Roscoff (France), 4-8 avril 2009

L'ARN au centre de la régulation génique

RNA at the center of gene regulation

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Rapport sur la Conférence

Conference Report

RESUME DU RAPPORT

Conférence Jacques Monod intitulée : L'ARN au centre de la régulation génique

Roscoff, 4-8 avril, 2009

La conférence Jacques Monod "L'ARN au centre de la régulation génique" s'est tenue à Roscoff (Bretagne) du 4 au 8 avril 2009. L'objectif principal de ce colloque a été de couvrir les résultats les plus récents et les plus remarquables dans le domaine des ARNs non codants, étant donné que ces ARNs apparaissent comme des partenaires cruciaux du contrôle de l'expression génique.

Les thèmes sélectionnés se sont avérés être de grand intérêt pour la communauté scientifique, car nous avons eu 109 participants provenant de 17 pays différents. La conférence a attiré la plupart des meilleurs spécialistes du domaine. La petite échelle de ce colloque, la sérénité de l'atmosphère et les excellentes commodités fournies par le CNRS à Roscoff, ont été des facteurs stimulants pour des discussions scientifiques en profondeur et l'initiation de collaborations.

Un fait remarquable est que ce colloque a réuni des scientifiques de cultures différentes, en particulier des spécialistes de systèmes prokaryotes et eukaryotes, ce qui s'est avéré très enrichissant. Nous avons favorisé la diversité et les approches interdisciplinaires, qui ont fourni une valeur ajoutée à la conférence, répartie en 6 sessions thématiques :

1/ Métabolisme de l'ARN, stabilité et transport

2/ Contrôle qualité de l'ARN

3/ Extinction génique, épigénétique

4/ Mécanisme d'action des microARNs

5/ ARNs régulateurs bactériens

6/ Régulations post-transcriptionnelles

Il y a eu 27 orateurs invités à faire une communication de 30 minutes, provenant de laboratoires français (10), européens (11) et non européens (6). De plus, nous avons sélectionnés 21 communications orales de 15 minutes à partir des résumés soumis à la conférence. Nous avons aussi organisé deux sessions de poster (2 x 24) de deux heures chacune. Les présentation orales et par affiche ont été d'excellente qualité et, bien que l'emploi du temps ait été très dense, tous les participants ont manifesté leur enthousiasme quant au succès de cette conférence et à la perspective de son renouvellement prochain.

CONFERENCE REPORT

Final report from the Jacques-Monod Conference entitled: RNA at the center of gene regulation

Roscoff, April 4-8, 2009

Summary

The CNRS-Jacques Monod conference "RNA at the center of gene regulation" was held in Roscoff, in Brittany, April 4-8, 2009. The main objective of this meeting was aimed at covering the most recent developments and exciting results in the field of non-coding RNAs, as such RNAs now are known to be ubiquitously present elements in the control of gene expression. The work presented and discussed by the selected speakers addressed both biological roles and mechanisms of action on RNA-mediated control processes. This conference highlighted new features that have emerged over the last few years on the RNA-based regulatory networks in eukaryotes – animals and plants – and in prokaryotes.

The selected topics were of high interest to the scientific community, indicated by turnout of applicants, a total of 109 from seventeen different countries (Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Italy, Japan, Russia, Spain, Sweden, Switzerland, The Netherlands, USA, United Kingdom). This conference featured many of the most highly recognized specialists in the fields covered. The relatively small scale of the meeting, the intimate and peaceful atmosphere, and the excellent facilities provided by the CNRS in Roscoff, stimulated many in-depth discussions and most likely initiated future collaborations. Much of this must be credited to Mrs Dominique Lidoreau and the personnel of the Roscoff center who took care of the practical organization (administration, lodging, poster room, computer facilities). We also want to emphasize the very good quality of housing and the excellent food. On one of the afternoons, an excursion was organized to the "Ile de Batz". This was a highly appreciated social event although the weather Gods were clearly not on our side.

A particularly valuable aspect of the meeting was that it brought together scientists from widely different cultures and scientific backgrounds, and that specialists in both eukaryotic and prokaryotic biological systems were communicating vividly. In planning this conference, we favored diversity and interdisciplinary approaches, and such a broad coverage was certainly appreciated and considered to be an 'added value' to this conference. Along these lines, we took care to balance contributions dealing with eukaryotic and prokaryotic systems and dispatched them into 6 sessions:

- RNA metabolism, turnover and transport
- RNA quality control
- Gene silencing and epigenetics
- miRNA mechanisms
- Bacterial regulatory RNAs
- Transcriptional and post-transcriptional regulation

A total of 27 speakers were invited to give 30 min talks. Of these, ten came from French laboratories, eleven from other European laboratories and six from the "rest of the world" (USA, Japan). In addition, 21 applicants were selected to give oral presentation (15 min talks), based on originality and novelty presented in their abstracts. Two poster sessions (two hours each, total of 48 posters) completed the scientific program. There was time and opportunity for questions and discussions in both platform talks and poster sessions, as well as during breaks and over lunch and dinner. The oral and poster presentations were of outstanding quality and, although the schedule was rather tight, the responses received by us indicated the enthusiasm of the participants for having attended this meeting. This convinces us that it would be important to cover this topic, with a timely focus, again in two or three years.

Scientific report.

RNA molecules are key players in numerous regulatory processes in all kingdoms of life. The Nobel Prize, awarded to Fire and Mello in 2006 for the discovery of RNA interference, testified to the importance and impact of research in this field. Small RNAs inhibit or activate genes by interacting with mRNAs, in pro- as well as eukaryotes and, as has become clear in recent years, also promote changes in (eukaryotic) chromatin to affect gene expression. This occurs by different molecular mechanisms and affects many cellular processes - from stress reponses, metabolism, development, maintenance of genome integrity, and defense against invaders. In addition to the plethora of trans-acting small RNAs in bacteria, miRNAs, siRNAs, piRNAs and others in eukaryotes, many structural elements within mRNAs mediate regulation or are the sites at which regulation is exerted. Gene expression is also affected by RNA turnover and by various quality control mechanisms that ensure that mRNAs encode functionally intact proteins. More and more links between RNAs and epigenetic phenomena have emerged and impact on our understanding of diseases. In the past few years, the ranges of subjects covered by this Jacques Monod Conference have spawned fascinating and important discoveries in these areas.

The Conference "RNA at the center of gene regulation" was aimed at covering the most recent exciting developments in this field. The work presented and discussed by the selected speakers addressed biological roles and mechanisms of RNA-mediated control processes. The talks were organized in six thematic sessions:

Session I : RNA metabolism, turnover, and transport

The path of RNA from transcription through processing, association with partner proteins, transport/ ecport, to its designated function and ultimately decay, is an exquisitely controlled process. Many contributions have been made to understand the various steps, and the points at which regulation is exerted. For this session, we invited speakers who made pioneering contributions in the last few years.

A) Degradation and control (chairperson : Dominique Morello)

RNA decay is one such field. Bacterial RNAs decay in an overall 5'-3'-direction. However, a puzzling observation was that bacteria appeared to lack 5'-exoribonucleases. The primary RNA degradation enzyme in many Gram-negatives is RNase E. J. BELASCO showed that in fact 5'-pyrophosphate removal from primary transcripts is the rate-limiting step in permitting fast RNase E-mediated (endo)-cleavage. He also reported on the autoregulatory mechanism in which the decay rate of RNAse E mRNA is a function of intracellular RNase E concentration. In this, a particular 5'-UTR element is the binding site for RNase E. C. CONDON showed

that RNase J1 in the Gram-positive bacterium *Bacillus subtilis* is, in addition to being an endoribonuclease, a *bona fide* 5'-3'-exonuclease involved in the degradation of full-length primary transcripts - thus ending a long quest for a type of enzyme previously known only in eukaryotes.

The rest of session 1A was on eukaryotic systems. C. TOMASETTO showed that MLN51, a component of the exon junction complex (EJC) expressed in many breast cancer cells, is present in stress granules (SGs) where it has a distinct function, essential for the formation of SG and for cell survival. Several classes of non-coding RNAs were presented for their involvement in mRNA degradation. Two talks (B. SERAPHIN and A. JACQUIER) were on a new class of ncRNAs called CUT RNAs (Cryptic Unstable Transcripts) in yeast. A. JACQUIER showed that this new class of RNA polymerase II transcripts results from bidirectional transcription from numerous pol II promoters, followed by premature termination. His data revealed that eukaryotic promoter regions are intrinsiqually bidirectional. B. SERAPHIN addressed the role of the exosome in selective elimination of CUT RNAs in the nucleus. As regards other classes of ncRNAs, M. SIMONELIG described the requirement of the piRNA (Piwi-interacting RNAs) pathway for maternal mRNA deadenylation and decay in the early *Drosophila* embryo, and C. VERHEGGEN presented a study of snoRNAs (guide RNAs for nucleotide modification on rRNA) showing that the carrier protein CRM1 plays a central role in transport of both capped and non-capped box C/D snoRNAs to nucleoli. Finally, M. SUBRAMANIAN talked about the role of the FMRP protein on mRNAs dendritic targeting and translational control, whereas K. KALANDITIS focused on gene silencing in plants, showing that the enhancer of RNAi, ERI1, negatively affects the concentration of pathogen-derived siRNAs but not that of an endogenous miRNA. He also showed interesting results indicating that light intensity is a major environmental factor for the induction and systemic spread of RNA silencing in plants.

B) Localization and transport (Chairperson Heike Lange)

Session IB included three talks. R. BUCHAN presented pioneering work on so-called P-bodies, demonstrating that RNA granules in *S. cerevisiae* have the same protein composition and a similar assembly mechanism as mammalian stress granules. He proposed the interesting hypothesis that P-bodies are important sites for decisions of mRNA fate, whereas stress granules may represent pools of mRNAs stalled in the process of reentry into translation from P-bodies.

J. LÖTVALL showed that mammalian exosomes carry many different RNAs which can be delivered upon fusion with target cells. Thus, the mRNA content of the exosomes is functional, and subsets of regulatory (miRNAs) are carried along as well. This indicates the exciting prospect of RNA-mediated cross-talk resulting from these transport events.

MicroRNA processing was addressed by J. CACERES, who found that hnRNP A1, a protein implicated in many aspects of RNA processing and translation, acts as an auxiliary factor for the processing of a microRNA precursor, pre-miR-18a, at the level of Drosha processing. These data show that auxiliary factors strongly affect processing of specific miRNAs.

Session II : RNA quality control (Chairperson François Dautry)

RNA quality control is very important. Much energy is invested into the biogenesis of RNAs, in particular mRNAs in eukaryotes, and hence it is an evolutionarily sensible strategy to control for proper functionality *before* possibly wasteful or aberrant gene products are produced. Nonsense mediated decay (NMD) is one such mechanism in which processed and cytoplasmically localized new mRNAs are subjected to a trial round of translation. In case of, e.g., premature stop codons being present, the RNA is destined to decay, whereas a successful

"pioneer round" will commit the mRNA to multiple rounds of translation. This session covered different aspects of this and related mechanisms in yeast and mammals. L. MAQUAT analyzed the role of the mammalian Staufen 1 protein (a dsRNA-binding protein) and showed that it recruits the NMD-factor Upf1 to 3'-UTR regions of mRNAs in order to elicit decay. She showed that the STAU-mediated decay (SMD) competes with NMD during myoblast differentiation, and that this contributes to myogenesis. M. MOORE introduced two other mechanisms of RNA decay: she demonstrated that *S. cerevisiae* possesses a novel quality control mechanism, nonfunctional rRNA decay (NRD), and showed that NRD utilizes the same proteins as those participating in the no-go mRNA decay (NGD) mechanism. P. NICHOLSON revealed nonsense-mediated transcriptional gene silencing (NMTGS) as a novel quality-control mechanism in mammalian cells acting at the level of chromatin rather than mRNA.

Three additional talks enriched this session: H. LE HIR presented an analysis of the EJC whose crystal structure, containing the RNA, was solved, allowing to reconstitute the NMD surveillance complex (EJC core and NMD factors) and revealing that this core complex serves as a binding platform for multiple factors in human cells. D. WEIL investigated the ultrastructure of GW bodies (also called P-bodies) following different stresses. The results showed that they are more compact than stress granules and that a distinct assembly pathway is present in mammalian cells. One talk in this session concerned bacteria. O. SHPANCHENKO presented the mechanism of trans-translation as an mRNA quality control system in bacteria; trans-translation is a process in which stalled/ nonstop mRNAs continue translation on tm-RNA, an RNA with dual function (tRNA-mRNA). This clears ribosomes and tags the abberant peptide for destruction.

Session III : Gene silencing and epigenetics (chairperson Henri Grosjean)

Gene silencing can occur on either the transcriptional or post-transcriptional level. Transcriptional gene silencing (TGS) generally depends on modification of either DNA sequences (DNA methylation) or of histones. This process is well-known in plants, but it is now also established that heterochromatin formation in fission yeast, and in many multicellular eukaryotes, is dependent on a functioning RNAi machinery and therefore needs RNA transcripts to be initiated. Several talks in the session focused on a new class of ≈30 nt long RNAs, piRNAs (Piwi-interacting RNAs), that are abundantly present in germlines of animals. M. SIOMI addressed the mechanism of action of *Drosophila* PIWI-proteins that are specifically associated with piRNAs, and identified that they have a Slicer activity that, via a ping-pong mechanism, generates the 5'-ends of piRNAs to set off their amplification. Furthermore, she established that the processing pathway of piRNAs also operates in somatic ovarian cells. S. CHAMBEYRON showed that the piRNA pathway mediates the repression of the *Drosophila* I element retroposon by a post-transcriptional mechanism. R. KETTING studied the Piwi proteins in zebrafish (Ziwi and Zili) and their roles in development, and N. STANDART identified by deep sequencing for the first time miRNAs and piRNAs in *Xenopus tropicalis*. In the frog, Piwi proteins (Xiwi and Xili) and Argonaute proteins are correspondingly present.

R. KETTING also analyzed the role of the nucleotidyltransferase CDE-1 in *C. elegans*, showing that CDE-1 restricts the production of siRNAs, and that such a process could as well operate in other animals, including mammals. SiRNAs in fission yeast were addressed by I. DJUPEDAL, who presented evidence that siRNAs, involved in the formation and maintenance of heterochromatin at the centromeres of *S. Pombe*, can be generated from endogenous centromeric transcripts that show fold-back structures. O. VOINNET has pioneered work on transcriptional and post-transcriptional silencing in plants. He reported on

the roles of different Dicers in plants under viral challenge, highlighting the roles of different classes of siRNAs in silencing and the generation of mobile signals. He identified proteins ARF 4 and ARF8 to be involved in siRNA-mediated gene silencing in plants. A. MAIZEL focused on the role of miRNAs and trans-acting siRNAs (tasiRNAs), showing that specific downregulation of ARF3 (auxin-responsive factor) by TAS3-derived tasiRNA is critical for leaf development, whereas ARF2/3/4 proteins and miR390 are required for root development.

Gene imprinting iun mammals often involves longer RNAs; a special case is dosage compensation. One of the X chromosomes must be silenced in female mammals. The key player is a very long RNA, Xist, which is part of the inactivation center (Xic). J.C. CHOW demonstrated that LINE1 elements (L1s) cooperate with Xist RNA in creating a silent compartment in which heterochromatin formation nucleates. Since siRNAs are generated from such genes linked to an L1, an RNAi-type mechanism may participate in the local propagation of X inactivation. C. KANDURI showed that the 91 kb-long antisense ncRNA *Kcnq1ot1*, one of several ncRNAs typically found in parentally imprinted regions in mammals, plays a role in lineage specific transcriptional silencing in mouse. This functional role requires a 0.9 kb region at the *Kcnq1ot1* RNA 5'end. Transcriptional silencing of the HIV-1 promoter was addressed by R. KIERNAN who showed that it is dependent on the nuclear exosome and the HIV-encoded TAR RNA. Finally, A. WERNER reported on mammalian and zebrafish natural antisense transcripts (NATs), suggesting a provokative scenario in which sense-antisense RNA pairs are processed into endo-siRNAs, possibly generating effects on monoallelic gene expression.

Session IV : miRNA mechanisms (chair person: Haru Siomi)

This session focused on mechanisms of action of both miRNAs and piRNAs. It was introduced by Z. MOURELATOS, who presented evidence that mouse, *Xenopus laevis* and *Drosophila melanogaster* Piwi family proteins (Piwi, Ago3, Aub) contain symmetrical dimethylarginines (sDMAs) revealing the significance of sDMA modification of Piwi proteins in the germline. J. MARTINEZ, reported on the roles of RNA modifying enzymes in RNAi/ miRNA-related mechanisms. His lab was searching for (t)RNA-ligases, after having observed that siRNAs undergo ligation in HeLa cell extracts. Several candidates for proteins with siRNA-ligase activity have been identified which could correspond to RNA-ligases involved in tRNA maturation.

The other talks illustrated new functions of miRNAs. A. LUND reported the interaction of miR-10a with the 5' untranslated region (by binding to the 5'TOP motif) of mRNAs encoding ribosomal proteins. Surprisingly, binding of miR-10a enhances translation and thus alleviates translational repression of ribosomal proteins mRNAs during amino acid starvation. S. PFEFFER focused on miRNAs encoded by mouse cytomegalovirus (MCMV) which are abundantly expressed during the lytic phase of infection. He showed that mutation of these miRNAs in MCMV can affect the virus' ability to infect newborn and adult mice. C. TOURIOL showed that miR-16 affects the translation of the vascular endothelial growth factor A (VEGF -A) mRNA that contains two distinct internal ribosome entry sites (IRESs). Interestingly, VEGF IRES-A activity was not altered by miR-16 targeting to the 3'UTR, while IRES-B was susceptible to miR-16 inhibition, showing that cellular IRESs are differently susceptible to miRNA translational inhibitory effect. Finally, J. PAZ-ARES identified a novel inhibitory mechanism of miRNA activity based on target mimicry in the plant phosphate starvation system of *Arabidopsis*. This mechanism relies on an ncRNA, IPS1, which has a region complementary to miR399, and acts by sequesteration of the miRNA.

Session V : Bacterial regulatory RNAs

A) sRNA function and mechanisms (chairperson François Vandernesch)

Small RNAs (sRNAs) are a heterogeneous class of RNAs found in genome-wide searches, until recently primarily in *E. coli*. Most of these are antisense RNAs that act in stress response regulation and virulence. The RNA binding protein Hfq is often required for control. Limited complementarity characteristic of many sRNA-target RNA complexes permits recognition of multiple, functionally related target RNAs. Clearly, ubiquitous post-transcriptional regulation by sRNAs is an important layer of control. The session was introduced by G. WAGNER, who summarized some of the biological roles of bacterial small RNAs (sRNAs) and presented results about a new regulatory mechanism involving two redundant antisense RNAs that inhibit the synthesis of the master regulator, CgD, of curli (proteinaceous surface structures in biofilm formation). J. VOGEL presented data showing how GcvB, RybB and MicC sRNAs regulate multiple structurally diverse mRNAs, by recognizing targets outside the canonical SD/AUG region and pairing with the upstream 5'UTR or with the coding sequence. P. ROMBY showed that sRNAs modulate the bacterial surface composition in *E. coli* and *S. aureus*. This feature is crucial as it is related to the involvement of sRNAs, in particular the *S. aureus* virulence regulator RNAIII, in the bacterial virulence trait. Bacterial virulence was also addressed by P. COSSART, who characterized 29 new ncRNAs in *Listeria monocytogenes* and demonstrated that one of them is involved in virulence, while one long antisense RNA identified is involved in control of flagellum synthesis. High density tiling array experiments showed that a number of ncRNAs follow the same expression patterns as virulence genes.

B) Defense mechanisms against viruses (chairperson Fabien Darfeuille)

Two talks focused on a new prokaryotic defense mechanisms against viruses and other invading genetic elements. P. HORVATH presented his data by which he established for the first time a nucleic acid-based immunity system encoded by the ubiquitous so-called CRISPR elements. CRISPR are repeated sequences present in many bacteria and almost all archea. Their functional significance had been elusive until very recently. CRISPR elements have identical repeats interspersed with unique spacer sequences. In *S. thermophilus,* the integration of phage-derived new spacers provides acquired immunity against the phages that contain identical sequences. Disruption of selected *cas* (CRISPR-associated) genes indicated their functions in immunity and spacer acquisition, respectively. M. LUNDGREN showed that CRISPR transcripts in *E. coli* are processed by a complex of five Cas proteins (denoted Cascade) This complex retains the RNA cleavage products which subsequently become the specificity determinants of the reaction that targets incoming DNA or their RNA products.

Session VI : Post-transcriptional regulation

Post-transcriptional regulation, and specifically translational regulation, is exceedingly complex. RNA structures are important determinants for the efficiency of translational initiation and, in all cases, protein complexes and ribonucleoproteins (RNPs) play crucial roles in determining the specificity and rate of reactions. In addition, dynamics is an integral part of regulation. This is particularly true in complex eukaryotes, and the multitude of protein factors is staggering. RNPs can be exchanged upon receiving environmental cues, and RNA structures can fold and unfold to affect the downstream processes. In this session, various aspects of translational regulation, and of RNP complexes in control, have been presented.

A) snRNPs (chairperson Anne-Catherine Dock-Bregeon)

C. BRANLANT presented data on snoRNP and sRNP (the equivalent in archea) structure-

function and assembly. RNPs are involved in regulation, splicing, and rRNA modification, whereas snoRNPs are involved in modification of rRNAs. A deep structure-function analysis of archeal H/ACA sRNPs was presented, based on reconstitution of the sRNP, on computer-based investigation on archeal sRNAs and their targets, and on knowledge of H/ACA sRNP 3D-structure. It was also shown that assembly of eukaryal snoRNPs in the cell is a complex process that involves nuclear factors not present in the mature particles.

T. KISS showed that 7SK RNA is a central regulator of cellular mRNA production through controlling the nuclear level of active positive transcription elongation factor b (P-TEFb), a cyclin-dependent kinase that phosphorylates the carboxy-terminal domain of RNA polymerase II. When not associated with P-TEFb, 7SK RNA associates with heteronuclear ribonucleoproteins (hnRNPs). The dynamic assembly and disassembly of these alternative complexes was shown to be instrumental in determining the level of active protein kinase which in turn is required for transcription elongation by RNA pol II. This topic was also addressed by O. BENSAUDE who showed that U1 snRNA can be co-immunoprecipitated with RNA pol II. His data are consistent with a constitutive association of U1 snRNA with RNA pol II and suggest that U1 by being associated with the transcription machinery might scan the nascent transcript to facilitate 5' splice site recognition.

B) Translation (chairperson Stéphane Pyronnet)

M. HENTZE discussed the regulation of messenger RNA translation by microRNAs. Using a cell-free system from *Drosophila* embryos his group identified chemical analogs of the physiological mRNA cap structure that convey increased regulation to *Drosophila* miR2. Since the same chemical modifications do not appear to affect general translation, these data strongly support the model that microRNAs regulate translation initiation at an early step at the cap structure.

A new mechanism of transcription-translation coupling was presented by A.C. PRATS. Fibroblast growth factor 1 (FGF1) is induced at both the transcriptional and translational levels during myoblast differentiation and muscle regeneration. Data show that translational induction involves the FGF1 IRES A and that IRES activity is strongly enhanced by the presence of a cis-acting element in the FGF1 promoter A. This suggests an effect of specific transcription factors in the recruitment of IRES trans-acting factors on the nascent mRNA.

M. SELMER showed high resolution crystal structures of the 70S ribosome from *Thermus thermophilus*, derived from functionally defined stage-specific complexes, assembled with sets of factors and RNAs. This enabled a study of ribosomal frame-shifting, providing insights into the mechanisms that lead to +1 and -1 frameshifts. A. ALARD focused on the eukaryotic initiation factors eIF-4GI and 4GII, two scaffolding proteins critical for the assembly of initiation complexes. She showed that the polo-like kinase (Plk) 2 binds to eIF-4GII and that the resulting complex is degraded in the proteasome, indicating a role for Plk2 in the control of translation initiation. Finally O. JEAN-JEAN reported on the involvement of human translation termination factor eRF3a in the mTOR signaling pathway required for the cap-dependent translation. The results indicated that eRF3a depletion inhibits cell cycle progression through the inhibition of mTOR signaling.

Conclusion and recommendations

This conference clearly emphasized that the field of RNA in gene regulation, in all its flavors, is in an extremely productive phase. It has spawned many totally unexpected developments, both with respect to the roles of small and large RNAs in regulation, but also with respect to mechanisms that were not envisioned previously. It does not take much more than a quick look at current journals to find that ncRNAs receive enormous attention, and rightly so. Thus,

the importance of RNA in control of gene regulation is obvious. Over the last few years, we have seen new classes of ncRNAs emerge, and new roles have been assigned to some RNAs discovered earlier. Deep sequencing approaches, now widely used, will undoubtedly expand the repertoire of RNA available to researchers. Biological roles of ncRNA, or elements within longer (m)RNAs, will be uncovered at a high rate. This applies to all kingdoms of life, from prokaryotes (bacteria/ archea) to eukaryotes such as protozoa, fungi, plants and animals. Each of these different organismal systems has its own interesting story to tell, sometimes of general implication, sometimes as a branch-specific specialty. The crucial roles that RNAs, and RNA-protein complexes play in, e.g., pathophysiological processes such as resistance to virulence, organ development and diseases, the fight against invading genetic elements, or appropriate regulation in response to changing conditions or stress, all let us expect exciting new developments in the RNA field during the next years.

In conclusion, the participants were overall happy with the content and the stimulating atmosphere of this conference. We heard several comments that indicated strong support for the perspective of pursuing a future Jacques Monod conference on RNA and regulation. The format of the conference was highly appreciated, and the mix between pro- and euaryotic model systems was considered very fruitful. A piece of advice for the future organizers, based on recommendations from participants concerns the very tight program. It might be worthwhile to concider to have a less dense schedule, so that there can be even more opportunity for free, non-scheduled discussions between the participants. We obtained a strong approval of the participants for the designated next president, Dr A.C. Prats, and the newly elected vice-president, Dr R. Ketting, and feel confident that they will be able to put together a very strong, exciting program