DR. PAUL JANSSEN AWARD

FOR BIOMEDICAL RESEARCH

Science Talk

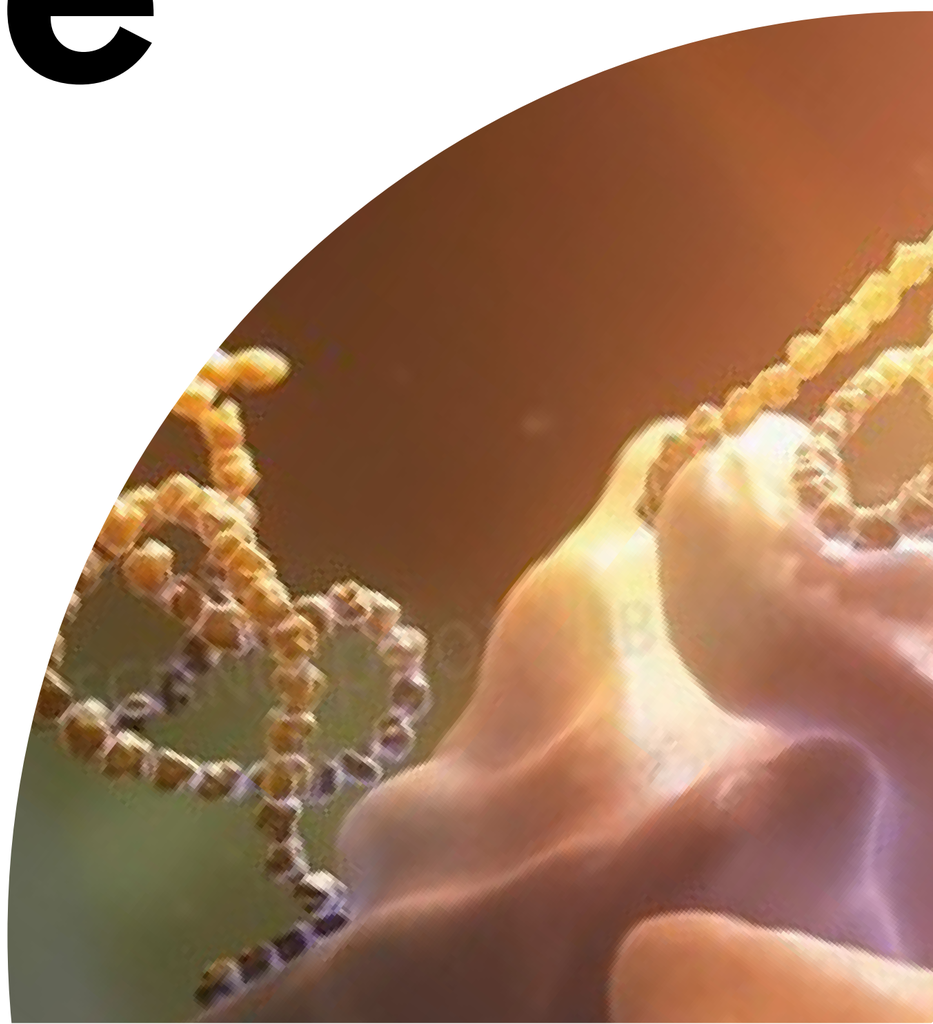
Protein Folding and Disease

27 September 2019

Campus Janssen Beerse

Belgium

2 pm



Meet protein folding pioneers Franz-Ulrich Hartl, M.D. of the Max Planck Institute of Biochemistry and Arthur L. Horwich, M.D. of Yale University School of Medicine who will receive the Dr. Paul Janssen Award for Biomedical Research 2019 for their revolutionary insights into chaperone-mediated protein folding.

This Science Talk, Protein Folding and Disease will showcase their work. Following award lectures from Drs. Hartl and Horwich, fellow prominent scientists will discuss the implications for human disease.

Arthur Horwich, M.D.

Sterling Professor of Genetics and Professor of Pediatrics, Yale School of Medicine and Investigator, Howard Hughes Medical Institute

Franz-Ulrich Hartl, M.D.

Director, Max Planck Institute of Biochemistry

Proteins are responsible for a wide range of functions in cells, including structure, catalysis, transport, and signaling. In order to carry out their myriad roles, these strings of amino acids must fold into proper conformation. Drs. Hartl and Horwich have dedicated their careers to better understanding the molecular machinery that drives protein folding, and the implications when a protein misfolds. Prior to their groundbreaking work, it was thought that proteins folded spontaneously within cells, with the structure determined by the amino acid sequence. While studying mitochondrial protein import, which importantly requires that proteins be unfolded and refolded, Drs. Horwich and Hartl hypothesized that the process may not be spontaneous but dependent on cellular machinery. Indeed, they discovered a new class of proteins that facilitate protein folding. These protein folders, part of the chaperone family of proteins, improve the efficiency of protein folding in cells and help avoid the formation of unfolded protein aggregates. Proper protein folding is important to human biology and health, as defects in folding are associated with aging and diseases including Alzheimer's disease, Parkinson's disease, Huntington's disease, and prion disease.

Introduction

Simon Lovestone
Vice President, Disease Area Leader, Neurodegeneration at Janssen

Science Talk by 2019 winners and Q&A

Drs. Horwich and Hartl will individually present their discoveries and recent work.

Science Dialogue – From chaperoning protein folding to therapeutic targets and clinical perspectives

Participants: Drs. Horwich and Hartl, Simon Lovestone (Janssen), Frederic Rousseau and Joost Schymkowitz (VIB Switch Laboratory, KU Leuven)

Panelists and the audience will talk about a number of key questions that must be addressed in the coming decade to harness the potential of this research. In addition, they will talk about how we can build on the groundwork to discover and develop new therapeutics targeting protein misfolding diseases such as Parkinson's, ALS, Alzheimer's, cancer.

Arthur Horwich, M.D.

Sterling Professor of Genetics and Professor of Pediatrics, Yale School of Medicine and Investigator, Howard Hughes Medical Institute

Dr. Arthur Horwich, a geneticist, received undergraduate and M.D. degrees from Brown University, trained in Pediatrics at Yale, was then a postdoctoral fellow first at Salk Institute in the Tumor Virology Laboratory, and then in Genetics at Yale, then joined the Yale faculty. His work was initially involved with protein import into mitochondria and resulted in discovery of a "folding machine" inside mitochondria, Hsp60. He has used genetic, biochemical, and biophysical tools to study the mechanism of action of these ring shaped so-called chaperonin machines that provide essential assistance to protein folding in many cellular compartments. More recently he has focused on neurodegenerative disease as caused by protein misfolding, seeking to understand how misfolded SOD1 enzyme in the cytosol of motor neurons leads to one form of ALS.

Franz-Ulrich Hartl, M.D.

Director of the Max Planck Institute for Biochemistry

Professor Dr. Franz-Ulrich Hartl, biochemist, was born in 1957 in Essen, Germany. He studied medicine at Ruprecht Karls University, Heidelberg, performed research at the Sloan-Kettering Institute and Howard Hughes Medical Institute, USA, from 1991 to 1997 and was a professor at Cornell University, New York, USA from 1993 to 1997. Dr. Hartl has been the director at Max Planck Institute for Biochemistry since 1997.

Hartl and his colleague Arthur L. Horwich, M.D., refuted the dogma that protein folding is generally a spontaneous process.

- Correct 3D-structure of proteins—molecular machines of the cell—is essential for their function
- Discoverer of molecular chaperones as protein folding helpers
- Chaperones (e.g. Hsp70 and Hsp60) shield proteins from harmful interactions during the folding process and prevent aggregation
- Misfolded proteins can form toxic aggregates in the cells
- Protein aggregations are involved in the development of neurodegenerative diseases and aging processes

Simon Lovestone B.M., Ph.D.

Vice-President, Disease Area Stronghold Leader,
Neurodegeneration Janssen Research & Development

Prior to his current role, Simon Lovestone was Professor of Translational Neuroscience at Oxford University where he initiated and was joint lead academic scientist with Chas Bountra of the Alzheimer's Research UK Drug Development Institute. Before this he spent close to 25 years at King's College London and the Maudsley Hospital including leading the NIHR Biomedical Research Centre, the UK's largest centre for experimental medicine in mental health and dementia and being Director of R&D for King's Health Partners, an Academic Health Sciences Centre working to integrate clinical sciences across three NHS Trusts and the University. He established and led the NIHR Translational Research Collaboration in Dementia, was co-coordinator of the European Medical Information Framework (IMI-EMIF) working closely with Bart Vannieuwenhuyse from Janssen and was instrumental in establishing the European Prevention of Alzheimer's Disease (IMI-EPAD) led by Serge Van der Geyten (Janssen) and Craig Ritchie (Edinburgh). He was crucial in establishing the Clinical Records Interactive Search (CRIS) system, enabling research access to electronic medical records, now active in NHS Trusts across England and Wales and covering approximately one third of all secondary mental health care in the NHS. His own research interests are in the mechanisms of Alzheimer's Disease and in the search for biomarkers and building on these, in drug discovery and experimental medicine. Underpinning all these studies is the use of informatics and the challenges of extracting value from very large variable datasets. He is also a practicing Old Age Psychiatrist specialising in dementia detection, diagnosis and management. He studied Microbiology at Sheffield University, Medicine at Southampton University and was awarded an MPhil and then a PhD from the University of London for research on mental health in new fathers and the role of GSK3 in phosphorylation of tau respectively. He was knighted for services to Neuroscience research in 2017.

Frederic Rousseau, Ph.D.

VIB Switch Laboratory, KU Leuven

Frederic Rousseau is an expert in protein folding and aggregation, both in human disease and in protein and peptide therapeutics. His laboratory is an interdisciplinary workplace with researchers from different backgrounds, such as bioinformatics, biophysics and cell biology. He has created a unique platform of technologies for studying protein aggregation, including biophysical, ultrastructural and cell biological instrumentations he has co-authored more than 120 high-level publications in the field of protein structure, folding and aggregation. Rousseau has made key contributions to the prediction of aggregation nucleating regions, such as the development of the TANGO (Nature Biotechnology, 2004) and WALTZ algorithms (Nature Methods, 2010). These prediction algorithms are being used to direct experimental cell biological and biomedical research, driving (i) the discovery of protein aggregation of tumor suppressors p53 (Nat. Chem. Biol., 2011) and PTEN in human tumors, (ii) the understanding of the aggregation mechanism of the Alzheimer beta peptide (EMBO J. 2008, 2010, 2012) and the demonstration that protein aggregation is a highly specific process (JMB, 2014) that can be exploited to trigger the aggregation of specific proteins as a knock-down technology in plants, bacteria and mammalian cells (Science 2016, Plant Phys 2016, Mol Microb 2015).

Joost Schymkowitz, Ph.D.

VIB Switch Laboratory, KU Leuven

Joost obtained his PhD in 2001 from the University of Cambridge (UK) where he worked on mechanisms of protein folding in the laboratory of Sir Alan Fersht. Frederic's postdoctoral work took place at the EMBL in Heidelberg (Germany) in the laboratory of Luis Serrano, where he contributed to the development of several structural modeling tools. He is now one half of a group leader duo at the Flanders Institute for Biotechnology (VIB) at the University of Leuven (Belgium) where he conducts research on mechanisms of protein misfolding and aggregation.

The Switch Lab endeavors to advance biological science via a combined approach of computational modeling and biophysical and cell biological experimentation. Specifically Switch investigates how sequence composition determines the structure of protein aggregates as well as their specificity, mode of interaction with molecular chaperones and toxicity to cells. Model systems are selected from disease cases, with a focus on neurodegerenation and cancer.

Joost is a scientific founder of-, and scientific advisor to Aelin Therapuetics, a privately held Belgian biotherapeutics company that develops the therapeutic applications of the Pept-inTM technology, invented in the Switch Lab. This technology harnesses the power of protein aggregation to specifically induce functional knockdown of a undruggable target protein, thereby creating a completely new class of antibiotics and first-in-class therapeutics against high-value human targets.

The Science Talk is free. Registration is required via www.janssen.com/belgium/dr-paul-janssen-award.

The Science Talk will be followed by the Award Ceremony and Dinner. Registration is required for both.

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