Gordon Research Conferences

Meeting Details

RNA Nanotechnology

Gordon Research Conference

Discovering and Assembling RNA Architectures for Materials, Therapeutics and Diagnostics

Dates

January 22-27, 2017

Location

Ventura Beach Marriott
Ventura, CA

Organizers

Chair:
Neocles B. Leontis

Vice Chairs:
Tushar Patel & **Thomas Hermann**

Application Deadline

Applications are no longer being accepted for this meeting. If you have been instructed to apply by the Conference Chair, please contact **Hillary Lussier** for further instructions.

Meeting Description

The 2017 GRC in RNA Nanotechnology will draw on the success of the first conference on this topic, held in 2015, to foster collaborations between scientists and engineers working in the diverse fields of chemistry, biochemistry, structural biology, microbiology, cancer biology, cell biology, biophysics, pharmacy, materials, and nanotechnology, with the purpose of promoting transformative advances that will enable the monitoring and improvement of human health and the diagnosis and treatment of diseases utilizing the unique modality provided by RNA-based nanoparticles.

RNA Nanotechnology has emerged from a series of important discoveries over the past 30 years, showing that: 1) RNA molecules, like proteins, can form complex and compact folded structures; 2) RNA molecules can function as enzymes, just like proteins, to catalyze important reactions in living cells macromolecules; 3) most RNA molecules in human cells are non-protein coding RNA (ncRNA) and play important roles in regulating gene expression; 4) most of the genome is transcribed and most of RNA produced is functional; 5) RNA is capable of self-assembly into complex quaternary structures, in association with other RNA molecules, proteins, or even DNA; and 6) RNA is capable of specifically binding small molecules and changing its structure in response to binding. Like proteins, RNA molecules form complex, hierarchically organized structures, that span several orders of magnitude.

In parallel with these discoveries, powerful new experimental methods have been developed to rapidly probe the solution structures of RNA with chemical and enzymatic probes, to establish atomic resolution structures by crystallography, NMR, and increasingly high-resolution cryo-electron microscopy (EM) and to evolve RNA molecules with new functionalities. Advances in computational analysis and 3D modeling of RNA have occurred in parallel, which have greatly improved our ability to 1) predict the 2D and 3D structures of RNA molecules based on sequence and 2) to design RNA molecules to fold into a desired 3D structure capable of self-assembling into a target supra-molecular assembly. Analysis of new 3D structures of large RNA molecules, beginning with catalytic Group I ribozymes and culminating with the ribosome revealed recurrent, modular 3D motifs and folds that can be reassembled to create novel architectures for constructing homogeneous nanostructures having defined size, shape, and stoichiometry; this pioneering concept demonstrated over 15 years ago by Prof. Peixuan Guo, Chair of the 2015 RNA Nanotechnology GRC and Prof. Neocles Leontis, Chair of the upcoming 2017 meeting.

The field has developed rapidly since then. The use of RNA as a medium for nanotechnology follows on the successful use of DNA, for this purpose pioneered by Nadrian Seeman and his many co-workers. RNA has recently catapulted as a nanotechnology platform due to its diversity in both structure and function. RNA is unique in comparison to DNA by virtue of its high thermodynamic stability, the formation of both canonical and non-canonical base pairings, the stabilization by base stacking, and distinctive *in vivo* attributes. (3) RNA nanotechnology is a unique field that is distinct from the classical studies of native RNA structure and folding that are decades old. In addition to intra-molecular (within a molecule) interactions that facilitate folding, special knowledge of inter-molecular interactions that enable supra-molecular self-assembly is required. (4) RNA nanoparticles can be purified to homogeneity and can be characterized or visualized by chemical, physical, biophysical, and optical methods. (5) Previously, the sensitivity of RNA to RNase degradation had been the biggest hurdle in the production of RNA for use as a construction material. Recently, simple chemical modifications, such as incorporation of 2'-fluorinated nucleosides, have provided resistance to enzymatic degradation, with little perturbation of folding properties and overall retention of biological function in certain cases. (6) Finally, RNA nanotechnology transcends conjugation of functional RNA modules to gold, liposome, dendrimer or polymer based nanoparticles, and more broadly encompasses application of bottom-up approaches to assemble nanometer scale particles composed primarily of RNA.

Related Meeting

This GRC will be held in conjunction with the **"RNA Nanotechnology" Gordon Research Seminar (GRS)**. Those interested in attending both meetings must submit an application for the GRS in addition to an application for the GRC. Refer to the **associated GRS program page** for more information.

Contributors

Gordon Research Conferences

Carl Storm Underrepresented Minority Fellowship

Predominantly Undergraduate Institution Fund (PUI)

National Institutes of Health
Turning Discovery Into Health

CHECKMATE

Bioconjugate Chemistry

ACS Combinatorial Science

Alnylam PHARMACEUTICALS

IONIS PHARMACEUTICALS

The RNA Society

Meeting Program

Sunday

4:00 pm - 8:00 pm	Arrival and Check-in
6:00 pm	Dinner

7:30 pm - 7:40 pm	Welcome / Introductory Comments by GRC Site Staff
7:40 pm - 9:30 pm	**RNA Computation and Modeling**
	The use of computational methodologies can significantly lessen the time and expense required to bring the design of RNA-based nano-constructs to experimental fruition. To advance RNA nanotechnology, we need to meet two complementary computational challenges: Predicting the 3D structures of cellular RNAs from sequence (the RNA folding problem) and designing RNA sequences to fold in specific structures (the "reverse folding" problem). These challenges are difficult because even structured RNAs contain flexible regions that adopt different conformations in response to changes in the environment and binding of ligands. Significant progresses in RNA 3D structure modeling and computation from the traditional intra-molecular interactions to inter-molecular interactions have been achieved, which will serve as guiding principles in this session.
	Discussion Leader: **Anne Condon** (University of British Columbia, Canada)
7:40 pm - 7:50 pm	Introduction by Discussion Leader
7:50 pm - 8:10 pm	**Eckart Bindewald** (Leidos Biomedical Research, USA) "Computational Characterization of Multistrand RNA Nanostructures"
8:10 pm - 8:20 pm	Discussion
8:20 pm - 8:45 pm	**Rhiju Das** (Stanford University, USA) "Calculating RNA Folding Energetics"
8:45 pm - 9:00 pm	Discussion
9:00 pm - 9:20 pm	**Craig Zirbel** (Bowling Green State University, USA) "Inferring the 3D Structure of RNA Internal and Hairpin Loops from Sequence"
9:20 pm - 9:30 pm	Discussion

Monday

7:30 am - 8:30 am	Breakfast
9:00 am - 12:30 pm	**RNA Folding and 3D Structure**
	Single-stranded RNA form complex 3D architectures composed of short Watson-Crick helices, interspersed with recurrent autonomous motifs, many of which are structurally well defined. Their modular properties allow them to be re-purposed as building blocks for nanoparticle assembly. For example, GNRA hairpin tetraloops mediate specific long-range interactions; UNCG hairpin loops nucleate folding; kink-turns and C-loops modulate the bending and twisting of helical elements; and many motifs provide specific protein binding sites. This session focuses on understanding the structural, energetic, and dynamic aspects of RNA 3D motifs to enable precise control of size, shape, geometry and positioning of functional groups to construct multifunctional RNA nanoparticles via inter-molecular interactions.
	Discussion Leader: **Sarah Woodson** (Johns Hopkins University, USA)
9:00 am - 9:15 am	Introduction by Discussion Leader
9:15 am - 9:45 am	**Juli Feigon** (University of California, Los Angeles, USA) "Telomerase RNA Folding and Function"
9:45 am - 10:00 am	Discussion
10:00 am - 10:30 am	**Jeffrey Kieft** (University of Colorado Denver School of Medicine, USA) "Viruses: The Master Inventors of Novel (and Perhaps Useful) RNA Folds"
10:30 am - 10:45 am	Discussion
10:45 am - 11:15 am	Coffee Break

11:15 am - 11:45 am	**Nils Walter** (University of Michigan, USA) "Folding of Single RNA Molecules in Nanomachines"
11:45 am - 12:00 pm	Discussion
12:00 pm - 12:30 pm	Poster Previews
12:30 pm	Lunch
1:30 pm - 4:00 pm	Free Time
4:00 pm - 6:00 pm	Poster Session
6:00 pm	Dinner
7:30 pm - 9:30 pm	**Basic Cellular Biology of Extracellular Vesicles**

This session will provide participants programming on basic cellular and molecular biology of extracellular vesicles, to facilitate interdisciplinary interactions between scientists with chemical and physical backgrounds and those with cellular and molecular biology backgrounds, this session will provide an overview of and recent developments in the basic cellular biology of extracellular vesicles with an emphasis on biogenesis, composition and uptake of extracellular vesicles.

Discussion Leader: **Tushar Patel** (Mayo Clinic, USA)

7:30 pm - 7:45 pm	Introduction by Discussion Leader
7:45 pm - 8:10 pm	**David Katzmann** (Mayo Clinic, USA) "Accepted Extracellular Vesicle Secretion from Apical and Basolateral Domains of Polarized Human Cholangiocytes"
8:10 pm - 8:20 pm	Discussion
8:20 pm - 8:45 pm	**Alissa Weaver** (Vanderbilt University School of Medicine, USA) "Signaling Regulation of RNA Trafficking to Exosomes"
8:45 pm - 8:55 pm	Discussion
8:55 pm - 9:20 pm	**Anna Krichevsky** (Brigham and Women's Hospital / Harvard Medical School, USA) "Insights from the Extracellular RNA Analysis of Cancer Stem Cells: On Protein-Coding and Non-Coding RNA"
9:20 pm - 9:30 pm	Discussion

Tuesday

7:30 am - 8:30 am	Breakfast
8:30 am	Group Photo
9:00 am - 12:30 pm	**RNA Synthetic Biology**

This session will focus on synthetic biology approaches that can contribute to and benefit from RNA nanotechnology applications. The session will address how new properties emerging from the assembly of RNA nanostructures will expand the repertoire of synthetic biology approaches. Noncoding RNA motifs including aptamers and ribozymes are already used in synthetic biology to create interacting networks of biological functionality. RNA nanotechnology adds an architectural dimension to organize functional RNAs in spatially defined structures. Stimulus-responsive nano-systems can be created by exploiting the self-assembly ability of functional RNA from building blocks by capitalizing on the modular nature of RNA architectures.

Discussion Leader: **Robert Batey** (University of Colorado Boulder, USA)

9:00 am - 9:15 am	Introduction by Discussion Leader
9:15 am - 9:45 am	**Lydia Contreras** (University of Texas at Austin, USA) "Assembling RNA Modules to Characterize Responsive Regulatory Networks *In Vivo*"

9:45 am - 10:00 am	Discussion
10:00 am - 10:30 am	**Ming Hammond** (University of California, Berkeley, USA) "Riboswitching on the Light: RNA-Based Fluorescent Biosensors to Image Bacterial and Immune Signals"
10:30 am - 10:45 am	Discussion
10:45 am - 11:15 am	Coffee Break
11:15 am - 11:45 am	**Julius Lucks** (Northwestern University, USA) "Measuring and Engineering RNA Co-Transcriptional Folding Pathways to Create New RNA Genetic Switches"
11:45 am - 12:00 pm	Discussion
12:00 pm - 12:10 pm	**Caroline Horizny** (Colleges of Nanoscale Science and Engineering, SUNY Polytechnic Institute, USA) "Development of Nanoscale RNA-Based Tools for Diagnostic Applications"
12:10 pm - 12:15 pm	Discussion
12:15 pm - 12:25 pm	**Jaimie Stewart** (University of California, Riverside, USA) "Self-Assembly of Multi-Stranded RNA Motifs into Lattices and Tubular Structures with Functional Capabilities"
12:25 pm - 12:30 pm	Discussion
12:30 pm	Lunch
1:30 pm - 4:00 pm	Free Time
4:00 pm - 6:00 pm	Poster Session
6:00 pm	Dinner
7:30 pm - 9:30 pm	**Pharmacology and Immunology of RNA Nanotechnologies** *The therapeutic application of RNA requires efficient delivery methods for electrically charged nucleic acids. Cellular delivery technologies are being developed which capitalize on unique properties of RNA nanoarchitectures, including their self-assembly from autonomous, interchangeable modules and the ability of ligand-modified RNA nano-objects to self-deliver through receptor-mediated pathways. For example, RNA-based constructs assembling to nanoscale objects, including RNA sponge materials for siRNA delivery, have proven successful in targeting cancer cells in vivo. This session will present a timely overview on delivery approaches useful for RNA-based nanoparticles and the implications of their immunological properties arising from different delivery technologies.* Discussion Leader: **Muthiah Manoharan** (Alnylam Pharmaceuticals, USA)
7:30 pm - 7:40 pm	Introduction by Discussion Leader
7:40 pm - 8:05 pm	**Kazunori Kataoka** (University of Tokyo, Japan) "Overcoming Hurdles to Clinical Translation of RNA Therapeutics"
8:05 pm - 8:20 pm	Discussion
8:20 pm - 8:45 pm	**Art Krieg** (Checkmate Pharmaceuticals, USA) "Therapeutic Applications of Activating Innate Immunity with Immune Stimulatory RNA or DNA"
8:45 pm - 8:55 pm	Discussion
8:55 pm - 9:20 pm	**Punit Seth** (Ionis Pharmaceuticals, USA) "Receptor Binding and Cellular Uptake of Therapeutic Oligonucleotides"
9:20 pm - 9:30 pm	Discussion

Wednesday

7:30 am - 8:30 am	Breakfast
9:00 am - 12:30 pm	**RNA Nanoparticles for Sensor and Therapeutics Development**
	This session will address the application of RNA nano-assemblies for sensing and therapy. RNA nanotechnology promises to combine the advantages of RNA therapeutics such as antisense binding and siRNA with emergent properties such as nuclease stability and extended tissue retention with the prospect to assemble therapeutics in a modular fashion from functional RNA motifs. Multivalent RNA nano-assemblies provide an opportunity to combine cell-specific sensing with targeted delivery, diagnostics and therapeutic functionality. Approaches for the design, assembly and testing of such multi-valent RNA nano-architectures will be discussed in this session.
	Discussion Leader: **Peixuan Guo** (The Ohio State University, USA)
9:00 am - 9:20 am	Introduction by Discussion Leader
9:20 am - 9:45 am	**Arkadiusz Chworos** (Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences, Poland) "Multimeric RNA Nanoparticles for Gene Expression Regulation"
9:45 am - 10:00 am	Discussion
10:00 am - 10:25 am	**Chengde Mao** (Purdue University, USA) "Rational Design and Construction of RNA Nanostructures"
10:25 am - 10:40 am	Discussion
10:40 am - 11:10 am	Coffee Break
11:10 am - 11:35 am	**Yoshiya Ikawa** (University of Toyama, Japan) "Programmable Formation of Catalytic RNA Triangles and Squares by Assembling Modular RNA Enzymes"
11:35 am - 11:50 am	Discussion
11:50 am - 12:15 pm	**Varathara Thiviyanathan** (University of Texas Health Sciences Center at Houston, USA) "Multi-Functional RNA Nanoparticles for the Targeted Delivery of Therapeutic Drugs to Cancer Cells"
12:15 pm - 12:30 pm	Discussion
12:30 pm	Lunch
1:30 pm - 4:00 pm	Free Time
4:00 pm - 6:00 pm	Poster Session
6:00 pm	Dinner
7:00 pm - 7:30 pm	Business Meeting
	Nominations for the Next Vice Chair; Fill in Conference Evaluation Forms; Discuss Future Site and Scheduling Preferences; Election of the Next Vice Chair
7:30 pm - 9:30 pm	**Extracellular RNA for Therapeutic Development**
	This session will focus on the therapeutic applications of extra-cellular RNA (exRNA). Emphasis will be on methods for identification of candidate RNA therapeutics in the vesicles; packaging of therapeutic synthetic siRNA and miRNA cargoes in extracellular vesicles; approaches for in vivo tracking of extracellular delivery vehicles; and in vivo functional assays to validate therapeutic outcome.
	Discussion Leader: **Samir El Andaloussi** (Karolinska Institute, Sweden)
7:30 pm - 7:40 pm	Introduction by Discussion Leader
7:40 pm - 8:10 pm	**Janusz Rak** (McGill University, Canada)

"Interrelationships Between Oncogenic and Vesiculation Pathways in Cancer"

8:10 pm - 8:25 pm Discussion

8:25 pm - 8:55 pm **Anastasia Khvorova** (University of Massachusetts Medical School, USA)
"Expanding the Chemical Diversity of Therapeutic Oligonucleotides"

8:55 pm - 9:10 pm Discussion

9:10 pm - 9:25 pm **Dajeong Kim** (University of Seoul, South Korea)
"Free-Standing RNA Film and RNA Nanosheets Fabricated by Enzymatic Approach and Their Therapeutic Application"

9:25 pm - 9:30 pm Discussion

Thursday

7:30 am - 8:30 am Breakfast

9:00 am - 12:30 pm

Extracellular RNA for Biomarker Development

One of the most exciting new areas of research is based on extracellular vesicles, such as exosomes and microvesicles. These biological nanovesicles are released by many different types of cells for inter-cellular communication and regulation of growth and differentiation. Exosomes are sized 40-100 nm, and contain specific subsets of host-cell proteins, RNA and lipids. This session will focus on extracellular RNA (exRNA) for biomarker development. Approaches for isolation of RNA cargo from human body fluids (urine, plasma, saliva, etc.) will be addressed and benchmarks for characterization of RNA as possible biomarkers that correlate with normal biological function, disease states or responses to treatment will be discussed.

Discussion Leader: **Jan Lotvall** (University of Gothenburg, Sweden)

9:00 am - 9:20 am Introduction by Discussion Leader

9:20 am - 9:50 am **Saumya Das** (Harvard Medical School, USA)
"Extracellular RNAs as Functional Biomarkers for Cardiac Remodeling"

9:50 am - 10:05 am Discussion

10:05 am - 10:40 am Coffee Break

10:40 am - 11:10 am **Louise Laurent** (University of California, San Diego, USA)
"Predicting Preeclampsia Using Circulating miRNA Biomarkers"

11:10 am - 11:25 am Discussion

11:25 am - 11:55 am **Kendall Van Keuren-Jensen** (Translational Genomics Research Institute, USA)
"Extracellular RNAs for Monitoring Central Nervous System Injury and Disease"

11:55 am - 12:10 pm Discussion

12:10 pm - 12:30 pm General Discussion: How Do We Develop a Translational Nanotechnology Consortium to Realize the Full Potential of RNA Nanotechnology?

12:30 pm Lunch

1:30 pm - 4:00 pm Free Time

4:00 pm - 6:00 pm Poster Session

6:00 pm Dinner

7:30 pm - 9:30 pm

Cross-Fertilization by DNA Nanotechnology

DNA nanotechnology has provided precedent on key features of RNA nanotechnology such as programmable self-assembly from recurring 3D modules, stimulus-responsive structural remodeling, and the development of techniques to study properties and structure of nucleic acid-based soft nanomaterials. This session will address approaches to construct and

characterize programmable nucleic acid nanoarchitectures for the assembly of soft materials including proteins arrays as tools in proteomics, crystallography and screening processes. Emphasis will be given to methods developed for DNA nanotechnology which have potential for application in the design and construction of RNA nano-assemblies.

Discussion Leader: **William Shih** (Harvard University, USA)

7:30 pm - 7:40 pm	Introduction by Discussion Leader
7:40 pm - 8:05 pm	**Mark Bathe** (Massachusetts Institute of Technology, USA) "Top-Down Design, Synthesis, and Functional Application of Designer DNA Nanoparticles"
8:05 pm - 8:15 pm	Discussion
8:15 pm - 8:40 pm	**Rebecca Schulman** (Johns Hopkins University, USA) "Isothermal Control of DNA Nanostructure Self-Assembly and Reconfiguration"
8:40 pm - 8:50 pm	Discussion
8:50 pm - 9:15 pm	**Georg Seelig** (University of Washington, USA) "DNA Strand Displacement from the Test Tube to the Cell"
9:15 pm - 9:30 pm	Discussion

Friday

7:30 am - 8:30 am	Breakfast
9:00 am	Departure

Funding for this conference was made possible NIH Common Fund, through the Office of Strategic Coordination/Office of the NIH Director. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention by trade names, commercial practices, or organizations imply endorsement by the U.S. Government.