EuroSciCon

DAY 1

Scientific Tracks & Abstracts

9th Edition of International Conference on

Mass Spectrometry

March 04-05, 2019 | Berlin, Germany

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Sessions

Analytical Chemistry | Chromatography | Mass Spectrometry Applications | New Advances and Development in Mass Spectrometry | Protein Mass Spectrometry | Proteomics | Tandem Mass Spectrometry

Session Chair
Milos Netopilik
Institute of Macromolecular Chemistry, Czech Republic

Session Co-Chair
YongNam Pak
Korea National University of Education, Republic of Korea

Session Introduction

Title: Using native, top-down mass spectrometry to characterize the interaction of amyloidogenic proteins with assembly modulator CLR01

Michael Nshanian, University of California, USA

Title: Models of chromatography separation and their application for improving SEC resolution

Milos Netopilik, Institute of Macromolecular Chemistry, Czech Republic

Title: Removal of interferences in ICP/MS using deuterium as a collision gas

Yong-Nam Pak, Korea National University of Education, Republic of Korea

Title: Understanding inhibitory mechanism of the selective inhibitors of Cdk5/p25 complex by molecular modeling studies

Amir Zeb, Gyeongsang National University, Republic of Korea

Title: Assessment of trace element-composition of cereals and legumes by ICP-MS

Mehmet Yaman, Firat University, Turkey

Title: Lansoprazole and simvastatin reduces the ability of clopidogrel to inhibit platelet aggregation in patients undergoing percutaneous coronary intervention in a tertiary health care system: A prospective drug–drug interaction study

Jinesh B Nagavi, Sarada Vilas College of Pharmacy, India

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Michael Nshanian, Int J Drug Dev & Res 2019, Volume 11
DOI: 10.21767/0975-9344-C1-005

Using native, top-down mass spectrometry to characterize the interaction of amyloidogenic proteins with assembly modulator CLR01

Michael Nshanian

University of California, USA

Alzheimer's disease (AD) is a complex neurodegenerative disorder that manifests itself through neuronal death and loss of synaptic transmission. Its complex pathophysiology includes a double proteinopathy characterized by aggregation of the amyloid -protein (A) and neurofibrillary tangles (NFT) of the microtubule-associated tau protein. Our group has effectively implemented high resolution mass spectrometry to study the interaction of amyloidogenic proteins with lysine specific molecular tweezer (MT) compound CLR01. CLR01 preferentially binds to Lys residues on unstructured proteins and modifies their assembly into non-toxic states. We have employed top down MS methods to gain structural insight into tau and tau:CLR01 complexes. In addition, we have discovered that performing top down ECD MS of noncovalent tau: CLR01 complex can reveal the site of inhibitor binding. Noncovalent interactions are generally stable enough for transition into the gas phase for structural and stoichiometric analysis. Furthermore, electron capture dissociation (ECD) based fragmentation preserves the labile post-translational modifications (PTMs) and only dissociates the covalent bonds of the noncovalent complexes, which is especially well suited to assigning the sites of ligand binding. Our top-down MS based methods have been successfully used to characterize the effects of CLR01 binding to 4R tau protein (45.8 kDa) and tau fragment (11 kDa). ESI-MS spectra were obtained for the unmodified and phosphorylated 4R repeat domain of tau fragment and tau/CLR01 complex in a 1:1 stoichiometric ratio. The intact protein-inhibitor complex was further subjected to ECD-MS to obtain sequence information and pinpoint the sites of inhibitor binding. ECD-MS data point to CLR01 binding sites in the microtubule binding region, implicated in aggregation. Since phosphorylation plays an important role in tau aggregation, we have also tested phosphorylated tau to map the sites of phosphorylation. ECD-MS confirmed phosphorylation at Ser-235. Our ion mobility experiments on the tau fragment revealed a shift towards a more compact structure in the presence of CLR01.

Biography

Michael Nshanian has completed his PhD in Biochemistry and Molecular Biology at the University of California, Los Angeles, under the guidance of Professor Joseph Loo. He is currently a Postdoctoral research fellow at Stanford University School of Medicine. He has spent several years in the Pharmaceutical industry in the San Francisco bay area, where he helped develop and characterize drug candidates using various analytical techniques. While working in the industry, he has also completed an MS in Chemistry under the guidance of Professor Joseph Pesek. He has published in JACS, Analytical Chemistry, International Journal of Mass Spectrometry and Electrophoresis. His most recent research on using native mass spectrometry and ion mobility spectrometry to study protein-inhibitor complexes will be published in the upcoming issue of the Journal of the American Society for Mass Spectrometry.

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Models of chromatography separation and their application for improving SEC resolution

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The effectivity of chromatography separation, i.e., resolution depends on construction of the chromatograph in the first place on the detectors cells volume and for polymer of given molecular weight, strongly on operational variables, as concentration and flow-rate. The effect of concentration is not important for polymers in theta solvents. However, the concentration effect is important for polymers in. The effective hydrodynamic volume of dissolved macromolecules decreases with increasing concentration. The spatial distribution of the analyte with respect to the longitudinal axis of the separation system, developing in time, can be approximated by the binomial distribution and the elution curve is obtained numerically from the spatial distributions developing in time. The elution curve is then obtained by observing the developing spatial distribution in a fixed point representing the detectors. The concentration effect is observed as deviations from this model which can be calculated numerically.

Biography

Milos Netopilik has completed his PhD at Institute of Macromolecular Chemistry and Postdoctoral studies from Virginia Polytechnic Institute and Technical University. Now, he works in Institute of Macromolecular Chemistry, Academy of Sciences of the Czech Republic and works in the theory of separation. He has published more than 68 papers in reputed journals.

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Removal of interferences in ICP/MS using deuterium as a collision gas

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The use of collision cell in ICP/MS has brought the removal of isobaric interferences in Ar ACP/MS especially for the species related to Ar background such as Ar dimers and Ar related molecular species. Determination of Fe or Se has been limited because of those interferences. However, the use of collision cell can eliminate or reduce molecular interferences. Hydrogen or Helium has been used as a collision gas. Different approaches such as reaction cell could be introduced instead of collision by using more reactive gases such as ammonia. However, the introduction of hydrogen in the collision cell does react with sample elements and produce molecular species to some degree. Matrix such as Br could react with hydrogen to make BrH to interfere on the determination of Se. The use of deuterium can alleviate this problem. The accuracy and precision could be improved by the use of deuterium especially for the complex matrix samples. Details of the improvement of complex matrixed sample such as oyster will be discussed.

Biography

Yong-Nam Pak has completed his PhD in Analytical Chemistry by University of Missouri. He has worked as Professor of Department of Chemistry at Korea National University of Education. He has published more than 80 papers in reputed journals and has serving as a Vice President of Korea Analytical Science and Technology.

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Amir Zeb, Int J Drug Dev & Res 2019, Volume 11
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Understanding inhibitory mechanism of the selective inhibitors of CdK5/p25 complex by molecular modelling studies

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Gyeongsang National University, Republic of Korea

Neurotoxic insults activate calpain, which in turn produces truncated p25 from p35. p25 forms hyperactivated CdK5/p25 complex, and thereby induces severe neuropathological aberrations including hyperphosphorylated tau, neuroinflammation, apoptosis, and neuronal death. Inhibition of Cdk5/p25 complex alleviates aberrant phosphorylation of tau to mitigate AD pathology. PHA-793887 and Roscovitine have been investigated as selective inhibitors of Cdk5/p25 with IC50 values 5nM and 160nM, respectively, but their mechanistic studies remain unknown. Herein, computational simulations have explored the binding mode and interaction mechanism of PHA-793887 and Roscovitine with Cdk5/p25. Docking results suggested that PHA-793887 and Rsocovitine have occupied the ATP-binding site of Cdk5 and obtained highest docking (GOLD) score of 66.54 and 84.03, respectively. Furthermore, molecular dynamics (MD) simulation demonstrated that PHA-793887 and Roscovitine established stable RMSD of 1.09 Å and 1.48 Å with Cdk5/p25, respectively. Profiling of polar interactions suggested that each inhibitor formed hydrogen bonds (H-bond) with catalytic residues of Cdk5 and could remain stable throughout the molecular dynamics simulation. Additionally, binding free energy calculation by molecular mechanics/Poisson–Boltzmann surface area (MM/PBSA) suggested that PHA-793887 and Roscovitine had lowest binding free energies of -150.05 kJ/mol and -113.14 kJ/mol, respectively with Cdk5/p25. Free energy decomposition demonstrated that polar energy by H-bond between the Glu81 of Cdk5 and PHA-793887 is the essential factor to make PHA-793887 highly selective towards Cdk5/p25. Overall, this study provided substantial evidences to explore mechanistic interactions of the selective inhibitors of Cdk5/p25 and could be used as fundamental considerations in the development of structure-based selective inhibitors of Cdk5/p25.

Biography

Amir Zeb is PhD student at Geyongsang National University, South Korea. His research interest is Computer Aided Drug Designing and Molecular Modelling. Mr. Zeb has been exposed to a number of proteins modelling projects and achieved excellent output. Currently, Mr. Zeb is trying to unveil the mechanistic studies of therapeutics targets in neurological disorders and their computational inhibition. He has published more than 15 papers in reputed journals.

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Mehmet Yaman, Int J Drug Dev & Res 2019, Volume 11
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Assessment of trace element composition of cereals and legumes by ICP-MS

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The determination of minerals and trace elements in foodstuffs is an important part of nutritional and toxicological analyses. Although copper, chromium, iron and zinc play an important role in human metabolism and so, they are essential micronutrients for human health, their higher intake as well as the prolonged intake of even low concentrations of toxic elements such as arsenic, chromium, cadmium, lead and nickel can cause serious toxic effects. The interest in those elements is increasing together with reports of relationships between trace element status and oxidative diseases. The importance of food safety is constantly increasing due to parallel import and export intensity among countries. Of all foods, cereals and legumes most adequately meet the recommended dietary guidelines for healthyful eating because they are high in carbohydrate and dietary fiber, mostly low in fat, supply adequate protein while being a good source of vitamins and minerals. In this study, concentrations of trace elements such as arsenic, chromium, cadmium, lead and nickel in cereals and legumes were determined by using ICP-MS. The samples were collected from Turkish markets and different regions. For sample preparation before measurement, microwave digestion system was used. It was found that the chromium and nickel concentrations are up to 3.0 mg/kg for beans taken from regions with high Ni and Cr in soils. To check the reliability, the SRM was examined for the studied elements.

Biography

Mehmet Yaman has completed his PhD at Inonu University in 1990. He has published more than 120 papers in reputed journals and has been serving as an Editorial Board Member of reputed journals. Between 2010 to 2013, he was selected as Member of Consultative Committee of the Scientific and Social Research Council of Turkey. He has an ınternational book chapter, "*Air Pollution Monitoring,Modelling, Health and Control*"; "*Comprehensive Comparison of Trace Metal Concentrations in Inhaled Air Samples*".

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Lansoprazole and simvastatin reduces the ability of clopidogrel to inhibit platelet aggregation in patients undergoing percutaneous coronary intervention in a tertiary health care system: a prospective drug–drug interaction study

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Clopidogrel, a prodrug is found to be less effective in inhibiting the platelet aggregation when administered along with PPI's and statins in patients undergoing cardiac stent, ST segment elevated Myocardial infarction (STEMI) followed by percutaneous coronary intervention (PCI). Clopidogrel binds to CYP2C19, a hepatic enzyme to get converted to its active metabolite in order to achieve desired pharmacological activity. The cytochrome P450 3A4 which is partially involved in the metabolism of clopidogrel also metabolizes PPIs like omeprazole, lansoprazole and pantoprazole; statins, mainly atorvastatin, rosuvastatin and simvastatin to the greater extent. In the current study, patients on PPI's with dual antiplatelet therapy and patients on PPI's and statins with dual antiplatelet therapy are considered to understand the potential drug–drug interactions (pDDI) among the South Asian population. Platelet aggregation was measured in 91 patients undergoing coronary artery stent implantation treated with clopidogrel and aspirin along with PPI's and statins.

It was observed that lansoprazole and simvastatin, but not omeprazole, pantoprazole and atorvastatin, rosuvastatin, inhibited the antiplatelet activity of clopidogrel. The percent platelet aggregation was 81 ± 2 (p = 0.012), 72 ± 6 (p = 0.001), and 43 ± 23 (p = 0.027) in the presence of clopidogrel with lansoprazole, omeprazole and pantoprazole respectively. Aggregation was found to be 91 ± 4 (p = 0.001), 51 ± 3 (p = 0.009) and 12 ± 23 (p = 0.031) in the presence of clopidogrel with atorvastatin and rosuvastatin respectively.

A prominent drug–drug interaction was observed with patients on dual antiplatelet therapy along with lansoprazole and simvastatin.

Biography

Jinesh Bahubali Nagavi has completed his PhD in Analytical Chemistry at JSS University. He has worked as an Instructor and Lecturer at RAK Medical and Health Sciences University, UAE. He has published more than 15 papers in reputed national and international peer reviewed journals, presented his research work in more than 10 International & national conferences. He has been serving as an Assistant Professor of Pharmaceutical Chemistry at Sarada Vilas College of Pharmacy, RGUHS, Karnataka, India. Dr. Jinesh has special interest in bioanalytical method development and validation with hyphenated techniques, pre-clinical trials, drug interactions, pharmacokinetic studies and clinical research.

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