmentalized RNA replication system. Proceedings of the National Academy of Sciences of the United States of America 113: 4045-4050.

How genetically interconnected is the global microbiome?

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ABSTRACT
Every milligram of soil is a habitat for a billion bacteria and their genetic inhabitants such as phages and conjugative plasmids. There is also history around each bacterium: naked DNA from past relatives, dormant endospores and viruses without a susceptible host. In these communities, local adaptations are inevitably important, such as resistance to contemporary viruses. Viruses similarly adapt to changing hosts. But does this evolutionary arms race make only locally co-evolved parasites capable to retain their infectivity in the community? This does not seem to be the case since we can find infectious phages for bacteria also from across the world. Further, conjugative plasmids are transferred from maladapted bacteria to local inhabitants and bacteria can obtain naked DNA from the environment. Given that millions of bacteria and viruses are deposited from the atmosphere to every square metre of Earth every single day, we can ask a question about the global microbiome: how genetically interconnected it actually is? As of now, there is little understanding of the role of this connectivity on the evolution of local communities. Is it relevant at all? Or could it be even a dominant feature that continuously dilutes or enhances the relevance of local adaptations? I am discussing various factors that can affect local and global evolution of microbes, including Black Queen evolution and "time-travel" via dormant bacteria as well as suggesting potential experiments to investigate the question.

Inevitability of genetic parasites and their role in mahor evolutionary transitions

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ABSTRACT
Viruses and other selfish genetic elements (genetic parasites) are ubiquitous in cellular life forms and are the most abundant biological entities on earth. Moreover, the great majority of cellular organisms are hosts to multiple classes of genetic parasites that differ with respect to their commensal or predator relationships with the host, from benign transposons to highly virulent lytic viruses. Thermodynamic arguments suggest that parasite-protected states of replicators are inherently unstable on the evolutionary scale, and therefore, emergence of parasites is a fundamental, inalienable feature of replicator systems. Well-mixed replicator systems collapse under the pressure of parasites due to the Tragedy of the Commons. Only compartmentalized host-parasite systems can be evolutionarily stable, i.e. parasites drive evolution of biological complexity. Although all hosts evolve diverse anti-parasite defense systems, mathematical modeling indicates, in agreement with empirical data, that at least in prokaryotes, parasites cannot be purged because horizontal gene transfer rates that are required for survival of clonal populations exceed those required for parasite persistence. Host-parasite interactions appear to have played key roles in major evolutionary transitions such as the origin of the first cells, eukaryotic cells, and multicellular organisms.

The life history of domesticated genes illuminates the evolution of novel mammalian genes

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ABSTRACT
Molecular domestications of transposable elements have occurred repeatedly during the evolution of eukaryotes. Mammals possess numerous single copy domesticated genes that have originated from the intronless multicopy transposable elements. The genesis and regulatory wiring of the Metaviridae-derived domesticated genes have been explained through phylogenomic analysis of more than 90 chordate genomes. Phylogenomic analysis has demonstrated that major diversification of these domesticated genes occurred in the ancestor of placental mammals. Mammalian domesticated genes have originated in several steps by independent domestication events. The analysis of active Metaviridae lineages in amniotes has demonstrated that domesticated genes originated from retroelement remains. The analysis of syntenic loci has shown that diverse domesticated genes and their chromosomal positions were fully established in the ancestor of placental mammals. During the domestication process, de novo acquisition of regulatory regions was crucial for the survival of the novel domesticated genes. The origin and evolution of de novo acquired promoters and untranslated regions in diverse mammalian domesticated genes have been explained by comparative analysis of orthologous gene loci. The origin of placental mammal-specific innovations and adaptations, such as placenta and newly evolved brain functions, was most probably connected to the regulatory wiring of domesticated genes and their rapid fixation in the ancestor of placental mammals.

Capsidocentric view on virus diversity, origins and evolution

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ABSTRACT
The origin of viruses is an outstanding question in Biology. A unique feature of the virus state, which distinguishes viruses from all other types of mobile genetic elements, such as plasmids and transposons, is the ability to form virions. Thus, the origin of viruses is likely to be concomitant with the origin of the major virion proteins. In my talk, I will present evidence from comprehensive sequence and structure analysis of major virion proteins across the virosphere which indicates that these proteins evolved on about 20 independent occasions. In many cases, the origins of the capsid proteins can be traced to diverse ancestral proteins of cellular organisms. Comparison of the evolutionary patterns of the major virion proteins with those of the major genome replication proteins reveals promiscuous association of the two functional modules, with multiple exchanges across different classes of viruses. This observation indicates that the evolution of virion morphogenesis modules is uncoupled from that of the genome replication modules and the type of viral nucleic acid. Collectively, these results shed light on the global structural diversity in the viral world and illuminate some general patterns of virus origins and evolution.

A-to-I RNA editing - immune protector and transcriptome diversifier

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ABSTRACT
Modifications of RNA affect its function and stability. RNA editing is unique among these modifications because it not only alters the cellular fate of RNA molecules but also alters their sequence relative to the genome. The most common type of RNA editing is A-to-I editing by double-stranded RNA-specific adenosine deaminase (ADAR) enzymes. Recent transcriptomic studies have identified a number of 'recoding' sites at which A-to-I editing results in non-synonymous substitutions in protein-coding sequences. Many of these recoding sites are conserved within (but not usually across) lineages, are under positive selection and have functional and evolutionary importance. However, systematic mapping of the editome across the animal kingdom has revealed that most A-to-I editing sites are located within mobile elements in non-coding parts of the genome. Editing of these non-coding sites is thought to have a critical role in protecting against activation of innate immunity by self-transcripts. Both recoding and non-coding events have implications for genome evolution and, when deregulated, may lead to disease.

Accelerated evolution by diversity-generating retroelements in phage, microbes, and microbiomes

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ABSTRACT
Diversity-generating retroelements (DGRs) have evolved to increase host fitness by diversifying ligand-binding domains of variable proteins in bacteria, archaea, and their viruses. DGRs function through a mutagenic retrohoming mechanism in which an RNA intermediate serves as both the primer and template for a unique form of reverse transcriptase-dependent cDNA synthesis in which adenines are specifically miscopied, producing adenine-mutagenized cDNA that replaces parental sequences in genes that encode variable proteins. Naturally-occurring DGRs have the potential to generate astronomical levels of diversity, corresponding in many cases to >1026 unique DNA sequences in diversified genes. DGRs focus their vast mutagenic potential to evolve protein function by positioning variable nucleotides at sites that encode solvent exposed resides in ligand-binding domains. We have discovered an enrichment of DGRs in prominent members of the human microbiome, including numerous Bacteroides species. Bacteroides DGRs are encoded on distinct yet related integrative and conjugative elements that undergo chromosomal excision and transfer in the GI tracts of gnotobiotic mice, and recent evidence suggests they diversify a family of proteins that function as tip adhesins on a newly discovered pilus family with highly modular components. Our results demonstrate the horizontal transfer of accelerated evolvability, highlighting the dynamic nature of microbial genomes.

New hyperthermophilic crenarchaeal virus with unusual genotype

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ABSTRACT
Although life is believed to have started about 4 billion years ago in an RNA-world, without a single exception all extant cells use double-stranded (ds-)DNA as their genetic material. The only exception in modern biology can be found in the virosphere. They can employ all possible types of nucleic acid structures: single-/double-stranded, DNA/RNA, circular/linear. Viruses of the archaea, especially those infecting hyperthermophilic crenarchaea, are known to consist a distinctive virosphere with extremely diverse morphology and genetic sequences. Despite of their remarkable diversity, all known archaeal viruses are DNA viruses, mostly dsDNA. Previously, we have described the first hyperthermophilic ssDNA virus, a spring/coil-shaped virus ACV, which eventually led to the establishment of the Spiraviridae family (Mochizuki et al., 2012). One of the biggest surprise was that despite of the harsh environment where this virus and its host (Aeropyrum pernix) survive (90-100 °C), it had the largest known ssDNA genome of 24 kb. But unfortunately pure virus-host system was never obtained, and this ssDNA virus is no longer available, and therefore the ssDNA stability mechanism under extreme temperature condition is unknown. Recently, we have succeeded in isolating several new hyperthermophilic archaeal viruses. All of these are DNA viruses, but preliminary results indicate that one of them may be a ssDNA virus. Sequence analysis of these new viruses are currently being done, and their features will be presented, with special focus on the new potential ssDNA virus.

What can viruses tell us about evolution?

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ABSTRACT
We analyzed Reverse Transcriptase (RT) and RNase H-like sequences and folds as lead structures arranged in phylogenetic trees of various, even rare and ancient species, indicating evolution. RNases H are among the most ancient protein folds and are very abundant, 60.000 RNase H-like species were described. RT and RNase H counteract each other, synthesis also requires degradation, removal or processing. Related structures are present in integrase, transposase, terminase, argonautes, Cas, RAGs, Prp8 and others. We tried to analyze evolutionary aspects of groupII introns, retrophages, virophages, phytoplasms, DGRs (diversity generating retroelements, RT in Bordetella pertrussis phage), Retrons, prions - what do they tell us about evolution? We are trying to understand the role of RNases H in numerous immune defense systems such as ribozymes, silencing, editing, Interferons, or antibody diversity. Ribozymes/viroids may be among the earliest biopolymers on our planet. The discovery of exoplanets stimulates the search for earliest signs of life. Can one speculate about the role of viruses during evolution based on contemporary viruses? Viroids/ribozymes are still present today as ncRNAs with catalytic acitivities. Other viruses also look like precursors of cellular components, Sirna or tRNA-like (TLR)viruses. Viroids or even viruses may have changed from independent entities to obligatory intracellular life-styles. Loss of genes is underestimated in its importance as evolutionary force known in mitochondria, chloroplasts, Rickettsia, plants, and retroviruses (retroelements). Gain and loss led to oncogenes in retroviruses some with relevance for human caner (e.g. Raf). Loss can be complemented by the host or helper viruses (HDV or Carnation viroid and (para)retrovirus). Loss can be enforced by changes in environmental conditions (Qbeta,1000xpassages, most recently in obesity). Ref: Moelling et al, Frontiers in Microbiol.8:1745(2017).

A small ribozyme as key mediator of diverse RNA processing pathways

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ABSTRACT
Functional RNAs that contribute to higher genetic complexity and extended functional space are of high relevance to RNA world scenarios. We have engineered hairpin ribozyme variants that mediate RNA processing reactions in diverse scenarios, including circularization, oligomerization, splicing and recombination. The hairpin ribozyme is a rather small RNA that can make itself from even shorter fragments, which cooperate to form a functional complex. Therefore, it is a good model, mimicking the emergence and further development of functional entities starting from short RNA strands to molecules of higher complexity with extended genetic space and functionality. The key feature of the hairpin ribozyme is its unique cleavage-ligation behavior. The internal equilibrium is shifted towards ligation. Therefore, ligation is the favored activity, if fragments are bound to the ribozyme in a stable complex. Cleavage is preferred, if less stable complexes are formed, and if fragments can fast and easily dissociate preventing re-ligation. Thus, the preference for either cleavage or ligation markedly depends on the structural features of the ribozyme-substrate complex and surrounding conditions. This allows modulation of ribozyme function by structural manipulation. At the example of the hairpin ribozyme, we have demonstrated that by careful structural manipulation the inherent cleavage and ligation activity can be tuned to support diverse RNA processing pathways, which in the RNA world may have contributed to (i) the emergence of RNAs with catalytic activity, (ii) the extension of genetic space by oligomerization and/or recombination, and (iii) the control of activity by splicing or allosteric regulation.

Lab Evolution of Group I Intron Spliceozymes in Cells

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ABSTRACT
We have developed variants of group I intron ribozymes that are able to remove 100-nt intervening sequences of a substrate RNA and join the flanking sequences, in vitro and in cells. These ribozymes were termed spliceozymes because they are ribozymes that act like spliceosomes. However, their performance is nowhere near that of spliceosomes because the 'generation 1' (G1) spliceozymes require specific substrate sequences, need to be expressed at high concentrations in cells, and convert a large fraction of substrate to side products. We are conducting lab evolution experiments in bacterial cells that aim to recapitulate biochemical steps in the evolution of the spliceosomes. After ten cycles of evolving the G1 spliceozyme, a G2 spliceozyme emerged with increased splicing efficiency due to reduced side product formation. This appears to be caused by a re-balancing between 5'-splice site activity and 3'-splice site activity. Lab evolution experiments are underway towards a G3 spliceozyme, which is able to work at lower concentrations, and shows less dependence on the substrate sequence.

RNA-mediated trans-generational inheritance in ciliates

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ABSTRACT
Transgenerational inheritance can be defined as heritable changes to the state of DNA that may be passed on to subsequent generations without alterations to the underlying DNA sequence. Although this phenomenon has been extensively studied in many systems, studies of transgenerational inheritance in mammals and other higher-level eukaryotes may be complicated by the fact that many epigenetic marks are reprogrammed during sexual reproduction. This, by definition, may obscure our interpretation of what is in fact truly transgenerational. Probably the most striking evidence for transgenerational inheritance is the RNA-mediated programming of genome content in ciliates, where maternal small RNAs guide DNA rearrangement in the genome of the progeny. This epigenetic transmission of information between maternal nuclei and the genome of the offspring mediates large-scale elimination of active and inactive transposable elements, which is not only required for genome stability but also enables genetic changes be passed on to the offspring.
I present recent progress in this dynamic field and argue that RNA-mediated DNA targeting pathways provide an optimal system for the transgenerational inheritance of acquired traits. Ciliates thus also demonstrate the evolutionary value of transposable elements, both as sources of sequence diversity and also as drivers of adaptive evolution by necessitating defensive systems.

How to package DNA: lessons from archaeal viruses

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ABSTRACT
One of the most intriguing results of the research on viral diversity on our planet is the revelation of unusual features of DNA viruses infecting Archaea, particularly those thriving in extreme thermal environments at temperatures above 80°C [1, 2]. Unusual features of this group of viruses include incredible diversity of elaborate virion architectures, many of which have never been observed among DNA viruses of Bacteria or Eukaryotes, as well as their genetic content, which in some cases is literally terra incognita, without a single gene with homologs in extant databases [3]. Hyperthemophilic archaeal viruses are remarkable also due to their capacity to withstand extreme conditions that are usually destructive for nucleic acids. The reconstruction of virion structures at near atomic resolution led to unexpected discoveries, such as the A-form DNA in virions and a new type of lipid membrane in virion envelopes, and revealed biological mechanisms protecting DNA at extremely high temperatures [4-6]. The results contribute to a deeper understanding of chemical and molecular basis for the stability of biomacromolecular complexes in adverse conditions.

References
1.Prangishvili D. 2013. The wonderful world of archaeal viruses. Ann. Rev. Microbiol. 67: 565-585.
2.Prangishvili D#, DH Bamford, P Forterre, J Iranzo, EV Koonin, and M Krupovic#. 2017. The enigmatic archaeal virosphere. Nat. Rev. Microbiol. 15: 724–739.
3.Krupovic M, V Cvirkaite-Krupovic, J Iranzo, D Prangishvili, and EV Koonin. 2018. Viruses of Archaea: Structural, functional, environmental and evolutionary genomics. Virus Res. 244: 181-193.
4.Ptchelkine D, S Gillum, T Mochizuki, S Lucas-Staat, Y Liu, M Krupovic, SEV Phillips, D Prangishvili#, and JT Huiskonen#. 2017. Unique architecture of thermophilic archaeal virus APBV1 and its genome packaging. Nat. Commun. 8: 1436.
5.Kasson P, F DiMaio, X Yu, S Lucas-Staat, M Krupovic, S Schouten, D Prangishvili#, and EH Egelman#. 2017. An envelope of a filamentous virus carries lipids in a horseshoe conformation. Elife, 6: e26268.
6.DiMaio F, X Yu, E Rensen, M Krupovic, D Prangishvili#, and EH Egelman#. 2015. A virus that infects a hyperthermophile encapsidates A-form DNA. Science 348: 914-917.

The small RNA landscape of hyperthermophilic archaea

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ABSTRACT
RNA-seq approaches revealed the production and processing of small RNA species in hyperthermophilic archaea. The extreme growth temperatures of these organisms pose significant challenges for RNA stability and folding. Our laboratory investigates several RNA stabilization mechanisms: (i) C/D box sRNA genes are abundant in hyperthermophilic archaea and are required for defining target sites of 2'-O methylation reactions. These RNA modifications increase RNA stability and are thought to assist rRNA folding. Examples of C/D box sRNA chaperones have been identified. C/D box sRNA genes have been discovered in different genetic contexts; they were shown to highjack promoters of adjacent genes and can utilize their start and stop codons for the generation of the signature C and D box motifs. In addition, C/D box sRNA genes have frequently been observed near gene fragmentation sites. (ii) One example for a genomic rearrangement event near a C/D box sRNA gene was identified in Thermoproteus tenax. Here, the gene coding for the universal RNA component of the signal recognition particle (SRP) was found to be permuted. The SRP RNA transcript is processed by the tRNA splicing endonuclease and an RNA ligase, generating a functional, circular SRP RNA molecule. The elevated stability of this RNA circle should provide an evolutionary advantage at high growth temperatures. (iii) Finally, stable double-stranded RNA molecules were investigated in Sulfolobus acidocaldarius and the involvment of an RNA duplex in biofilm formation was discovered.

Piggybacking the Immune System and Pathogens

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Most bacterial pathogens are lysogens, cells carrying prophage. Acquisition of prophage creates lysogens in situ and reinforces pathogenic ecosystems. Recently, we have also shown that phage, released from lysogens in the microbome, form a bacterial selective, adaptive immune system protecting the mucosal surfaces of animals. This is probably the origin of the selective immune system. Underlying both of these phenomena are an ecological process called Piggyback-the-Winner that facilitates evolutionary, Red Queen dynamics.

Giant viruses as protein-coated amoeban mitochondria?

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ABSTRACT
Mimivirus' genome includes parts of 5S, 16S and 23S ribosomal RNAs encoded by Acanthamoeba's mitogenome, the giant virus' host. Two non-exclusive hypotheses for rRNA remnants in giant viruses are examined: 1. mitogenomes invade viral genomes as they do for nuclear chromosomes (producing numts); 2. megaviral genomes evolved from an ancestral mitogenome. Alignment analyses confirm mitochondrial, rather than alphaproteobacterial origins of megaviral rRNAs. Other mitogenes have likely megaviral homologues. These megaviral homologues coevolve to much larger extents than candidate rRNA homologues, suggesting rRNA decay in viruses. Megaviral mitogene homologues overall follow mitochondrial gene order, suggesting mitogenome ancestry. Ancestral synteny decreases with megaviral genome size, suggesting that subsequent random mitogene insertions blur ancestral gene order and that defenses against DNA invasion conserve mitogene order in short megaviral genomes. Synteny between mitogenome and megaviral genomes confirms the RNA/DNA polymerase-homologies-based hypothesis that giant viruses have mitochondrial-like ancestors, viral rRNA remnants are corollary of mitogenomic origins of megaviral genomes. Note that giant viruses, mitochondria and bacterial spores all have double membranes, spores and viruses have protein coats. Rare, still undescribed spore-like structures formed by mitochondria might have produced megaviruses.
Key words: shared synteny; genome invasion; gene order; Rickettsia; Acanthamoeba castellanii.

No Genome is an Island: Developing a 21st Century Agenda for Experimental Evolution

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ABSTRACT
Conventional 20th Century evolution thinking was based on the idea of isolated genomes for each species. Any possibility of life-history inputs to the germ-line was strictly excluded (Weismann's doctrine), and genome change was attributed to random copying errors. Today we know that many life-history events lead to rapid and non-random evolutionary change mediated by specific cellular functions. These include cell mergers and activation of natural genetic engineering by stress, infection and interspecific hybridization. In addition, we know of molecular mechanisms for transmitting life history information across generations through gametes. These discoveries require a new agenda for evolutionary experiments to determine the genomic impacts of abiotic stresses, biotic interactions, and sensory inputs from environmental conditions. The presentation will offer some generic recommendations for enriching evolution experiments to incorporate new knowledge and find answers to previously excluded questions.

LINE-1 ORF2p-dependent chromatin remodeling, in response to stressing stimuli

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ABSTRACT
Long Interspersed Nuclear Elements (LINE-1) are autonomous retrotransposable elements that encode the protein ORF2p, comprising reverse transcriptase (RT) and endonuclease (EN) activities, both required for LINE-1's own mobilization. LINE-1-encoded ORF2p is highly expressed in human cancers. Inhibition of ORF2p- derived RT using the nonnucleoside inhibitor efavirenz antagonizes cancer proliferation, both in preclinical studies and in a phase-II human trial, suggesting that ORF2p overexpression has functional roles in tumorigenesis.
We show that, unexpectedly, efavirenz up-regulates the expression of ORF2p, which undergoes nuclear translocation and accumulation. Efavirenz selectively inhibits the RT activity of ORF2p, whereas EN retains an unaltered ability to cleave nuclear DNA. This generates double-strand breaks, concomitant with the fragmentation and eventual disappearance of the nuclear lamina. Thus, unrestricted LINE-1-derived EN activity, uncoupled from RT, releases nuclear scaffold-associated domains and induces a chromatin conformation highly prone to variations. Indeed, RT inhibition induces changes in key epigenetic hallmarks associated with a global reprogramming of expression of coding genes, microRNAs (miRNAs) and genomic ultra-conserved regions (UCRs). These variations are reversible, as cells revert to their original condition upon discontinuation of the efavirenz treatment.
These results provide a mechanistic key to understand the implication of ORF2p in cancer. Furthermore they suggest that LINE-1 ORF2p mediates a stress-responsive phenomenon, inducible by a variety of stressors, in which the chromatin organization can be rapidly reformatted and acquire roles in cell fate determination that can contribute to adaptive processes over evolutionary time.

The evolutionary journey of Fv1

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ABSTRACT
Both exogenous and endogenous retroviruses have long been studied in mice, and some of the earliest mouse studies focused on the heritability of genetic factors influencing sensitivity to infection. The prototypic retroviral restriction factor, Fv1, is now understood to exhibit a degree of control across multiple retroviral genera and is highly diverse within the genus Mus. To better understand the age and evolutionary history of Fv1, a comprehensive survey of the Muroidea was conducted, allowing the progenitor integration to be dated to ~45 million years. Intact coding potential is visible beyond the genus Mus and sequence analysis revealed strong signatures of positive selection within field mice, Apodemus. Fv1's survival and evolution over such a period implies a recurring and shifting retroviral burden imparting the necessary selective pressures – an influence likely also common to analogous factors. Patterns of variability across Fv1 highlight its preference for repeated structures and suggest that the functionally constrained properties of the retroviral capsid lattice present a common target in the evolution of virus binding restriction factors.

The origin of the central dogma through conflicting multilevel evolution

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ABSTRACT
Molecular biology embodies three asymmetries between genomes and enzymes. Information flows from genomes to enzymes, but not from enzymes to genomes: informatic asymmetry (i.e. the central dogma of molecular biology). Genomes serve as templates, whereas enzymes serve as catalysts: functional asymmetry. Genomes are less abundant than enzymes per cell: numerical asymmetry. How did these asymmetries first arise in primordial cells? Although existing theories can explain subsets of them, no theory has been able to explain all at one stroke. Here we provide such a theory by showing that all these asymmetries can spontaneously arise from conflicting multilevel evolution. Our model assumes a population of protocells, each containing a population of self-replicating catalytic molecules. The model incorporates a conflict between evolution at the molecular level and evolution at the cellular level, which arises from a trade-off between a molecule's catalytic activity and templating ability. We found that this conflicting multilevel evolution forms a positive feedback loop with the asymmetric flow of information between the molecules, which induces the division of labor between primordial genomes and enzymes. Our results provide a novel evolutionary explanation for the origin of the fundamental molecular asymmetries underlying all life.

Roles of RNA transcripts from endogenous bornavirus-like elements in host evolution

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ABSTRACT
Bornavirus, a nonsegmented negative-strand RNA virus, is unique among animal RNA viruses in that it not only replicates in the cell nucleus, but also establishes a persistent infection without any cytopathic effects. Interestingly, bornavirus has been shown to integrate a DNA genome copy into the host chromosomal DNA by using host retrotransposon, such as LINE-1. We have also discovered that bornaviruses have left their own endogenous elements, called endogenous bornavirus-like elements (EBLs), in the genomes of many animal species, including humans, as footprints of their ancient infection. Despite millions of years of evolution as endogenous viruses, many EBLs still show high sequence homology with current bornaviruses and are transcribed into the RNA in the host cells. Therefore, it is intriguing to investigate whether EBLs have acquired functions as RNAs and affected host evolution. In this talk I will present our recent results of the roles of RNA transcripts from EBLs in human genome and discuss about significance of RNA virus endogenization in host evolution. Our data would provide new insights into the evolutionary relationship between RNA viruses and hosts.

RNA virus opens the door from fittest type to RNA collectives: a personal account

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ABSTRACT
For many years, Gunther Witzany and I have promoted the view that viruses provide major influence on the origin of host and acquisition of host complexity. But from the accepted neo Darwinian stance (post modern synthesis of evolutionary biology), viruses are 'extremely selfish' fittest types whose creative role would simply be to provide variation that can sometimes be exapted by host survivors to attain higher individual fitness. This is the conceptual framework (room) most of us occupy. But the virosphere itself dictates host survivors and virus-host symbionts present clear advantages. Even more compelling, RNA (and retro) viruses have experimentally demonstrated quasi species (QS) behaviors that are much more consortial then initially proposed. "Unfit' minorities can interact to direct the outcome of a virus population. I initially encountered this phenomena studying defective interfering virus of VSV in the early 1970s while characterizing the virion associated RNA polymerase. In time, it became clear that small non-coding viral RNAs with some dsRNA character were generally directing regulation (transcription, replication) and mediating interference. However, to a large extent, the experimental observations of consortial RNA viruses QS have been ignored. But if we generalize these RNA virus features, we open a new conceptual door to collective behaviors from which interacting RNA networks (and communication) naturally emerge. From this perspective, we can propose a pathway for the origin of RNA consortia based life. We can also account for why various distinct retroviruses were involved in acquisition of complex phenotype, such the species specific origin of mammalian placentas or programming stem cells.

The many faces of antisense transcripts

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ABSTRACT
Large proportions of the human genome do not code for proteins and were long considered as junk. Recent studies, however, show that transcription occurs in noncoding regions and also in the opposite direction of protein coding genes. The resulting antisense transcripts and noncoding RNAs have emerged as essential and abundant regulators of eukaryotic gene expression.
Natural antisense transcripts are defined as RNAs from the opposite strand of protein coding genes that share complementarity with the cognate sense transcript. The production of antisense transcripts is counterintuitive since the formation of double stranded RNA (dsRNA, as a result of co-expressed sense and antisense transcripts) activates protein kinase R, the immune system and may eventually kill the cell. Nevertheless, antisense transcripts are found in all tissues but are particularly prevalent in testis. To investigate the physiological role(s) of natural antisense transcripts we have immune-precipitated RNA-RNA duplexes from mouse testis followed by RNA-seq. Several thousand genes give rise to dsRNA, some of which were confirmed by RT-qPCR, moreover, we find more bi-directionally expressed genes in testis as compared to other tissues.
In order to investigate the cellular consequences of convergent transcription we have established a HEK293 cell line system where we can transiently induce the transcription of the sense gene (SLC34A1) and the antisense RNA (read-through transcript, alternative splice form of PFN3) using dexamethasone. Transcriptional changes are paralleled by epigenetic modifications. These studies are complemented with HEK293 cells that carry transcriptional termination signals either in SLC34A1 or PFN3 upstream of the potential RNA overlaps.

An evolutive and integrated view of the genetic code

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ABSTRACT
An integrative view of all the complex interaction networks between messenger RNA, transfer RNA, and ribosomal RNA is described: the stability of codon-anticodon trimers, the conformation of the anticodon stem-loop of transfer RNA, the modified nucleotides, and the interactions with bases of ribosomal RNA at the decoding site. An information-rich, alternative representation of the codon table is derived. The new organization of the 64 codons is circular with an asymmetric distribution of codons and leads to a clear segregation between GC-rich 4-codon boxes and AU-rich 2:2-codon and 3:1-codon boxes. The advantage of integrating data in this circular decoding system is that all transfer RNA sequence variations can be visualized, within an internal structural and energy framework, for each organism and anticodon. Within this new representation, the multiplicity and complexity of nucleotide modifications, especially at base positions 34 and 37 in the anticodon loop, segregate meaningfully and correlate well with the necessity to stabilize AU-rich codon-anticodon pairs and to avoid miscoding in split codon boxes. Further, chemical modifications of base U34 are critical to decode purine-ending codons in split codon boxes. These chemical modifications allow for diversity in codon usage depending on the genomic GC content as well as on the number and types of isoacceptor tRNAs. This structure-based network of interactions results in an energetically uniform decoding of all native and fully modified tRNAs. Depending on presence or levels of modifications, translation can adapt to the cellular constraints. The evolution and expansion of the genetic code is viewed as originally based on GC content and "old" amino acids (like Ala, Gly, Pro) with the progressive introduction of A/U codons and additional amino acid decoding together with tRNA modifications and the modification enzymes. Because of the coupling with metabolism and enzymatic machineries, although universal, the genetic code is not translated identically and codon use and bias differ between organisms in the three kingdoms of life. To decipher diversely but efficiently the genetic code, cells developed sophisticated co-evolution patterns between transfer RNA pools and modifications, anchored in the cellular metabolic enzymatic pathways and guaranteeing protein homeostasis.

RNA-protein interactions and the structure of the genetic code

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ABSTRACT
The relationship between mRNA and protein sequences as embodied in the universal genetic code is a cornerstone of modern-day molecular biology. I will provide evidence supporting a novel claim that the genetic code can be seen as a Rosetta stone for understanding RNA-protein interactions in general. Conversely, I will defend the idea that RNA-protein interactions could have been an important driving force behind the origin of the genetic code. Specifically, we have recently revealed a robust, statistically significant matching between the composition of mRNA coding sequences and the nucleobase-binding preferences of their cognate protein sequences. For example, purine-density profiles of mRNA sequences mirror the guanine-affinity profiles of their cognate protein sequences with quantitative accuracy (median Pearson correlation coefficient |R| = 0.80 across the entire human proteome). Overall, our results support as well as redefine the stereochemical hypothesis concerning the origin of the genetic code, the idea that it evolved from direct interactions between amino acids and the appropriate bases. Moreover, our findings support the possibility of direct, complementary, co-aligned interactions between mRNAs and their cognate proteins even in present-day cells, especially if both are unstructured, with implications extending to different facets of nucleic-acid/protein biology. In particular, I will discuss the implications of the complementarity hypothesis in the context of viral capsid assembly.

The evolutionary versatility of group II introns

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ABSTRACT
Group II introns are ancient catalytic RNAs and mobile DNAs that have spread among bacterial, archaeal, mitochondrial and chloroplast genomes. Although not present in nuclear genomes, they are the likely ancestors of eukaryotic pre-mRNA introns as well as non-LTR retroelements. As retroelements, group II introns proliferate selfishly, yet they harm their hosts relatively little because they splice out of interrupted genes after transcription. Group II introns have evolved into a surprising number of derivative and specialized forms in both bacteria and organelles, which will be summarized. For both catalytic RNAs and mobile DNAs is it often challenging to obtain robust phylogenetic data to infer their evolution. While this is true of group II introns, it is nevertheless possible to outline an evolutionary history to account for the development of the major intron lineages, their derivative forms, their migrations among organisms and cellular compartments, and their eventual evolution into spliceosomal introns and non-LTR retroelements.

Introduction: A new Definition of Life will lead to a new Theory of Evolution

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Three levels of biocommunication (cell-cell communication, RNA-RNA/DNA/Protein interactions, virosphere) are essential for organizing and coordinating all life processes. If one level is completely missing, we could not speak seriously of life.

The interactions between these three levels (cells, RNA Networks, virosphere) sheds light onto evolutionary processes depending on genetic novelty and genomic variations beyond the error replication (mutations) narrative.

POSTER
Abstracts

Penelope retrotransposons in flatworms: diversity, evolution and ribozyme-coding properties

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ABSTRACT
Retrotransposons are a group of mobile genetic elements capable to transposition through RNA intermediate. They are known to be a major part of eukaryotic genomes and drivers of genomic evolution. In this work I present genome-wide data on diversity, phylogeny, evolutionary dynamics and structure of Penelope-like elements (PLE) in flatworms. PLE is an enigmatic and ancient class of retrotransposons found in genomes of many eukaryotes and known for their ability to encode HH-ribozymes. For this particular research a computational pipeline was developed allowing a researcher to retrieve coding sequences of retrotransposons from genome assemblies. This pipeline was applied to genome assemblies of 36 flatworm species including those of medical and veterinary importance. It was found that the diversity of PLE in genomes of flatworms is underestimated: the data suggest that there are many previously unknown PLE families in the genomes of Trematoda and some Cestoda worms. On the contrary, some Cestoda genomes demonstrate full absence of nearly active PLE copies (genera Echinococcus and Hymenolepis). Moreover it was found four species from different classes with very high and therefore unusual level of PLE activity. Also the collected data suggest that PLE do not fit "master copy" model of retrotransposition.
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Keywords: genomics, retrotransposons, penelope, evolution, flatworms

Implementing protein structure information to detect ancient endogenous viral elements

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ABSTRACT
It is known that the number of viruses in different biotopes exceeds the number of cells usually by an order of magnitude. Also, most, if not all, organisms are under permanent attack of viruses. Hence, the flow-through of viral genetic material for organisms is huge. So, it is not surprising that from this very intensive flow-through some of the (not just retroviral but also non-retroviral) viral genes have been integrated into eukaryotic genomes. Some of these genes are not only integrated but also fixed in population and spread over the world (however, in most cases the reason for that is not yet very clear).

All these virus-to-host (V2H) transfers have been identified using BLAST analysis. Viruses are very fast evolving units and thus, the detectable sequence similarity may disappear. I am using the power of Hidden Markov Models of protein domains together with structural information to detect more ancestral V2H transfers. I have been concentrating in one particular integration: relatives of tobamoviral (Virgaviridae) sequences that have been identified in different fly genomes (including Drosophila melanogaster). These homologous sequences have not been identified using BLAST analysis. Hence, the aim of my work is that HMMs and structural information should be implemented in EVE detection protocols. Applying this method allowed to find more ancestral V2H transfers and give us more comprehensive picture/knowledge on the role of viruses in biosphere.

When does RNA become Alive?

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ABSTRACT
A question is posed whether RNA can exhibit critical features of life. If RNA can catalyze its own synthesis, replication, and control the errors in duplicating the RNA sequence, and if it can control energy flows for such processes, then RNA could be called "alive". First, life is defined. Using the data base of organisms in the biosphere and non-living entities in the geosphere, a generalized definition of life is constructed. This is further universalized by eliminating biases reflective of the contemporary terrestrial biosphere being confined to narrow chemical constructs and restricted sources of energy (Clark 2004, 2018). Non-enzymatic copying of RNA is considered first as the most primitive. The error catastrophe in such copying can be avoided, since mismatches in copying stall the copying process. The proper matches result in higher copying rates and are thus selected (Leu et al. 2012; Rajamani 2010). These properties of RNA constitute the critical steps on its path to becoming alive, whether on Earth, Mars, or an Ocean World. References: Clark, B. C. 2004. In ALIFE IX, ed. M. Bedau et al., pp. 96-102. Boston, Mass.; Clark, B. C. 2018. Handbook of Astrobiology, Part12; CRC; Leu, K. et al., JACS 2012. 135: 354-366; Rajamani et al., 2010. JACS 132: 5880-5885.

Bacteria-Phage Interplay: Resistance Conversation in Genomic Level

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ABSTRACT
Bacteriophages are extremely abundant in the biosphere and bacteria strive in order to avoid phage infections by adaptation. In this study, we investigated the phage-resistance conferring genomic mutations of two multidrug resistant Klebsiella pneumoniae strains against eight naturally occurring phages. All the phages were isolated from community sewage water and selected to efficiently cross-infect both K. pneumoniae strains. Phages were further characterized to differ from each other. In order to investigate the genomic interplay with bacterial hosts and phages, both bacterial strains were exposed to all eight phages individually, sequentially and as a cocktail. Fitness costs of acquired resistances were measured and genetic mutations corresponding to resistances were determined. Resistance cost originating from the simultaneous exposition to multiple phages were significantly higher compared to those resulting from a single or sequential phage exposition.

Understanding the influencing factors in a development of resistance is crucial, especially when implementing phages into antibacterial applications. In a sense, bacterial genome is a logbook of ist past encounters with phages. The resulting logbook markings show a dependence both on previous discussions and on whether individual intercourses have been dialogs or conversations with multiple phage participants. By deciphering the details behind resistance formation, we can learn to utilize phages to their maximal potential as well as better understand the evolution of bacterial genomes.

Keywords: Phage, Klebsiella pneumoniae, Mutation, Resistance, Fitness cost

Mixed infections of plant viruses: how does potato virus Y and pepino mosaic virus coinfection affects disease symptomatology and dynamics of virus populations?

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ABSTRACT
Plant viruses are often present in nature in mixed infections and, if pathogenic, the outcome of the disease in plant can be dependent on the type of the interaction between the viruses present in mixed infection. This can range from synergistic (one or both viruses increase in their titer) to antagonistic (one or both viruses decrease in their titer). Moreover, the severity of disease symptoms these viruses are causing in plants can be increased or decreased, depending on the type of the interaction. The most known reports on the synergistic interaction is between some potyviruses (family Potyviridae) and potexviruses (family Alphaflexiviridae). In the present research, we have established mixed infections of two economically important virus species with partially overlapping host ranges: Potato virus Y (genus Potyvirus) and Pepino mosaic virus (genus Potexvirus). Single infections, coinfections (infection with both viruses at the same time) and superinfections (first infection with one virus, later with the other) were established in tomato (Solanum lycopersicum) and Nicotiana benthamiana. Virus titers in plants were measured four weeks after the infection using quantitative PCR and compared between different modes of infection. A change in severity of disease symptoms was observed; most notably, N. benthamiana plants coinfected with both viruses showed much more severe symptoms than if infected only with one virus. Further, to elucidate the effect of mixed infection on the within-plant population structures and evolutionary dynamics of both viruses, we have performed an evolution experiment in which both viruses were serially passaged in N. benthamina plants in single and mixed infections. Viral titers were determined for selected passages and population structures of the viruses were characterized using small RNA deep sequencing.

V-table - an approach in structuring Virosphere by arranging viral taxa according to the similarity of their sets of characteristics.

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ABSTRACT
The fact, that after 100 years of research in a field of virology, there is no visualization of viral diversity, e.g. no structure unifying all known viruses, except for alphabetic lists of taxa within corresponding taxonomic groups, is unprecedented. Virus taxonomy does not provide information on how viral families are related whereas the ranks, higher than family and order are implausible.

The absence of universal genes and common ancestor complicate visualization of viral phylogeny. However, constantly growing number of new viral taxa, along with expanding spectrum of their molecular characteristics cause a need in a structured overview on virosphere.

Imaging virosphere allows making trends of viral diversity visually comprehensive for both scientific community and broader audience. In http://v-table.com/ we applied hierarchic categorization of characteristics, first grouping viruses according to the most basic characteristics. Type of genome and host form the grid for tabular arrangement. Other characteristics including size, form and segmentation of genome, type and size of capsid, envelope and replication location are applied within the aforementioned grid.

Comparing viruses by multiple characteristics simultaneously allows creating a structure, reflecting the relations between distantly related groups of viruses. Hence, the idea of V-table is to combine virus taxonomy, biological properties and phylogeny.

Keywords: Virosphere, virus diversity, taxonomy

ZAP inhibits Echovirus 7 mutants with high CG dinucleotides frequencies.

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ABSTRACT
There is a dinucleotide frequency bias in cytoplasmically expressed mRNA sequences of different eukaryotes. Neighbouring CG dinucleotides are markedly suppressed and so are UA pairs. The same suppression is visible in viruses infecting these, suggesting a specific selection and evolution against CG and UAs dinucleotides for host and viruses.

Picornaviruses also suppress CG dinucleotide frequencies. Artificially increasing this frequency in Echovirus 7 (E7) leads to impaired replication. Previous studies established that the difference in phenotype between E7 Wild Type virus and a high CG mutant occurs early during infection, before IFNβ production and translation of the viral polyprotein.

How the High CG mutant E7 is recognised in the cell has been unclear. A targeted screen using a combination of inhibitors, overexpression and siRNA to potential host factors identified Zinc- Finger antiviral protein (ZAP) as a restriction factor that would specifically inhibit transcripts enriched in CG motif. Depletion of ZAP by CRISPR/Cas9 in A549 cells, markedly increased the replication kinetics for CG High mutant viruses. In contrast overexpression of ZAP lead to suppressed viral RNA levels, and cross-linking immuno-precipitation showed interaction.

Our results demonstrate that ZAP inhibits virion production when cells are infected with CG enriched E7. This conclusion highlights two interesting points, first that the innate immune system recognises mRNA CG motives as 'non-self' and consequently this becomes a selective pressure constraining viral genomic variations. Detection of dinucleotide motives in RNA transcripts is a newly uncovered mechanism in innate immunity.

Transgenerational RNAs - Inheritance of Immunological Identity?

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ABSTRACT
In the paper I shall argue that the transmission of small RNAs to subsequent generations can be interpreted as the transmission of an alternative kind of identity - the immunological self instead of the genetic self: Small RNAs can respond to environmental stimuli, such as for example viruses. By the synthesis of small interfering RNAs, which target RNAs of viral origin, the organism is both capable of fending off the viral infection and is as well "immunized" against future viral challenges. Thus, small RNAs keep a memory of the non-self. This memory can be passed on and confer immunity to several subsequent generations. In addition, it was suggested that other classes of small RNAs can confer memory of the self, by licensing previously expressed messenger RNAs for expression in future generations. Taken together, this suggests that in addition to genetic information an immunological self/nonself paradigm can be inherited. Small RNA memory qualifies as an alternative source for phenotypic novelty in several ways: it is short-term, flexible and adaptive. There are also indications of small RNA directed effects on stretches of DNA which could suggest a capacity of the self/non self paradigm to even induce genetic novelty.

These thoughts do also imply considerations on larger scales. Philosophical as well as biological theories of the self / identity rely very much on a theory of evolution by random (DNA-based) selection. However, the small RNA based paradigm of immunological memory opens up a different perspectives for considering identity.

Distribution of predicted Retrotransposon LTRs in gene flanking regions of the *Pinus taeda* genome v.2.0.

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ABSTRACT
Transposable elements (TEs) contribute to regulation of gene networks by embedding transcription factor binding sites (Feschotte 2008; Sundaram *et al.* 2014; Zhao *et al.* 2018). The most prevalent TEs in conifer genomes are LTR retrotransposons, which contain transcription initiation and termination signals, cis-acting elements, polypurine tracts, integrase binding signals, tRNA primer binding sites (Kumar, Bennetzen 1999). The aim of this study was the analysis of genes containing LTRs in flanking regions in the *Pinus taeda v.2.0.* genome. Uppsala Multidisciplinary Center for Advanced Computational Science resources were used for manipulation of genome sequences. 5kB sequences from 5' and 3' flanking regions were extracted and were divided into 1kB regions. Predicted conifer LTR sequences were BLASTed to the flanking sequences. Ratio of hit number to the number of extracted flanking regions was similar for all regions (0.1-0.11), except for the 0-1 kB region (0.16-0.18), indicating that in proximal regions, the higher hit number is not dependant on the higher number of extracted regions. 160 LTRs that were present in all ten regions were analysed, each LTR hit from 19 to 820 unique gene flanking regions. 40 LTRs were significantly (p=0.001, t-test) more frequent in the 0-1 kB region. Frequencies of seven LTRs were significantly increased in the 0-2kB region (p=0.001). Gene groups defined by presence of particular LTRs were further functionally analysed using Gene Ontology terms. As a result LTRs were identified that were enriched in gene regions and contain multiple TFBS (MYB, TATA-box, GT-1, WRKY etc.).
Key words: retrotransposons, gene networks, gene regulation.

Shifts of TE replication strategy revealed by small RNA sequencing

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Summarizing sentence: We investigated small RNA expression in different Drosophila species and found patterns that indicate shifts of the replication strategy for some families of transposable elements.

ABSTRACT
Small RNAs (sRNAs) are involved in the regulation of cellular processes but also contribute to an intracellular immune system against viruses and transposable elements (TEs). This work aims to shed light on the evolution of sRNAs employed in TE control. For this purpose, sRNA libraries (18-30 nucleotides) of three different tissues (embryo, ovary, carcass) from seven Drosophila species (D. melanogaster, D. simulans, D. mauritiana, D. yakuba, D. erecta, D. ananassae and D. pseudoobscura) were sequenced with an Illumina HiSeq 2500. We mapped the reads to transcript annotations of these species and found that substantial fractions of reads aligned to TEs. For most TEs, sRNA expression showed conserved patterns. However, the silencing response to some TEs displayed patterns that indicate shifts of of their replication strategy. Our results highlight that inferences based on single species, such as D. melanogaster, may yield a biased picture of TE biology. To unravel the evolutionary strategies of TEs, it will be necessary to study TE dynamics in many diverse species.

Keywords: Transposable elements, small RNA, Drosophila, piRNA

Adaptation to Nonsense as Nonself

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A third of 7000 known rare diseases are caused by premature termination codon (PTC) mutations. The introduction of an unscheduled stop codon, leading to a truncated and potentially deleterious LAMB3 protein (nonself/nonsense), causes severe blistering of the skin in rare skin disease JEB-H (Junctional epidermolysis bullosa-Herlitz). Consequently, the trimeric laminin 332 anchor - linking epidermis and dermis - cannot be formed in the absence of a functional LAMB3 protein (self/sense). Discrimination between self and nonself or sense and nonsense is not absolute. Evolution of environments, cells and viruses is driven by interactive adaptive processes of progression through available resources, actions and responses.
To establish self-integrity, cells respond to internal or environmental changes upon proper recognition and discrimination. Cycles of exo- and endocytosis, constantly exchanging self and nonself, are also exit- and entry-points for truncated proteins, RNAs, viruses and cell renewal. A limited number of cellular pathways is responsible for internalization, recognition and labeling of potential invaders or matrisomal defects of internal/external origin. In all cases, the cellular response relies on a cell's inherited/acquired damage and repair mechanisms. Such defense of the transcription and translation machinery is essential to cellular resource management and requires nonself/nonsense labeling for further repair, termination, decay and/or externalization.