

Giovanni Armenise Harvard Foundation 17th Symposium

Quantifying Biology in Space and Time

June 9 – 12, 2019

[Park Hotel ai Cappuccini](#), Gubbio, Italy

Summary

The 17th Symposium of the Giovanni Armenise-Harvard Foundation was held, for the second time, in Gubbio, at Park Hotel ai Cappuccini, the venue that had hosted the 2016 meeting. Once again, researchers from Italian, European, and American institutions immersed themselves in the beautiful landscape of the Umbria hills, as well as into a three-day-long journey into the latest developments of biology.

The theme chosen for this symposium was “Quantifying Biology in Space and Time”. As Harvard Medical School’s Dean (and Armenise Harvard Foundation President) George Daley commented, the title is a reference to the remarkable technologies that are transforming life sciences. “Biology is becoming increasingly subject to the kind of razor-like focus that has traditionally been associated to physics or chemistry”, Daley explained. “We now have amazing imaging technologies that allow us to see with finer and finer resolution not just individual cells, but the structure within cells itself. And we also have a whole new set of tools that allow us to see single cells in isolation, and even single molecules within them.”

The meeting started out with a keynote lecture by Karen Adelman, who leads a lab in Harvard Medical School’s Department of Biological Chemistry and Molecular Pharmacology. Her lab is focused on the regulation of gene expression, and in particular on enhancers – short sequences of DNA that make the transcription of a particular gene more likely. “You can think about our genome as a book”, she explained. “Every cell in the body has the same book, but every part of the body reads different parts of the book. Gene regulation is the process that says which part of the book must be read”. Enhancers, in particular, are pieces of DNA that are recognized by proteins in the cells called transcription factors, which in turn are the key activators of genes. “What is interesting is that the enhancers and the transcription factors don’t necessarily bind next to the gene they activate. It’s action at a distance”, Adelman explained. “My lab tries to understand what happens at an enhancer, and how it is able to talk to a gene in another place.”

To do this, Adelman’s lab uses a recently-developed method to isolate genetic material at the exact moment when the DNA sequence of an enhancer is being copied into RNA, then reads the RNA sequence and maps it back to the corresponding DNA, thus identifying the enhancers. It is a typical example of the innovative technologies and tools that were the focus of the meeting. As Adelman went on to explain, studying enhancers also exemplifies curiosity-driven basic research that has clear connections to clinical problems. “In many cancers, the fundamental problem is that a cell does things it is not supposed to do. And that is all related to the proteins the cell expresses, and how it responds to signals to grow. For us to understand why this happens, we need to understand why the genome thinks it gets the signal to turn that gene on. We’ve looked around genes for many years and have not

understood that process. But now that we look to enhancers, we begin to understand how genes get that aberrant information to turn on in the wrong situation.”

Dr. Daley’s and Adelman’s opening addresses that first evening were followed by a “Jeffersonian dinner” that set the tone for the next two days, and helped bridge the gap between senior and junior, Italian and American researchers. At each table, a moderator led the conversation through a series of open questions about researchers’ life, ambitions and challenges. Then, on Monday, the scientific program (on the following pages) kicked off, and included many highlights: spectacular sub-cellular imaging that allows the study of cell-to-cell communication; the study of cancer evolution as a way to control the emergence of drug resistance; research on microRNAs’ role as gatekeepers in brain wiring; the study of transcription factors with quantitative biology tools; the investigation of how cells count how many centrosomes there are.

Overall, more than 20 talks over three sessions, half each by American and often presenting ground-breaking and yet-unpublished research, and ending with Pier Paolo di Fiore’s closing keynote on subverted endocytosis and cancer. In the end, participants had had a unique overview and discussion of how, in the words of HMS Dean George Daley, “technology is opening up whole new vistas on biology.”

Giovanni Armenise Harvard Foundation 17th Symposium
Quantifying Biology in Space and Time
June 9 – 12, 2019

PROGRAM

SUNDAY, JUNE 9, 2019

Arrivals and Check-in

5:30 PM Registration

6:30 PM Welcome and Introduction
George Daley, Dean, Harvard Medical School (HMS)

6:45 PM Keynote Address
Karen Adelman, BCMP, HMS
Controlling transcription at coding and non-coding RNA loci



7:30 PM Welcome Reception and Opening Dinner

MONDAY, JUNE 10, 2019

7:00 - 8:30 AM Breakfast

Session 1 Session Title: Cell circuits in space and time

Session Chair: Steve Blacklow, BCMP, HMS
20 minute talks plus 10 minutes for Q & A

8:30 AM Tommy Kirchhausen, Cell Biology, HMS
Imaging subcellular dynamics from molecules to multicellular organisms

9:00 AM Andrea Ciliberto, IFOM, FIRC Institute of Molecular Oncology, Milan
Stopping the unstoppable: why and how cells escape from a mitotic arrest

9:30 AM Andrew Kruse, BCMP, HMS
Structural basis for rapid desensitization of GPCR signaling

10:00 AM Break

10:15 AM Diego di Bernardo, Telethon Institute of Genetics and Medicine, Naples
Cybergenetics: engineering and control of transcriptional circuits

10:45 AM Adrian Salic, Cell Biology, HMS
Lipid-dependent regulation of a developmental morphogen

11:15 AM Francesca Ciccarelli, The Francis Crick Institute, London
Systems Biology to Study Cancer Evolution

11:45 AM Break

12:00 PM Steve Blacklow, BCMP, HMS
A molecular mechanism for feedback inhibition of notch signaling

12:30 PM Alberto Bardelli, Oncology, Candiolo Cancer Institute IRCCS, University of Turin
Cancer evolution as a therapeutic target

1:00 PM Lunch

Session 2 Session Title: Single-molecule measurement of transcriptional circuits

Session Chair: Michele Caselle, University of Turin
20 minute talks plus 10 minutes for Q & A

2:30 PM Kevin Struhl, BCMP, HMS
Extensive structural differences of closely related 3' mRNA isoforms: links to Pab1 binding and mRNA stability

3:00 PM Marie-Laure Baudet, Center for Integrative Biology, University of Trento
microRNAs: gatekeepers of space and time in brain wiring

MONDAY, cont'd

- 3:30 PM Luigia Pace, Italian Institute of Genomic Medicine
Epigenetic and transcriptional control during T cell fate commitment
- 4:00 PM Davide Cacchiarelli, Telethon Institute of Genetics and Medicine, Naples
Understanding transcription factors through quantitative biology
- 4:30 PM Break (15 minutes)
- 4:45 PM Luca Giorgetti, Friedrich Miescher Institute for Biomedical Research, Basel
Towards a quantitative understanding of chromosome structure and transcriptional regulation
- 5:15 PM Giocchino Natoli, European Institute of Oncology & Humanitas, Milan
Access to the genomic regulatory information and the control of inflammatory gene expression
- 6:00 PM Poster Session, with Wine/Prosecco and Hors d'oeuvres
- 8:00 PM Dinner

TUESDAY, JUNE 11, 2019

- 6:30 - 8:30 AM Breakfast
- 7:45 AM Guided Excursion to Assisi (optional)
Free morning for those not participating in the excursion
- 1:30 PM Lunch
- Session 3** **Session Title: Detecting biological mishaps one molecule at a time**
Session Chair: Rosa Bernardi, San Raffaele Scientific Institute, Milan
20 minute talks plus 10 minutes for Q & A
- 2:30 PM Johannes Walter, BCMP, HMS
The acrobatics of replication-coupled DNA repair
- 3:00 PM Luca Fava, Center for Integrative Biology, University of Trento
How do cells count centrosomes?
- 3:30 PM David Pellman, Pediatric Oncology, Dana-Farber Cancer Institute
Rapid genome evolution from catastrophic cell division errors
- 4:00 PM Francesca Demichelis, Center for Integrative Biology, University of Trento
Synthetic lethal candidates nominated through orthogonal data driven search
- 4:30 PM Break

TUESDAY, cont'd

- 4:45 PM Susan Shao, Cell Biology, HMS
Mechanism of ribosome-associated quality control
- 5:15 PM Sun Hur, BCMP, HMS
Ubiquitin E3 ligases in innate immunity
- 5:45 PM Federico Forneris, University of Pavia
Molecular mechanisms of collagen lysyl hydroxylases and glycosyltransferases
- 6:15 – 7:00 PM Closing Keynote
Pier Paolo Di Fiore, European Institute of Oncology, University of Milan
Subverted endocytosis and cancer: much more than meets the eyes
- 8:00 PM Dinner

WEDNESDAY, JUNE 12, 2019

- 6:30 - 10:30 AM Breakfast
- 11:00 – All Day Hotel check-out and Departures

