

## **FINAL REPORT**

### **U.S. Department of Energy**

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"Post-Transcriptional Control of Gene Expression: Effectors of mRNA Decay"

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## Final Report

FASEB Summer Conference, Tucson, Arizona

Post-Transcriptional Control of Gene Expression: Effectors of mRNA Decay

July 6-11, 2002

The 2002 meeting "Post-Transcriptional Control of Gene Expression: Effectors of mRNA Decay" was held at the Omni Tucson National Golf Resort and Spa in Tucson, Arizona from July 6<sup>th</sup>-11<sup>th</sup>. The goal of this meeting was to provide an interactive forum for scientists working on prokaryotic and eukaryotic mRNA decay. The meeting began with an informal get-together over margaritas, chips and appetizers before dinner and, after dinner, a special one-hour seminar by Dr. Roy Parker, a leader in the field of mRNA decay in *S. cerevisiae*. Roy presented the "big picture", with a focus on what is known and what needs to be determined not only for yeast but for other organisms. His seminar was followed by a lively questions-and-answers session.

This was the most interactive meeting that this organizer has ever attended, in large part because of the nature of the participants. These participants, when asked in advance to plan for the meeting, did so. This was also the largest meeting in this meeting's history, with 110 attendees. The large attendance probably reflects the current awareness that mRNA decay is a key player in gene regulation in a way that is affected by the many steps that precede mRNA formation. As evident from the list of session titles (see below), the meeting covered many aspects of these influential steps. Therefore, there was tremendous cross-fertilization of topics as well as organisms studied. Attendees included mostly graduate students and post-doctoral fellows with a very healthy dose of principle investigators. The organizers were aware that student and post-doctoral attendance would be high and made sure that all sessions began with a 10-minute overview of the topic to be covered. This overview included significance, our current status of understanding, and issues that remain to be resolved. All told, there were 48 women and 62 men. There were 35 invited speakers and an additional two speakers chosen from abstracts. The organizers raised enough money to support in full all speakers, including the additional two. Of the speakers, eight were women, of which two were also session chairs.

There were eight sessions. The sessions, in chronological order, were entitled: (1) mRNA transport and mRNP; (2) Multicomponent eukaryotic nucleases; (3) Nonsense-mediated mRNA decay and nonsense-associated altered splicing; (4) *Cis*-acting sequences/*Trans*-acting factors of mRNA decay; (5) Translational accuracy; (6) Multicomponent bacterial nucleases; (7) Interplay between mRNA polyadenylation, translation and decay in prokaryotes and prokaryotic organelles; and (8) RNA interference and other RNA mediators of gene expression.

In addition to talks, there were three "round table" discussions that worked amazingly well and were attended by essentially everyone. The availability of beer provided a relaxed and interactive environment where ideas flowed freely. Topics were purposefully controversial, and discussants handled themselves with remarkable aplomb. Topics, in chronological order, were (1) Does translation occur in the nucleus? (2) Differences and

similarities in the mechanisms of mRNA decay in different eukaryotes, and (3) RNA surveillance in bacteria? Notably, each round table occurred following one or more sessions that provided state-of-the-art background information. Participants came prepared per the organizer's instructions. Each round table (actually a long table in the front of the room that was outfitted with multiple microphones in addition to the microphones available to the audience) had a pre-designated chair who oversaw the discussion and, with the help of the organizers, planned the round table during the weeks before the meeting. The idea was to recapitulate the type of scientific conversation that principle investigators would have at the bar – causal but informative and opinionated. All participants were notified of the round table topics in advance of the meeting so they could come prepared with data and ideas for presentation. Each round table lasted 1-1.5 hour.

There were two poster sessions, each of which was extremely well attended. Beer was made freely available during these sessions, too. A pre-designed committee of four principle investigators who had access to all poster abstracts from graduate students and post-doctoral fellows in advance of the meeting carefully evaluated each poster on site. Per the committee's recommendations, the organizers presented four awards for scientifically best posters during the final dinner. Awards consisted of a nice certificate for framing and \$100. Through Dorit Zuk, a meeting participant and editor of the journals *Cell/Molecular Cell*, the organizers were able to supplement the top award with an annual subscription to *Molecular Cell*.

In Summary, the Conference was extremely well received, and the organizers got lots of compliments both on site and after the meeting in the form of letters, card and emailings. A few speakers are working on a meeting review for publication. Key to the integrity of the meeting was the Abstract Book. This Book consisted of 118 pages and included the contents page, personal thanks, contributions, program at a glance, complete program, author index, speaker abstracts, poster session organization, poster abstracts, and the list of participants with contact information.

At the business meeting, there was a unanimous decision to hold another meeting in two years. The site of first choice was Montana, just for a change. Aside from the heat, everyone generally liked Tucson. In addition to on-site amenities, the organizers took advantage of the proximity of the Kartchner Caverns and organized tours in advance of the meeting that supplemented events organized by FASEB. Maybe, there are other facilities worth visiting in the future, such as the government reserve of retired airplanes.

The Chairperson for the 2004 meeting will be George Mackie of the University of British Columbia. The Vice-Chairperson will be Roy Parker of the University of Arizona.

**Post-transcriptional Control of Gene Expression:**  
**Effectors of mRNA Decay**

Tucson                      July 6, 2002 to    July 11, 2002

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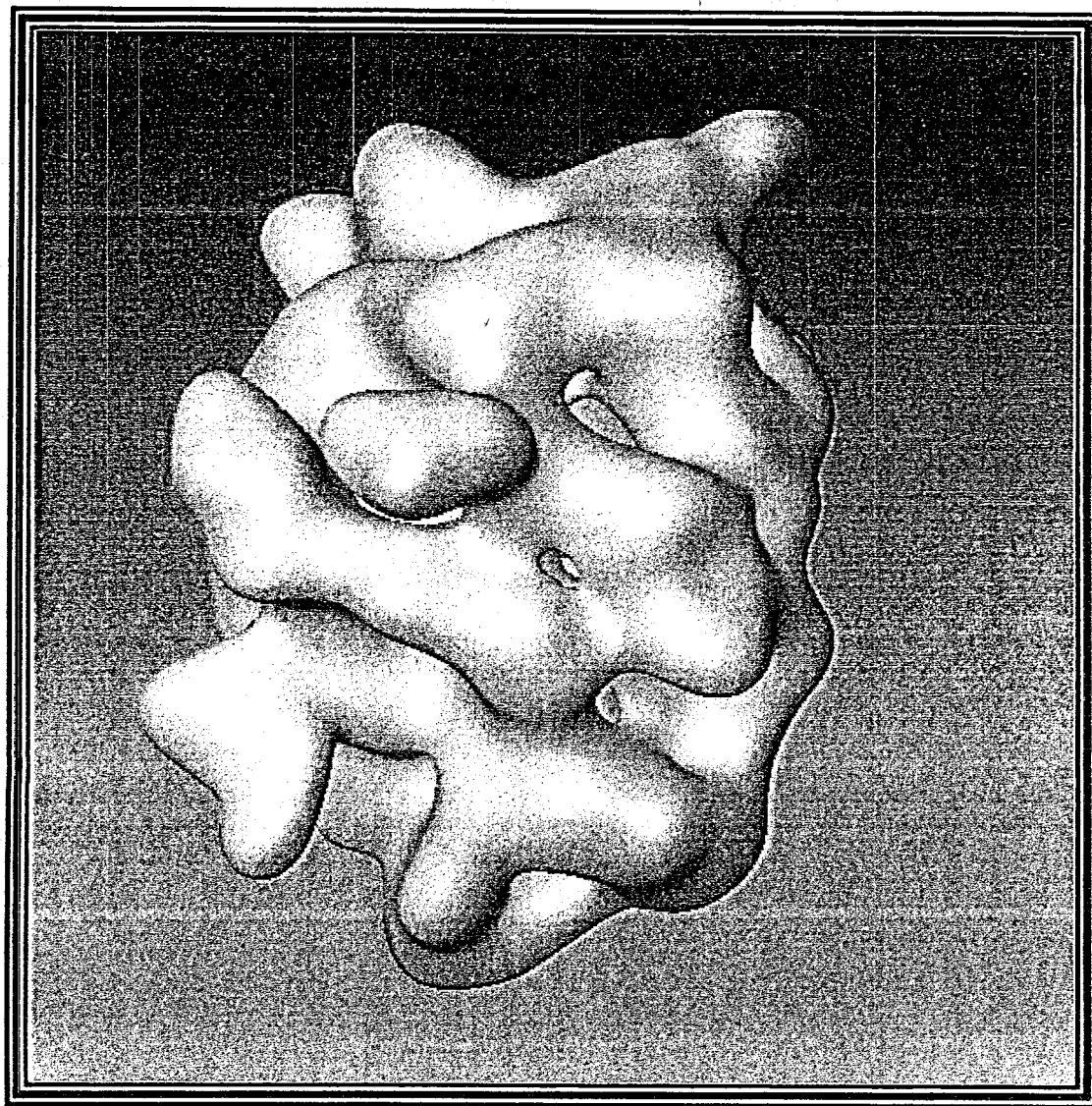
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Monday, December 09, 2002

# Post-Transcriptional Control of Gene Expression: Effectors of mRNA Decay

July 6 – 11, 2002  
Omni Tucson National Golf Resort and Spa  
Tucson, Arizona



Cryo-EM reconstruction of the yeast exosome at 17Å resolution  
Courtesy of Holger Stark (IMP, Göttingen)

Organizer: Dr. Lynne Elizabeth Maquat, University of Rochester, New York  
Co-organizer: Dr. Cecília Maria Arraiano, Universidade Nova de Lisboa, Portugal

## Personal Thanks

Cecilia and Lynne would like to thank Stephanie Scoville in the Department of Biochemistry and Biophysics at the University of Rochester Medical Center and Julie Levin at FASEB, each of whom were tremendous help in organizing this meeting. Stephanie contributed in a multitude of ways. She helped solicit funds from corporations and keep track of finances, collect information from and send updates to meeting participants, and put together this abstract book. Julie was a fountain of knowledge from the early days of fund raising to the last phases of working out arrangements with the Omni. Thanks, Stephanie and Julie! We would have been hard pressed to organize this meeting without you.

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2002 FASEB Summer Research Conference  
 Post-Transcriptional Control of Gene Expression: Effectors of mRNA Decay  
 Program At a Glance

Saturday, July 6	Evening	Opening reception and dinner Special Seminar
Sunday, July 7	Morning	mRNA transport and mRNP
	Afternoon	Multicomponent eukaryotic nucleases
	Evening	Nonsense-mediated mRNA decay and nonsense-associated altered splicing Round table discussion – Does translation occur in the nucleus?
Monday, July 8	Morning	free
	Afternoon	Cis-acting sequences/trans-acting factors of mRNA decay
	Evening	Poster Session 1 Round table discussion – Differences and similarities in the mechanisms of mRNA decay in different eukaryotes
Tuesday, July 9	Morning	free
	Afternoon	Translational accuracy Poster Session 2
	Evening	Multicomponent bacterial nucleases
Wednesday, July 10	Morning	Interplay between mRNA polyadenylation, translation and decay in prokaryotes and prokaryotic organelles
	Afternoon	Round table discussion – RNA surveillance in bacteria?
	Evening	Dinner and announcement of poster awards
Thursday, July 11	Morning	RNA interference and other RNA mediators of gene expression

**2002 FASEB Summer Research Conference**  
**Post-transcriptional Control of Gene Expression: Effectors of mRNA Decay**

**Saturday July 6**

**Evening**

4:00 p.m. – 9:00 p.m.

Conference Registration

6:00 p.m. – 7:00 p.m.

FASEB Opening Reception

7:00 p.m. – 8:30 p.m.

Dinner

**8:30 p.m.**

***Welcome/Orientation:*** Lynne Maquat and Cecilia Arraiano

***Special Seminar***

- ♦ Roy Parker – Mechanisms and control of mRNA turnover in a simple eukaryote

**Sunday July 7**

7:30 a.m. – 9:00 a.m.

Breakfast

**Morning**

**9:00 a.m. *mRNA transport and mRNP***

**Introduction: Melissa Moore**

- ♦ Peter Cook – Transcription factories and nuclear translation
- ♦ Piergiorgio Percipalle – Pre-mRNP assembly and transport: a function for actin?

*Group Photo and Coffee Break*

- ♦ Melissa Moore – Exploring connections between pre-mRNA splicing and mRNA metabolism
- ♦ Joan Steitz – SR proteins: yet another link between splicing and export
- ♦ Jim Dahlberg – Export of ribosomes from cell nuclei

**12:30 p.m. – 1:30 p.m. Lunch**

**Afternoon**

**2:00 p.m. *Multicomponent eukaryotic nucleases***

**Introduction: Mike Kiledjian**

- ♦ David Tollervey – Pre-mRNA turnover and processing: lessons from stable RNA synthesis

- ♦ Mike Kiledjian — Regulatory components of mammalian mRNA turnover

Coffee Break

- ♦ Jeff Wilusz — Regulation of exosome-mediated mRNA turnover in mammalian cells
- ♦ Pam Green — Rapid mRNA decay mechanisms in plants: a genomics perspective

6:00 p.m. – 7:00 p.m.

Dinner

## Evening

**7:00 p.m. *Nonsense-mediated mRNA decay and nonsense-associated altered splicing***

**Introduction: Allan Jacobson**

- ♦ Allan Jacobson — Substrates for NMD: identification of the genome-wide cast, decay susceptibilities of new vs. old mRNAs, and a requirement for aberrant termination
- ♦ Lynne Maquat - Nonsense-mediated mRNA decay in mammals: The dynamics of exon-exon junction proteins detected on CBP80-bound but not eIF4E-bound mRNA, and new factors involved in decay
- ♦ Miles Wilkinson — Nonsense codons retain mRNAs in the nuclear fraction of cells
- ♦ Josh Mendell — Genetically separable roles for rent1/hUpf1 in nonsense-mediated decay and nonsense-mediated alternative splicing

***Round Table Discussion with beverages and munchies:*** Does translation occur in the nucleus?

Discussion Leaders: Peter Cook (moderator), Jim Dahlberg, Murray Deutscher, Melissa Moore, Joan Steitz

## Monday July 8

7:30 a.m. – 9:00 a.m.

Breakfast

**Morning – Free** (*Organized events include Jeep tour, horseback riding, guided hike, desert museum*)

12:15 p.m. – 1:30 p.m. Lunch

## Afternoon

**2:00 p.m. *Cis-acting sequences/Trans-acting factors of mRNA decay***

**Introduction: Ann-Bin Shyu**

- ♦ Stu Peltz - Regulation of ARE-mediated decay in yeast
- ♦ Ann-Bin Shyu – Deadenylation: the first step on the road of mammalian mRNA decay
- ♦ Nancy Standart - Novel role of ARE-binding proteins in translational control during *Xenopus* oogenesis

*Coffee Break*

- ♦ Betsy Goodwin – GLD-1 regulates the translation and RNA stability of the *tra-2* mRNA in *C. elegans*
- ♦ Bill Marzluff – Mechanism and regulation of histone mRNA degradation
- ♦ Jack Hensold – Regulation of mRNA decay in differentiating mammalian cells

6:00 p.m. – 7:00 p.m.

Dinner

**7:00 p.m. Poster Session 1** (*all posters in this and the subsequent session will be evaluated on the basis of scientific merit by the award committee: Ann-Bin Shyu (chair), Betsy Goodwin, George Mackie and Bill Marzluff*)

## Evening

**8:30 p.m. Round Table Discussion with beverages and munchies:**

Differences and similarities in the mechanisms of mRNA decay in different eukaryotes.

Discussion Leaders: Pam Green, Allan Jacobson, Mike Kiledjian, Roy Parker, Stu Peltz, David Tollervey (moderator), Jeff Wilusz

## Tuesday July 9

7:30 a.m. – 9:00 a.m.

Breakfast

**Morning – Free** (*Trip to Kartchner Caverns for those who signed up*)

12:15 p.m. – 1:30 p.m. Lunch

## Afternoon

**2:00 p.m. Translational accuracy**

Introduction: Phil Farabaugh

- ♦ John McCarthy – Novel cap-associated functions in budding and fission yeast
- ♦ Phil Farabaugh - Programmed alternative decoding of mRNAs: an approach to a mechanistic explanation
- ♦ Yoshi Nakamura – Regulation of translation termination

## 4:00 p.m. Poster Session 2

6:00 p.m. – 7:00 p.m.

Dinner

## Evening

### 7:00 p.m. *Multicomponent bacterial nucleases*

Introduction: George Mackie

- ♦ Murray Deutscher – RNA quality control
- ♦ Cecília Maria Arraiano – Regulation of exonucleases and RNA stability in *Escherichia coli*
- ♦ Bob Simons – Bacterial RNA processing and decay at low temperatures

Coffee Break

- ♦ George Mackie – Structure-function relationships in the enzymes of mRNA decay in *Escherichia coli*
- ♦ Stan Cohen – Modes of target site selection by RNase E and related enzymes
- ♦ Joel Belasco – RNA degradation by RNase E

## Wednesday July 10

7:30 a.m. – 9:00 a.m.

Breakfast

## Morning

### 9:00 a.m. *Interplay between mRNA polyadenylation, translation and decay in prokaryotes and prokaryotic organelles*

Introduction: Marc Dreyfus

- ♦ Marc Dreyfus – 5' end-independent mRNA decay in *Escherichia coli*: the importance of translation
- ♦ A.J. Carpousis – Function in *Escherichia coli* of the non-catalytic part of RNase E: role in the degradation of untranslated mRNA

Coffee Break

- ♦ Philippe Régnier – Are the RNase E- and poly(A)-dependent pathways of RNA degradation independent in *Escherichia coli*?
- ♦ Sid Kushner – Complex interactions among RNase E, polynucleotide phosphorylase, poly(A) polymerase and other proteins help govern mRNA decay in *Escherichia coli*

- ♦ Gadi Schuster – Polyadenylation and degradation of RNA in chloroplast and prokaryotes: similarities and differences

12:15 p.m. – 1:30 p.m. Lunch

### Afternoon

**2:00 p.m. Round Table Discussion with beverages and munchies: RNA surveillance in bacteria?**

Discussion Leaders: A. J. Carpousis (moderator), Murray Deutscher, Marc Dreyfus, Sid Kushner, George Mackie, Philippe Régner

### Evening

**6:00 p.m. Dinner and Announcement of Poster Awards  
DJ/Dancing**

## Thursday July 11

7:30 a.m. – 9:00 a.m.

Breakfast

### Morning

**9:00 a.m. RNA interference and other RNA mediators of gene expression**

Introduction: Amy Pasquinelli

- ♦ Rich Jorgensen – Sense cosuppression in plants
- ♦ Scott Hammond – RNA interference: mechanism and applications
- ♦ Amy Pasquinelli – Post-transcriptional gene regulation by ~22 nucleotide RNAs

*Coffee Break*

- ♦ Kazunari Taira – RNA targeting at any site of interest by a novel RNA-protein hybrid ribozyme, and gene discovery based on hybrid ribozyme libraries
- ♦ Stu Peltz – RNA as a target in drug discovery

12:15 p.m – 1:30 p.m.

Box Lunches Available