

CNIO-“la Caixa” Foundation Frontiers Meeting- 2nd-4th MAY 2017

MOLECULAR CHAPERONES IN CANCER

In memory of Dr. Susan Lindquist

Venue:

Spanish National Cancer Research Centre – CNIO Auditorium
Madrid, Spain

Chairpersons and organizing committee:

Nabil Djouder, Spanish National Cancer Research Centre, Madrid, Spain
Wilhelm Krek, Institute for Molecular Health Sciences, ETH, Zurich, Switzerland
Paul Workman, The Institute of Cancer Research, London, UK
Xiaohong Helena Yang, Cancer Cell, Cambridge, USA

Rationale:

Molecular chaperones play key roles in the folding, stability and activity of proteins in normal cell homeostasis and disease pathology, including cancer. However, despite recent progress we have much to learn in comprehending the precise details of the molecular function of chaperones and how they support cancer development. This conference will focus on recent developments in our understanding of the structure and function of molecular chaperones such as HSP90, including use of model organisms. We will also address how chaperones act in networks with other proteins to create cancer phenotypes, how chaperones facilitate and support cancer evolution, and how better to target chaperones for cancer treatment.

Speakers

Banerji, Udai
Buchner, Johannes
Bukau, Bernd
Chiosis, Gabriela
Cuervo, Ana María
Golemis, Erica
Heikenwälder, Mathias
Kalodimos, Charalampos
Karin, Michael
Kaufman, Randal J.
Llorca, Oscar
Mayer, Matthias
Mendillo, Marc
McAlpine, Shelli R.
Moll, Ute
Montoya, Guillermo
Morimoto, Richard
Nagata, Kazuhiro
Ohkubo, Shuichi
Pearl, Laurence
Pincus, David
Sistonen, Lea
Van Oosten-Hawle, Patricija
Vaughan, Cara

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Tuesday May 2nd, 2017

13:00 Registration - welcome coffee for all participants

14:45-15:00 Welcome address **Wilhelm Krek**

15:00-16:00 Keynote Lecture
Chair: Wilhelm Krek

Proteostasis Networks in Development, Aging and Cancer
Richard Morimoto, Northwestern University, Evanston, US

16:00-16:30 *Coffee break*

16:30-18:30 Protein Quality Control
Chair: Wilhelm Krek

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

16:30 – 17:00 Protein quality control in the ER: ERAD and autophagy
Kazuhiro Nagata, Kyoto Sangyo University, Japan

17:00 – 17:30 Dynamics of Hsp70 and Hsp90 mediated Regulation of the Conformation of p53 and p53 Cancer Variants.
Matthias Mayer, ZMBH, Heidelberg, Germany

17:30 – 17:45 short talk

17:45 – 18:00 short talk

18:00 – 18:30 The epichaperome in cancer – role and significance
Gabriela Chiosis, Memorial Sloan-Kettering Cancer Center, New York, US

19:00-21:00 *welcome cocktail with speakers*

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Wednesday May 3rd, 2017

08:30 - 12:30 Folding, misfolding and aggregation

Chair: Udai Banerji

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

08:30 – 09:00 Regulation of chaperone machineries

Johannes Buchner, TUM Technische Universität München, Germany

09:00 – 09:15 short talk

09:15 – 09:30 short talk

09:30 – 10:00 Mechanisms of protein disaggregation by molecular chaperones

Bernd Bukau, ZMBH, University of Heidelberg, and DKFZ - German Cancer Research Center, Germany

10:00 – 10:30 Structural basis for the interaction of molecular chaperones with non-native proteins

Charalampos Kalodimos, College of Biological Sciences, University of Minnesota, St. Paul, US

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

11:30 – 12:00 Structural and Functional Basis of Protein Phosphatase5 Specificity

Cara Vaughan, Birkbeck University of London, UK

12:00 – 12:30 Structural and functional analysis of human CCT/TriC

Guillermo Montoya, Novo Nordisk Foundation Center for Protein Research Faculty of Health and Medical Sciences, University of Copenhagen, Denmark

12:30-14:00 *Lunch*

14:00-17:30 UPR and Stress mechanisms

Chair: Guillermo Montoya

This session will discuss the unfolded protein response programmes and other stress mechanisms

14:00 – 14:30 Essential Function and Dynamic Regulation of Heat Shock Factor:

A Paradigm from Yeast for its Role in Cancer

David Pincus, Whitehead Institute for Biomedical Research, Cambridge, US

14:30 – 15:00 Synergistic and opposite effects of heat shock transcription factors in cell stress and cancer.

Lea Sistonen, Åbo Akademi University, Turku, Finland

15:00 – 15:15 short talk

15:15 – 15:30 short talk

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15:30-16:00 *Coffee break*

16:00 – 16:30 *Tba*

Wilhelm Krek, Molecular Health Sciences Institute, ETH Zurich, Switzerland

16:30 – 17:00 Cryo-EM structure of the HSP90 co-chaperone required for assembly of the ATM/ATR/mTOR family of kinases

Oscar Llorca, CIB, Madrid, Spain

17:00 – 17:30 Delineating and exploiting stress response network addictions in malignancies

Marc Mendillo, Northwestern University, Chicago, US

17:45-19:45 Poster session – Snack for all participants

20:30 *Dinner for the speakers*

Thursday May 4th, 2017

08:30-13:00 Chaperones in Cancer

Chair: Nabil Djouder

This session will present recent advances and breakthroughs of in vivo models generated to understand chaperones' biological relevance in cancer and how alterations in protein quality control contribute to cancer.

08:30 – 09:00 Chaperone-mediated autophagy, helping cancer survival one protein at a time

Ana María Cuervo, Albert Einstein College of Medicine, New York, US

09:00 – 09:30 On the role of Hsp60 and mitochondrial UPR to drive intrahepatic cholangiocellular carcinoma

Mathias Heikenwälder, German Cancer Research Center, Heidelberg, Germany

09:30 – 10:00 The transcription factor PQM-1 is a novel regulator of proteostasis and mediator of transcellular chaperone signalling in *C. elegans*

Patricija Van Oosten-Hawle, University of Leeds, UK

10:00 – 10:15 short talk

10:15-11:00 *Coffee break (certificates and invoices will be available at the reception desk)*

11:00 – 11:30 p62/SQSTM1: A multifunctional autophagy receptor controlling inflammation and cancer

Michael Karin, University of California, La Jolla, US

11:30 – 12:00 Improving survival by exploiting tumor dependence on stabilized mutant p53 in mouse models.

Ute Moll, Stony Brook University, New York, US

12:00 – 12:30 *ER protein misfolding causes mitochondrial dysfunction leading to oncogenesis*

Randal J. Kaufman, Sanford|Burnham Medical Research Institute, La Jolla, US

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12:30-14:30 *Lunch*

14:30-18:00 Targeting chaperones: chaperonotherapy
Chair: Lea Sistonen

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.

14:30 – 15:00 Pathways of HSP90 client protein degradation
Laurence Pearl, University of Sussex, Brighton, UK

15:00 – 15:30 *What have we learned from the clinical development of HSP90 inhibitors?*
Udai Banerji, The Institute of Cancer Research, London, UK

15:30 – 15:45 short talk

15:45 – 16:00 short talk

16:00-16:30 *Coffee break*

16:30 – 17:00 Strategies for designing heat shock protein inhibitors: new inhibitors that target Hsp90, Hsp70, and Hsp27
Shelli R. McAlpine, University of New South Wales, Sydney, Australia

17:00 – 17:30 The discovery and development of oral HSP α / β inhibitor, TAS-116
Shuichi Ohkubo, Taiho Pharmaceutical Co., Ltd, Tokyo, Japan

17:30 – 18:00 HSP90 inhibition in cancer versus ciliopathies
Erica Golemis, Fox Chase Cancer Center – Philadelphia, US

18:00-18:15 Prizes for best poster and best short talk

18:15-18:55 Closing Lecture
Drugging the cancer genome and the cancer state with inhibitors of HSP90, HSP70 and the HSF1 pathway
Paul Workman, The Institute of Cancer Research, London, UK

Wrap up and concluding remarks

19:00 – 19:15 **Paul Workman**

Farewell Snack for all participants