DAY 1

Keynote Forum

EuroSciCon conference on

Protein, Proteomics and Computational Biology

December 06-07, 2018 | Amsterdam, Netherlands

EuroSciCon

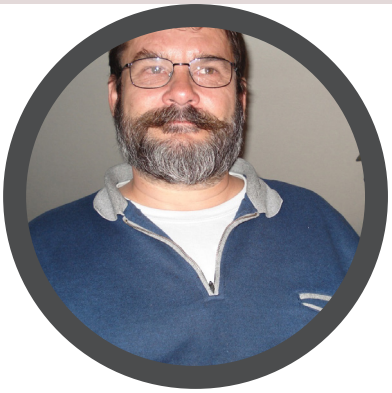
EuroSciCon conference on

Protein, Proteomics and Computational Biology

December 06-07, 2018
Amsterdam, Netherlands

Soren Naaby Hansen et al., Biochem Mol biol J Volume:4
DOI: 10.21767/2471-8084-C5-019

OXYGEN-SENSITIVE INTERACTIONS BETWEEN GLYCOLYTIC ENZYMES AND A CANCER-TESTIS ANTIGEN ESTABLISHED SIGNALLING SCAFFOLD ARE REGULATED BY LYSINE ACETYLATION



Soren Naaby Hansen[1], Arabinda Mandal[2] and Allan Stensballe[3]

[1]Aalborg University Hospital, Denmark
[2]University of Virginia, USA
[3]Aalborg University, Denmark

Reactivation of the male gametogenic expression program is tightly associated with the most malignant and metastasis-prone tumours and the emergence of aggressive sub clones of tumour cells, which are highly resistant to stress-induced apoptosis. While the cancer-testis antigens (CTAs) CABYR and AKAP3/4 roles during gamatogenesis and their importance for flagellar movement have gradually emerged, their function in cancer cells have remained obscure. In this study, we combine immunoprecipitation (IP), mass spectrometry (MS) and Western blot (WB) analysis to unravel their functional roles in therapy resistant lung and ovary adenocarcinoma cells by identifying their interaction partners. CABYR variants were shown to oligomerize and interact with AKAP proteins to generate a HMW signal scaffold structure, which was found to bind several glycolytic enzymes and signal transducers. Forward and reverse IP experiments followed by WB confirmed interactions between CABYR and LDH, ALDO, PFK, TPI-1, GAPDH, ENO-1 and GSK3b. Transistion from normoxic to hypoxic growth conditions disrupted the associations between glycolytic enzymes and the CABYR-AKAP signaling scaffold in the cancer cells, leading to a 3.2-fold increase in their production and secretion of lactic acid. Hypoxic growth conditions resulted in increased acetylation of lysine residues in both CTAs, and triggered deacetylation of lysines in LDH and aldolase. Treatment with resveratrol prevented hypoxia-induced dissociations, suggesting that the regulation of oxygen-sensitive protein interactions within the CABYR-AKAP-glycolysome complex involve changes in the acetylation of lysines in the engaged proteins. MS analysis of IPs finally revealed interactions between CABYR and proteins associated with the cancer cells contractile cytoskeleton. Based on these findings, it is tempting to speculate that hypoxia-induced release and subsequent local activation of glycolysomes from cytoskeleton-associated CABYR-AKAP scaffold structures might be instrumental for cancer cells ability to maintain a steady energy supply to their contractile cytoskeleton and thereby sustain their migratory and invasive capability despite encountering severe reductions in environmental oxygen levels.

Biography

Soren Naaby Hansen has graduated as MD from Copenhagen University in 1991. Following Residential Training, he went on to train as a Postdoctoral Fellow at the Department of Cell Biology, University of Virginia (1993), where he later became Group Leader in Proteomics. In 1999, he became Assistant Member and Head of Biochemical Proteomics, Ludwig Institute for Cancer Research, Royal Free and University College London Medical School, UK. He became Lecturer in Biochemistry and Molecular Biology, University College London, in 2000. In 2006, he returned to Denmark where he was appointed as Senior Scientist at the Department of Clinical Immunology, Aarhus University Hospital, Aalborg. He completed a Doctorate in Medical Sciences at Aarhus University in 2012, and is currently employed at the Department of Psychiatry, Aalborg University Hospital, where he directs a study of the pathophysiology underlying depression disorders.

sonh@rn.dk

EuroSciCon

EuroSciCon conference on

Protein, Proteomics and Computational Biology

December 06-07, 2018
Amsterdam, Netherlands

Nekane Guarrotxena, Biochem Mol biol J Volume:4
DOI: 10.21767/2471-8084-C5-019

SENSITIVE AND MULTIPLEXED RESPONSE OF SERS-BASED PLASMONIC NANO-DUMBBELL PLATFORMS IN DISEASE BIOMARKERS DIAGNOSTICS

Nekane Guarrotxena

Institute of Polymer Science and Technology-Spanish National Research Council (ICTP-CSIC), Spain

A rapid, sensitive and accurate response of analytical techniques to resolve health issues, such as low limit identification in special biological environment (i.e. complex mixtures of proteins) remains to being a key aspect in modern proteomics. In fact, extensive efforts to obtain sensitivity enhancements with detection limits even down to the single molecule have been devoted in the nanotechnology framework. Recently, innovative approaches based on the properties of colloidal nanoparticle (NP) assemblies have led to the development of novel diagnostic methods with sensitivity enhancements for single molecule protein monitoring/identification/detection. Among them, surface-enhanced Raman spectroscopy (SERS) benefits from its higher detectable response to binding of a single protein (sensitivity) and also, very importantly, from its multiplexing capabilities due to the narrow nature of detected peaks from Raman reporter molecules. Since SERS retains the fingerprinting capabilities of Raman spectra, the internal modes of a reporter molecule brought at metallic NPs junctions, where strong field enhancement occurs, can be used as diagnostic tools. Specific attention has been given to SERS-based immunoassays. Indeed, the combination of the high sensitivity provided by SERS and the strong binding specificity of antibody-protein ensures that SERS-based detection platform are suitable tools for biomedical and biochemical analysis, clinical diagnosis and biosensor. Therefore, the superior capabilities of SERS readout strategy such as high sensitivity and simultaneous detection of a multiple proteins in complex matrices will be highlighted in this presentation.

Biography

Nekane Guarrotxena has completed her PhD in Chemistry from Complutense University, Madrid-Spain and Postdoctoral research positions from ENSAM, Paris-France and University of Science II, Montpellier-France. She was the Vice-Director of the Institute of Polymer Science and Technology (ICTP-CSIC) (2001-2005), a Visiting Professor in CPOS of University of California, Santa Barbara-US and CaSTL of University of California, Irvine-US (2008-2011). She has published in more than 60 papers in reputed journals, four books (also co-editor) and 24 book chapters, and has been serving as an Editorial Board Member of repute, an Organizing Committee Member of scientific and technological events, and an External Expertise Consultant on I+D+I Management and Policy for National and International Agencies. Her research interest focuses on the synthesis and control-assembling of hybrid nanomaterials, smart-stimuli nanostructures, nanoplasmonics and their applications in bio-imaging, drug delivery, therapy and sensing.

nekane@ictp.csic.es

EuroSciCon

EuroSciCon conference on

Protein, Proteomics and Computational Biology

December 06-07, 2018
Amsterdam, Netherlands

J. Boudet et al., Biochem Mol biol J Volume:4
DOI: 10.21767/2471-8084-C5-019

COMBINATION OF NMR METHODS TO SOLVE KEY STRUCTURES OF THE PRN1 PRIMASE IN COMPLEX WITH ITS SUBSTRATES

J. Boudet[1], J.-C. Devillier[2], T. Wiegand[3], L. Salmon[1], B. Meier[3], G. Lipps[2] and F. H.-T. Allain[1]

[1]Institute of Molecular Biology and Biophysics (ETH Zurich, Switzerland)
[2]Institute of Biochemistry and Bioanalytics (University of Applied Sciences of Northwestern Switzerland, Muttenz, Switzerland)
[3]Institute of Physical Chemistry (ETH Zurich, Switzerland)

Primases are single-stranded DNA dependent polymerases that synthesize RNA/DNA primers during replication. A primase, a DNA polymerase and an helicase compose the replication machinery of the archaeal plasmid pRN1[1]. The structure of the archaeal functional primase domain has been solved by X-ray crystallography[2,3] and it revealed an heteromeric structure with a catalytic prim/pol domain tethered to a novel helix bundle domain. We investigated the NMR structure of the functional pRN[1] primase domain in complex with a single-stranded DNA template containing the GTG motif[4]. We showed that the catalytic prim/pol domain of this 38 kDa enzyme is not required for template binding. Intermolecular contacts detected exclusively between the helix bundle domain and the DNA led us to isolate specifically this structurally independent unit. Our results are compatible with a conformational switch between a template-bound open state and a closed active complex[3,5,6]. We used multiple NMR dataset to solve the solution structures of the helix bundle domain in complex with the single-stranded DNA template alone and upon cofactors addition. Affinity measurements validated our structural data demonstrating the importance of residues located in helices 10 and 12 for the interaction with the GTG motif and confirmed the specificity improvement observed upon cofactors binding. In association with functional assays, these novel transient structures bring new perspectives and will help us to characterize the molecular steps required for priming.

Biography

Julien Boudet received his PhD degree in structural biology and biophysics from the University of Grenoble (Joseph Fourier University) in France under the supervision of Prof. Jean-Pierre Simorre. During his thesis, he learned nuclear magnetic resonance (NMR) spectroscopy and used this powerful method to investigate proteins and oligonucleotides structures, molecular mechanisms underlying antibiotic resistance and viral proteins interactions. After graduating, Julien joined the group of Prof. Frédéric Allain in ETH Zurich as a postdoctoral research associate. He focused his investigations on the DNA replication machinery and, in particular on the primase-mediated catalysis. He set up innovative computational methods to investigate challenging biological systems and demonstrated the role of cofactors in improving the specific template recognition by the pRN1 primase. He is currently developing computational and analysis tools to assist therapeutic oligonucleotides design.

boudet.julien@gmail.com

EuroSciCon

EuroSciCon conference on

Protein, Proteomics and Computational Biology

December 06-07, 2018
Amsterdam, Netherlands

Zajonc, Biochem Mol biol J Volume:4
DOI: 10.21767/2471-8084-C5-019

MODULATING IMMUNE RESPONSES WITH DESIGNED GLYCOLIPID ANTIGENS THAT TARGET NATURAL KILLER T CELLS USING A STRUCTURAL-FUNCTIONAL APPROACH

Zajonc
Friedrich Alexander University (Erlangen, Germany)

Natural Killer T (NKT) cells are a unique T cell population characterized by features of both the innate and adaptive immune response. Two main classes of NKT cells (Type I and II) exist that express different antigen receptors (TCRs) and respond to different glycolipids presented by the shared antigen-presenting molecule CD1d. Type I NKT cells respond rapidly to the prototypical antigen -galactosylceramide (-GalCer) and can secrete both pro- and anti-inflammatory cytokines, while Type II NKT cells recognize the self-glycolipid sulfatide and are thought to be controlling autoimmunity. The cytokine profile of Type I NKT cells can be altered using modified synthetic glycolipids to produce the cytokine response of choice. Through biophysical TCR binding affinity measurements, as well as crystallographic studies of how the TCR engages different CD1d-presented glycolipids, we and others have identified the structural basis of glycolipid recognition by NKT cells. The TCR of Type I NKT cells binds to CD1d with a conserved footprint, while inducing structural changes in both CD1d and the glycolipid antigens. This conserved TCR binding mode allows for the design of glycolipid antigens, predominantly analogs of -GalCer in an attempt to obtain glycolipids that elicit a particular cytokine profile. We are especially interested in identifying novel antigens that elicit pro-inflammatory cytokines, since they have great potential as vaccine adjuvants. I will present our ongoing work on characterizing novel CD1d-restricted antigens, which led us to a surprising discovery.

Biography

Prof. Zajonc obtained his Ph.D. in Biology from the Friedrich Alexander University in Erlangen, Germany in 2001, working on fatty acid elongation and sphingolipid metabolism in yeast. For his postdoctoral work, he joined the laboratory of Ian A. Wilson at the Scripps Research Institute in La Jolla, California, where he worked on the structural basis of glycolipid presentation by the CD1 family. At that time, he made seminal findings of how glycolipids can be recognized by T cells. In 2006, he started his own lab at the La Jolla Institute for Immunology, where he continued to work on microbial antigen recognition by T cells, antibody recognition of viral antigens, as well as viral interference with immune recognition. He has published over 90 peer-review papers in top tier journals including Science, Nature Immunology, Journal of Experimental Medicine, Immunity and PNAS.

dzajonc@liai.org

Proteomics and Computational Biology 2018