

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, 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. Eugenia Clerico - University of Massachusetts Amherst

Dr. Benoit Coulombe - Montreal Clinical Research Institute (IRCM), University of Montreal

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

Dr. Elke Deuerling - Konstanz University

Dr. Walid Houry - Biochemistry, University of Toronto

Dr. Ursula Jakob - University of Michigan

Dr. Matthias Mayer - Center for Molecular Biology Heidelberg (ZMBH)

Dr. Rahul Samant - Babraham Institute

Dr. Ritwick Sawarkar - University of Cambridge

Dr. Lea Sistonen - Turku Centre for Biotechnology

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Monday June 10th, 2024

13:00-14:45 Registration - welcome coffee

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

15:00-16:00 Keynote Lecture

The TRiCky business of folding proteins in the cell
Judith Frydman, Stanford University, Stanford, US

16:00-16:30 *Coffee break*

16:30-18:45 Protein Quality Control I

Chair: Óscar Llorca

16:30 – 17:00 Regulation of the heat shock transcription factor Hsf1 by the Hsp70 chaperone network
Matthias Mayer, Center for Molecular Biology Heidelberg – ZMBH, Germany

17:00 – 17:15 **short talk 1** The Critical Properties of the Chaperonins for Their Function in Mitochondria. **Lingling Chen**, Indiana University, Bloomington, US

17:15 – 17:45 Co-Translational Protein Modification Principles and Their Potential Implications in Cancer
Elke Deuerling, Konstanz University, Konstanz, Germany

17:45 – 18:00 **short talk 2** Bag1 has a key role in the Hsp70-assisted, proteasome-mediated degradation Pathway. **Jorge Cuéllar**, National Centre for Biotechnology, Madrid, Spain

18:00 – 18:15 **short talk 3** Protein phosphatase-2A regulates the formation of cytotoxic protein aggregates through HSP70. **Oliver Krämer**, University Medical Center Mainz, Nackenheim, Germany

18:15 – 18:45 Regulation of chaperone machineries
Johannes Buchner, Technical University of Munich (TUM), Garching, Germany

18:45-20:00 *Welcome cocktail for all participants*

Tuesday June 11th, 2024

09:00 - 12:30 Protein Quality Control II

Chair: Lea Sistonen

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 4** Cotranslational folding of the eukaryotic proteome is mediated by inter-chaperone dynamics. **Mauricio Aguilar Rangel**, Stanford University, US

09:45 – 10:00 **short talk 5** Prefoldin associates to human chromatin where it interacts with the FACT histone chaperone and regulates nucleosome dynamics during transcription elongation. **Sebastián Chávez Canonical**, Institute of Biomedicine of Seville (IBiS), Spain

10:00 – 10:30 Selectivity versus Promiscuity in Client Binding by Hsp70s
Eugenia Clerico, University of Massachusetts 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**
Chair: Gabriela Chiosis

14:00 – 14:30 The PAQosome, a HSP90 co-chaperone for protein complex assembly and maturation; implication in disease
Benoit Coulombe, Montreal Clinical Research Institute (IRCM), University of Montreal, Québec, Canada

14:30 – 15:00 CryoEM studies of the R2TP cochaperone
Óscar Llorca, Spanish National Cancer Research Centre (CNIO), Madrid, Spain

15:00 – 15:15 **short talk 6** Regulation of oncogenic kinases by HSP90 molecular chaperone complexes.
Jasmeen Oberoi, University of Sussex, Brighton, UK

15:15 – 15:30 **short talk 7** Structural recognition and stabilization of tyrosine hydroxylase by the J-domain protein DNAJC12. **Jimena Muntaner Pérez-Urria**, Spanish National Centre for Biotechnology (CNB-CSIC), Madrid, Spain

15:30-16:00 *Coffee break*

16:00 – 16:30 Towards understanding the functions of the PAQosome and its subcomplexes
Walid A. Houry, Biochemistry, University of Toronto, Ontario, Canada

16:30 – 16:45 **short talk 8** Structures of the Tubulin cofactors as GTP-dependent multi-subunit chaperone for alpha/beta-tubulin biogenesis. **Jawdat Al-Bassam**, University of California – Davis, US

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16:45 – 17:00 **short talk 9** J-domain proteins: the role of their dimeric state in the Hsp70 Chaperone Machinery. **Veronika Lashkul**, Center for Molecular Biology of Heidelberg university (ZMBH), Germany

17:00 – 17:30 Elucidating the structural basis of the URI prefoldin-like complex
Nabil Djouder / Rayan Naser, Spanish National Cancer Research Centre, Madrid, Spain

17:30-19:00 Poster session - Refreshments

Wednesday June 12th, 2024

09:00-11:15 Chaperones in disease and chaperonotherapy I
Chair: Walid Houry

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

09:30 – 10:00 Polyphosphate - An Ancient Player in Proteostasis and Cancer
Ursula Jakob, University of Michigan; Molecular Chaperones in Metabolism, Ann Arbor, US

10:00 – 10:15 **short talk 10** Nucleolar stress as a driver of aging and neurodegeneration: A ribosomal perspective. **Óscar Fernández Capetillo**, Spanish National Cancer Research Centre, Madrid, Spain

10:15-10:45 *Coffee break*

10:45 – 11:00 **short talk 11** p53 protein degradation redefines the initiation mechanisms and transitional mutations in colorectal cancer. **Irene Herranz**, Spanish National Cancer Research Centre, Madrid, Spain

11:00 – 11:15 **short talk 12** Point mutations of the mitochondrial chaperone TRAP1 affect its functions and pro-neoplastic activity. **Claudio Laquatra**, University of Padua, Italy

11:15-15:30 Chaperones in disease and chaperonotherapy II
Chair: Nabil Djouder

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

11:45 – 12:00 **short talk 13** The chaperone AGR2 contributes to the complex interplay between endoplasmic reticulum stress and inflammation in pancreatic cancer. **Irene Felipe Abrio**, Spanish National Cancer Research Centre, Madrid, Spain

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12:00 – 12:15 **short talk 14** Expression of mitochondrial Hsp40 chaperone is beneficial for mitochondrial biogenesis. **Grzegorz Ciesielski**, University of North Florida, US

12:15 – 12:45 Clinical applications of targeting HSP90 and other molecular chaperones
Udai Banerji, The Institute of Cancer Research; The Royal Marsden NHS Foundation Trust, London, UK

12:45-14:15 *Lunch at the cafeteria*

14:15 – 14:30 **short talk 15** From Chaperones to Epichaperomes: Phosphorylation Triggered Shape and Function Shifting of HSP90. **Tanaya Roychowdhury**, Memorial Sloan Kettering Cancer Centre, NY, US

14:30– 15:00 Exploring chaperone vulnerabilities in (cancer) senescence
Rahul Samant, Babraham Institute, Cambridge, UK

15:00-15:30 *Closing Lecture*

Targeting the Cell's Stress Pathways for Therapeutic Benefit in Cancer
Paul Workman, Centre for Cancer Drug Discovery, The Institute of Cancer Research, London, UK

15:30 – 15:45 Wrap up: Nabil Djouder

15:45 – 16:00 Poster/short talk prizes