

CNIO – CaixaResearch Frontiers Meeting
MOLECULAR CHAPERONES IN CANCER AND PROTEIN QUALITY CONTROL
June 10th – 12th, 2024

Venue:

Spanish National Cancer Research Centre – CNIO Auditorium, Madrid, Spain

Chairpersons and organizing committee:

Gabriela Chiosis, Memorial Sloan Kettering Institute, USA

Nabil Djouder, Spanish National Cancer Research Centre-CNIO, Spain

Judith Frydman, Stanford University, USA

Oscar Llorca, Spanish National Cancer Research Centre-CNIO, Spain

Paul Workman, Centre for Cancer Drug Discovery, The Institute of Cancer Research, London, UK

Rationale:

Molecular chaperones play a crucial role in maintaining protein folding, stability, and function in both normal and disease states, including cancer. Despite significant advances, our understanding of the precise molecular mechanisms underlying chaperone function and their role in cancer development remains incomplete. This conference will focus on recent progress in elucidating the structure and function of molecular chaperones, particularly HSP90, using model organisms. Additionally, we will explore the role of chaperones in networks with other proteins in cancer phenotypes, how chaperones support cancer evolution, and approaches to better target chaperones for cancer treatment. By bringing together researchers and clinicians from diverse disciplines, we aim to foster collaboration and advance our understanding of the critical role of chaperones in cancer biology.

SPEAKER LIST

Chairpersons and organizing committee:

Dr. Gabriela Chiosis

Dr. Nabil Djouder

Dr. Judith Frydman

Dr. Oscar Llorca

Dr. Paul Workman

Speakers:

Dr. Udai Banerji - The Institute of Cancer Research; The Royal Marsden NHS Foundation Trust

Dr. Jeffrey L. Brodsky - University of Pittsburgh, Kenneth P. Dietrich School of Arts and Sciences

Dr. Johannes Buchner - Technical University of Munich

Dr. Benoit Coulombe - Institut de recherches cliniques de Montréal

Dr. Chengkai Dai - Center for Cancer Research, National Cancer Institute

Dr. Elke Deuerling - Konstanz University

Dr. Lila Gierasch - University of Massachusetts Amherst

Dr. Manajit Hayer-Hartl - Max-Planck-Institute of Biochemistry

Dr. Walid Houry - Biochemistry, University of Toronto

Dr. Ursula Jakob - University of Michigan

Dr. Matthias Mayer - Center for Molecular Biology Heidelberg – ZMBH

Dr. Leonard Neckers - Center for Cancer Research, National Cancer Institute

Dr. Rahul Samant - Babraham Institute

Dr. Ritwick Sawarkar - University of Cambridge

Dr. Lea Sistonen - Turku Centre for Biotechnology

Dr. Peter Walter - Howard Hughes Medical Institute, University of California

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Monday June 10th, 2024

13:00-14:45 Registration - welcome coffee

14:45-15:00 Welcome address: Oscar Llorca

15:00-16:00 Keynote Lecture

Stages of phase-separation during biogenesis of a bacterial microcompartment

Manajit Hayer-Hartl, Max-Planck-Institute of Biochemistry, Martinsried, Germany

16:00-16:30 Coffee break

16:30-18:30 Protein Quality Control

Chair: Oscar Llorca

This session will present recent work and discuss how proteins are appropriately folded to ensure their proper functions.

16:30 – 17:00 Regulation of the heat shock transcription factor Hsf1 b

y the Hsp70 chaperone network

Matthias Mayer, Max-Planck-Institute of Biochemistry, Martinsried, Germany

17:00 – 17:30 Co-Translational Protein Modification Principles and Their Potential Implications in Cancer

Elke Deuerling, Konstanz University, Konstanz, Germany

17:30 – 17:45 short talk

17:45 – 18:00 short talk

18:00 – 18:30 Regulation of chaperone machineries

Johannes Buchner, Technical University of Munich (TUM), Garching, Germany

18:30-20:00 Welcome cocktail for all participants

Tuesday June 11th, 2024

09:00 - 12:30 Folding, Misfolding and Aggregation

Chair: Lea Sistonen

This session will cover the most recent mechanistic advances of how chaperones and other stress-inducible proteins recognize and deal with misfolded and damaged proteins inducing their aggregation and degradation.

09:00 – 09:30 The intersection between cellular stress response pathways, proteostasis, and cancer cell survival

Jeffrey L. Brodsky, University of Pittsburgh, Kenneth P. Dietrich School of Arts and Sciences, Pittsburgh, US

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09:30 – 09:45 short talk

09:45 – 10:00 short talk

10:00 – 10:30 How Hsp70s Bind Many Substrates But Not All

Lila M. Gierasch, University of Massachusetts Amherst, Amherst, US

10:30-11:30 *Coffee break and group picture*

11:30 – 12:00 Proteomic Instability of Cancer and Non-oncogene Addiction: Heat Shock Factor 1 (HSF1) as an Oncogenic Enabler

Chengkai Dai, Center for Cancer Research, National Cancer Institute, Bethesda, US

12:00 – 12:30 Function of Heat Shock Transcription Factors in Epithelial-Mesenchymal Plasticity

Lea Sistonen, Faculty of Science and Engineering Åbo Akademi University Turku Centre for Biotechnology, Turku, Finland

12:30-14:00 *Lunch at the cafeteria*

14:00-17:30 **Chaperones, Molecular Mechanisms and Structure I**

Chair: Gabriela Chiosis

This session will present recent advances and breakthroughs on the mechanisms and structural bases of chaperones how alterations in protein quality control contribute to cancer.

14:00 – 14:30 Recent advances in the characterization of the Particle for Arrangement of Quaternary structure (PAQosome)

Benoit Coulombe, Montreal Clinical Research Institute (IRCM), University of Montreal, Québec, Canada

14:30 – 15:00 CryoEM studies of the R2TP cochaperone

Oscar Llorca, Spanish National Cancer Research Centre (CNIO), Madrid, Spain

15:00 – 15:15 short talk

15:15 – 15:30 short talk

15:30-16:00 *Coffee break*

16:00 – 16:30 **Ursula Jakob**, University of Michigan; Molecular Chaperones in Metabolism, Ann Arbor, US

16:30 – 17:00 Towards understanding the functions of the PAQosome and its subcomplexes

Walid A. Houry, Biochemistry, University of Toronto, Ontario, Canada

17:00 – 17:30 Digging into the URI Prefoldin-Like Complex

Nabil Djouder, Spanish National Cancer Research Centre, Madrid, Spain

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17:30-19:15 Poster session - Refreshments

Wednesday June 12th, 2024

08:30-11:45 Chaperones, Molecular Mechanisms and Structure II
Chair: Walid Houry

This session will present recent advances and breakthroughs on R2TP and prefoldin complexes and their potential role in protein quality control.

08:30 – 09:00 Epichaperomes in Cancer: Unraveling Molecular Complexity for Therapeutic Innovation and Diagnostic Advancements
Gabriela Chiosis, Memorial Sloan Kettering Cancer Center, New York, US

09:00 – 09:30 **Leonard M. Neckers**, Center for Cancer Research, National Cancer Institute – NIH, Rockville, US

09:30 – 09:45 short talk

09:45-10:15 *Coffee break*

10:15 – 10:45 The TRiCky business of folding proteins in the cell
Judith Frydman, Stanford University, Stanford, US

10:45 – 11:00 short talk

11:00 – 11:15 short talk

11:15-17:00 Targeting Chaperones: Chaperonotherapy
Chair: Nabil Djouder

This session will discuss the chemistry, drug design and allosteric regulation with recent advances in generating new therapeutic approaches to target chaperones for cancer treatment.

11:15 – 11:45 How HSP90 helps cancer proliferation
Ritwick Sawarkar, University of Cambridge, UK

11:45-13:45 *Lunch at the cafeteria*

13:45 – 14:15 Discovery and development of NXP800: a clinical stage GCN2/ISR activator that inhibits HSF1 transcription for the treatment of ARID1A mutant ovarian cancer
Paul Workman, Centre for Cancer Drug Discovery, The Institute of Cancer Research, London, UK

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14:15 – 14:45 Clinical applications of targeting HSP90 and other molecular chaperones
Udai Banerji, The Institute of Cancer Research; The Royal Marsden NHS Foundation Trust, London, UK

14:45 – 15:00 short talk

15:00 – 15:15 short talk

15:15-15:45 *Coffee break*

15:45– 16:15 Exploring chaperone vulnerabilities in (cancer) senescence
Rahul Samant, Babraham Institute, Cambridge, UK

16:15-16:45 *Closing Lecture*

Targeting the Cell's Stress Pathways for Therapeutic Benefit
Peter Walter, Altos Lab and UCSF, California, US

16:45 – 17:00 Wrap up: Nabil Djouder

17:00 – 17:15 Poster/short talk prizes