Science brings Europe and India closer

2nd European Indian INDIGO Meeting

on VOC biomarkers for disease detection

06. – 08. June 2016

Universität Rostock Traditio et Innovatio

ROSTOCK MEDICAL ROMBAT BREATH RESEARCH ANALYTICS & TECHNOLOGIES

MedAirv

Steinbeis

2nd European Indian INDIGO Meeting on VOC biomarkers for disease detection

Date:

Rostock 06.-08. June 2016

Location:

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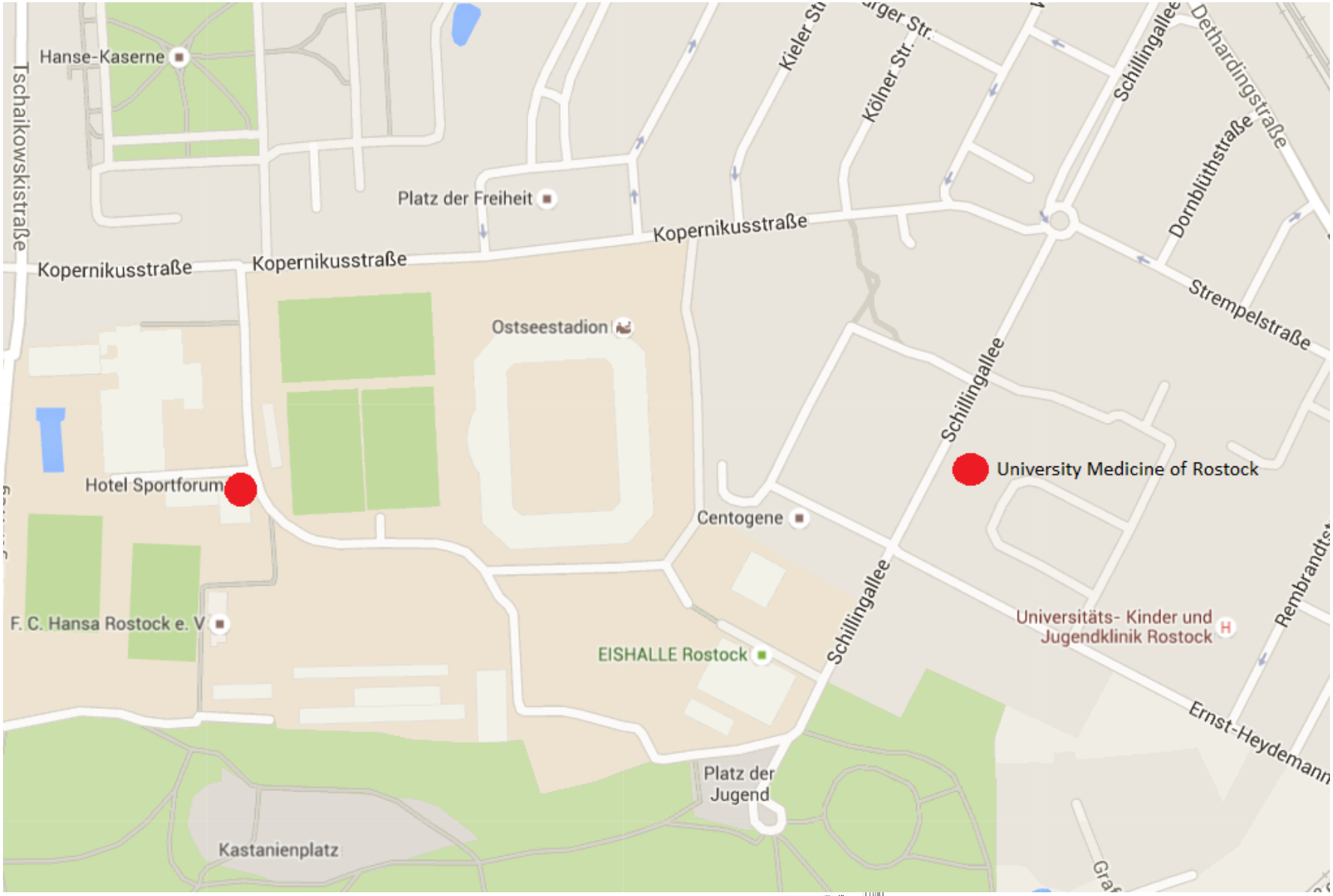

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Science brings Europe and India closer

NEW INDIGO

INNO INDIGO POLICY

ROMBAT BREATH RESEARCH ANALYTICS & TECHNOLOGIES

MedJurv

Steinbeis

Time	Monday, 06.06.2016	Time	Tuesday, 07.06.2016	Wednesday, 08.06.2016
9:00	Welcome and registration in room "Ostseestadion"	9:00	Welcome in room "Olymp"	**7:30 Pickup @ Sporthotel** **8:00 Station Thierfelder Str.**
9:15	Welcome and introduction/overview *Jochen Schubert (Rostock, Germany)*	9:05	*Wojciech Filipiak (Innsbruck, Austria)* "VOC-Measurements from cell cultures"	Steam and Waves: Tour to the Baltic Sea
9:30	*José Câmara (Madeira, Portugal)* "HCV project – a little contribute against fight cancer"	9:50	**Hands-on-Workshop 2:** *Ann-Christin Bischoff (Rostock, Germany)* "How to measure volatile organic compounds in vitro over cultures?"	
10:15	*Srikanth Rapole (Pune, India)* "HCV project in India - Results and future prospects"			
10:45	Coffee break	11:00	Coffee break	
11:15	Student lecture: *Priscilla Porto-Figuera (Portugal, Madeira)* "Exploring the potential of a new analytical approach NTDs/GC-MS for establishment the volamtomic pattern of urine samples"			
11:40	Student lecture: *Khushman Taunk (Pune, India)* "Alterations on VOCs in breast and lung cancer"	11:30	*Jorge Pereira (Madeira, Portugal)* "Characterization of saliva volatiles as potential biomarkers for cancer diagnosis – preliminary studies with breast and lung cancers"	
12:05	Student lecture: *Pritam Sukul (Rostock, Germany)* "Physiological influences on real-time breath biomarker profiles"	12:15	**Workshop 3:** Conferee Networking: Jochen Schubert "Blood- Breath-Saliva - What do we need for diagnostic applications?"	
12:30	Lunch	13:00	Lunch	Lunch
13:30	*H.A. Nagarajaram (Hyderabad, India)* "A database for human volatome"			
14:10	*Wolfram Miekisch (Rostock, Germany)* "VOC-Biomarkers - New perspectives and old problems"	14:15	*Jens Herbig (Innsbruck, Austria)* "Real time MS - Basics & Applications"	**End of meeting**
14:50	Panel Discussion: "VOC biomarkers for cancer detection"			
15:15	Coffee break	15:00	Coffee break	
15:45	**Hands-on-Workshop 1:** *Phillip Trefz (Rostock, Germany)* "Data interpretation of complex volatomic data"	15:30	Panel discussion: "Perspektives for EU-Indian cooperations within NewIndigo and InnoIndigo-Projects"	
17:00	End	16:15	End	
19:30	Conference Dinner			

Monday, 06.06.2016

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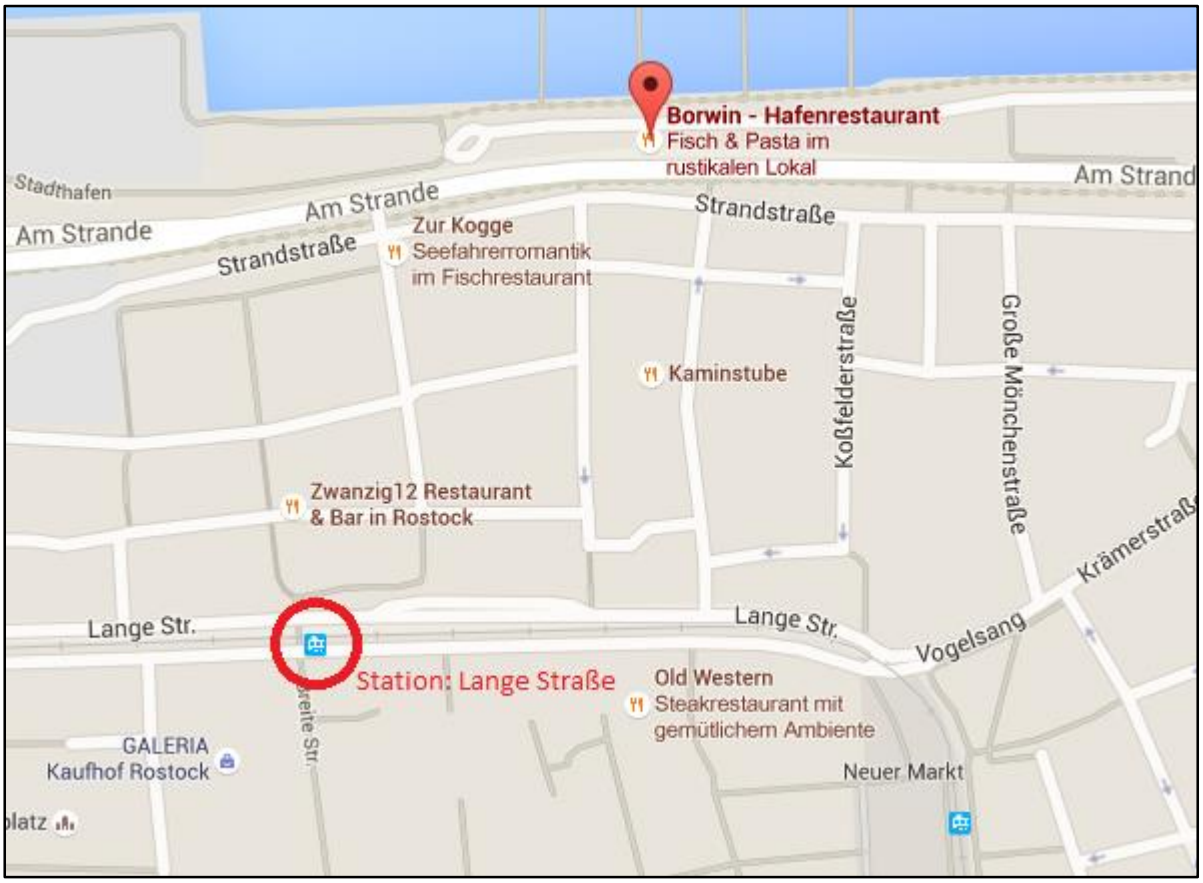
17:00	End	
19:30	**Conference Dinner**	

Conference Dinner:
Restaurant: Borwin
Am Strande 2
18055 Rostock
Station: Lange Straße



HCV-Project – a little contribute against fight cancer

9:30

José S. Câmara, Jorge Pereira
CQM – Centor de Química da Madeira, Campus Universitário da Penteada; Faculty of Exact Sciences and Engineering, University of Madeira. Funchal. Portugal; e-mail address: jsc@uma.pt

Currently, the frequency of cancer malignancies is increasing worldwide. According to World Health Organization, deaths due to cancer, worldwide, will continue to rise to over 11 million/yr by 2030. This sobering fact, in itself, is a strong argument for need to do continued research, both basic and clinical, to find improved ways to prevent, diagnose and treat cancer. The diagnosis and treatment of cancer in its early stages can often increase the 5-year-survival rate 3-4 fold. Currently available diagnostic tests for most cancers are extremely costly or involve invasive procedures (e.g. bronchoscopy, biopsy, etc) that are not without complications. In recent years, many studies on different screening methods have been undertaken. A desirable screening method should be non-invasive, painless, inexpensive and easily accessible to a large number of patients. Analysis of volatile organic metabolites (VOMs), from urine and exhaled breath, consumed or released by cancerous cells is emerging as a new, attractive and non-invasive approach for cancer diagnostics. The principle behind this approach is based on the fact that cancer cells can be distinguished from normal cells by their altered metabolic rate, their changed apoptotic pathways and their altered protein expression patterns thereby leading to the production and/or consumption of cancer-specific VOMs. These VOMs, detected either directly from the headspace of cancer cells or via the exhaled breath, urine and/or saliva, could lead to the establishment of a set of volatile biomarkers that could be used for the early detection of cancer and for the discrimination between different types of cancer. Hopefully, improved characterization of the disease progression could be also achieved. Obtaining this kind of discrimination could have significant, positive impacts with respect to clinical decisions and patient outcomes.

In this project we analyzed the volatomic profile of up to 130 urine samples and 100 saliva samples of breast cancer patients from India and Portugal; 50 urine and saliva samples from lung cancer patients and about 30 urine and saliva samples from colon cancer patients as well as 30 urine and saliva samples from age-matched healthy controls, using solid phase microextraction in headspace mode (HS-SPME) as pre-concentration technique combined with GC-MS analysis. The obtained bioanalytical data matrix was subjected to multivariate analysis using SPSS software in order to differentiate between cancer patients and healthy subjects and to detect volatile metabolites able to differentiate the target groups.
In addition we evaluate the potential ability of different nanosorbent materials to isolate the volatile metabolites from biofluids, as a platform to construct a nanosorbent-based device directed towards volatile extraction. The main results obtained and the synergistic empowerment from the collaborative studies, will be reported.

Keywords: *Cancer, differentiation, volatile organic metabolites (VOMs), MVA*

Acknowledgements:
The authors acknowledge the financial support of the FP7 New INDIGO Partnership Programme through the HCV project (New-INDIGO/0003/2012 project, ERA- NET) and Fundação para a Ciência e a Tecnologia (FCT) with funds from the Portuguese Government (Project PEst-OE/QUI/UI0674/2011) and the MS Portuguese Network (Rede/1508/RNEM/2011)

HCV Project in India – Results and future prospects

10:15

Srikanth Rapole*, Khushman Taunk, Ravindra Taware,
**Proteomics Lab, National Centre for Cell Science, Ganeshkhind, Pune-411007, MH, India.*

Cancer remains a major cause of mortality worldwide. The major reason for this high mortality rate is lack of awareness and late diagnosis. Early diagnosis of cancer improves the likelihood of successful treatment and can save many lives. But, it requires successful strategies for early detection and screening of the disease. The present diagnostic techniques involve methods which are expensive and invasive. This restricts a majority of world population to avail them. Therefore, there is an urgent need to develop diagnostic methods which would be less expensive and non-invasive in nature. The use of urine and saliva as samples for disease monitoring and diagnosis is a promising option in early diagnosis.

Here, we propose a very simple and non-invasive methodology using HS-SPME followed by GC-MS analysis capable of identification of cancer specific volatile organic compounds (VOCs) which could easily discriminate between cancer subjects and healthy controls. In this project, we studied urinary and saliva volatomic biosignatures of cancer patients and healthy individuals (control group) and to explore the VOCs as potential biomarkers in cancer diagnosis at early stage. In case of breast cancer, 69 breast cancer patients and 69 healthy control urine samples were subjected for volatomics analysis. A total of 98 VOCs ware identified in which 25 VOCs are differentially regulated. Saliva volatomics data of 25 breast cancer patients along with age and sex matched healthy control revealed 52 VOCs out of which 19 VOCs are statistically significant. Good discrimination within breast cancer and control groups was achieved with urine and saliva volatomics data. Total 42 VOCs were detected and identified in control (n = 11) and lung cancer group (n = 11) of urine samples and subsequent statistical interpretation of data identified 7 VOCs with increased abundance while 4 VOCs with decreased abundance in lung cancer urine as compared to healthy controls. The results from HCV project, challenges and future prospects will be presented.

Exploring the potential of a new analytical approach NTDs/GC-MS for establishment the volatomic pattern of urine samples

11:15

Priscilla Porto-Figueira[1], Jorge Pereira[1] and José S. Câmara[1,2]

1. *CQM—Centro de Química da Madeira, Universidade da Madeira, Campus Universitário da Penteada, Funchal 9000-390, Portugal;*
2. *Faculdade de Ciências Engenharia da Universidade da Madeira, Campus Universitário da Penteada, Funchal 9000-390, Portugal.*

Currently, a small number of diseases, particularly cardiovascular (CVDs), oncologic (ODs), neurodegenerative (NDDs), chronic respiratory diseases, as well as diabetes, form a severe burden to most of the countries worldwide. Hence, there is an urgent need for development of efficient diagnostic tools, particularly those enabling reliable detection of diseases, at their early stages, preferably using non-invasive approaches. Advanced sampling procedures (solid-phase and needle traps microextraction) coupled with modern analytical technologies (proton transfer reaction mass spectrometry, selected ion flow tube mass spectrometry, ion mobility spectrometry, e-noses, *etc.*) allow the characterization of biological fluids composition to an unprecedented level.

In this work a new extraction procedure, based on a Needle Trap Device (NTDs), was optimized and combined with GC-MS to establish the volatomic profile of urine samples. In order to improve the extraction efficiency several influencing experimental parameters, such as temperature, equilibrium time, volume of headspace, ionic strength, pH and agitation, were investigated. NTDs (triple-bed) constituted by combinations of Divinylbenzene/Carbopack X/Carboxen 1000 was selected and used for screening the volatile composition of urine samples. The new extraction procedure showed a good performance, comparable with traditional techniques such as SPME and SPE.

Keywords: *Disease diagnosis; volatile organic metabolites (VOMs), NTD*

Acknowledgements: The authors acknowledge the Portuguese Foundation for Science and Technology (FCT) through the Pluriannual base funding RD Units Strategic Plan - 2013/2015 (UID/QUI/00674/2013), the MS Portuguese Networks (RNEM/2014) and New-INDIGO/0003/2012 project (ERA- NET, FP 7)

Alterations of VOCs in breast and lung cancer: An Indian study

11:40

Khushman Taunk*, Ravindra Taware and Srikanth Rapole
**Proteomics Lab, National Centre for Cell Science, Ganeshkhind, Pune-411007, MH, India.*

Management of cancer thrives to be most challenging especially in late stage diagnosed cancer cases. Early detection of cancer can play a key role in its efficient management as well as high survival rates in patients. Adopting novel strategies which are easy to use, robust, inexpensive and least painful to patients can be of high importance towards screening of cancers and thus early detection of cancer. In context to these objectives we have used non-invasive body fluids like urine and saliva of Breast and Lung cancer patients and subjected them to analytical extraction technique HS-SPME. The proper extraction conditions and methodology were standardised for optimum efficiency. The VOCs of urine and saliva were adsorbed on the SPME fiber and analysed by GC-MS. The identified VOCs were subjected to multivariate statistical analysis and the statistically significant features were extracted. These significant features will be further analysed with bioinformatics tools to elucidate their biological interpretation.

Various mutations inside the cells are one of the major reasons towards the transformation of normal cells to cancerous. These mutations can be studied in cell lines by knocking down the genes responsible for the particular mutation and comparing it with its wild type cell line. Presently, these kind of experiments utilize the genomics and proteomics tools to study the biological questions. We have taken this aspect to a volatomics approach to identify VOC signatures responsible for cancer. We have studied the VOCs that result from the condition media of the cell lines (both gene knock-down and the wild type) when they grow in the culture medium up to a confluency of 75%. We used the HS-SPME extraction methodology followed by GC-MS analysis to elucidate the VOC profile of the gene knock-down cell lines. The overall challenges of the GC-MS based volatomics will also be discussed.

Physiological influences on real-time breath biomarker profiles

12:05

Pritam Sukul
Department of Anaesthesiology and Intensive Care, ROMBAT, University Medicine of Rostock, Schillingallee 35,18057 Rostock, Germany.

Breath research is an interdisciplinary field of science that involves physiology and medicine with analytical chemistry and engineering. It holds great promise towards noninvasive applications in relation to clinical diagnosis as well as physiological and therapeutic monitoring. Exhaled VOC patterns have been proposed as a future diagnostic tool for early detection of cancer, diabetes, cystic fibrosis and liver cirrhosis etc.. During the inception of this field, scientists were aiming at the discovery of trace (~ppbV to ~pptV ranges) gases in human breath as unique disease biomarkers. During the last decade, the presence of several hundred volatile organic compounds (VOCs) had been described in human exhalation by means of GC-MS. Despite the identification and quantification of many compounds, actual clinical interpretations of biomarkers are challenging. Till date, not a single substance has been transformed as unique disease biomarker into clinical practice. This might be the consequence of inadequate basic knowledge on the origin and physico-chemical properties, distribution and exhalation kinetics of individual markers as well as insufficient understanding of complex physiological effects on biochemical pathways.

Physiology plays the most important role on VOC exhalation. Simple changes in physiological factors may have sudden and profound effects on breath VOC concentrations. Studies have already indicated that hemodynamic and respiratory changes induced by different breathing patterns have immediate effects on VOC exhalation. Such effects could be specific for compounds. Pronounced changes were observed in certain substance classes, whereas other remained almost consistent.

Potential confounders such as environmental, dietary intake or bacterial emission and clinical contaminations are contributing to VOC patterns similarly as pathophysiological conditions or biological processes. Recent development and application of advanced real-time mass-spectrometric techniques such as SIFT-MS, and different PTR-MS in association with online end-tidal (alveolar) sampling have significantly lowered many confounding factors related to storage and time of analysis and mixed breath samples. Such progresses in sampling and analysis have indicated that rapid changes in concentrations are rather important than any unique breath biomarkers.

Nowadays, real-time monitoring of physiology induced immediate changes in exhaled VOC concentrations, is possible without losing analytical sensitivity. This helps clinicians to understand and relate various metabolic and biochemical pathways. We designed several studies, to evaluate the importance of the origin, physico-chemical characters of VOCs as well as the role of hemodynamic and respiratory parameters for clinical interpretation of exhaled substances in terms of breath biomarker. We introduced different breathing pattern, changes in postures and forced respiratory maneuvers in spontaneously breathing healthy human subjects to induce physiological effects onto the composition of exhaled breath. We have found that comprehensive overviews on hemodynamics, ventilation, ventilation/perfusion ratio, compartmental distribution, and substance origin and physico-chemical properties are mandatory during clinical interpretations of exhaled VOCs as breath biomarkers.

13:30

A database for human volatome

H.A. Nagarajaram, Rajkishore Mohapatra@ and Rahul Dhakne@
Laboratory of Computational Biology, Centre for DNA Fingerprinting & Diagnostics (CDFD), Gruhakalpa, Nampally, Hyderabad 500 001, Telangana State, India.
@Equal contribution

We have developed a relational database to store various types of data pertaining to volatile metabolites detected by our collaborating partners. This database can hold (a) patient's (as well as control's) demographic information, (b) information on samples analyzed, (c) essential experimental details and (d) the detected volatiles along with their abundances. Data deposition can be made by using either manual data-entry method or by uploading data sheets. A prospective user has to register and a strict protocol is followed for his authentication before he makes data entry or data retrieval. Currently, we are developing add-on tools to retrieve and integrate, on-the-fly, using various public domain data resources, known physicochemical, pathways and other relevant biological information available for various volatile metabolites deposited in this database.

We have also developed a statistical software suite based on R-platform for volatome data analysis. This suite includes tools for:

(a) Missing data imputation,

(b) Multivariate analysis,

(c) Supervised and unsupervised data modelling,

(d) data dimensionality reduction etc.

This will also be hosted alongside the volatile database on the project web-portal.

VOC-Biomarkers - New perspectives and old problems

14:10

Wolfram Miekisch, Jochen K. Schubert
Department of Anaesthesiology and Intensive Care, ROMBAT, University Medicine of Rostock, Schillingallee 35,18057 Rostock, Germany.
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During the past decades, breath research was mainly focused on the detection of biomarkers or VOC patterns for the detection of pathologic conditions. Cross-sectional studies often revealed differences in marker patterns between patients and controls but identified “disease specific” VOC “markers” or “marker patterns” could not be reproduced within other studies. In this way, hundreds of different VOC- “marker sets” for diseases such as cancer, metabolic disorders or organ failure have been published. None of the proposed VOC marker sets or devices has ever reached clinical relevance.

In parallel techniques in the field of breath research e.g. real time mass spectroscopy and PoC sensor systems have advanced remarkably and nowadays enable continuous real time monitoring with the patient as his own control. Based on this type of research we have now started to understand that concentrations of breath biomarkers are not only affected by pathological conditions but also through:

- Normal physiology
- Bacterial presence
- Acute and previous (environmental) loads
- Nutrition, medication

As “unique” or “exclusive” breath markers for certain diseases do not exist, these effects have to be taken into account for the interpretation of clinical studies. For cross sectional studies control and standardisation of sampling, of ventilatory and hemodynamic parameters is a mandatory pre-requisite for reproducible and reliable results.

In contrast to conventional methods such as blood or tissue analysis, breath biomarker concentrations may change rapidly (even within seconds) and may immediately reflect physiological effects as well as pathological changes. Therefore, individual monitoring of volatile compounds may provide unique and immediate insides into body processes. In combination with innovative technology, such as m-health applications, a new era of personal monitoring could be established, if basic biochemical mechanisms and parameters affecting exhalation of breath VOCs are known. This talk will give an overview of the most important factors affecting breath biomarker profiles. Based on most recent findings ([I],[II],[III],[IV],[V]) examples and brisk perspectives for future applications of breath biomarkers for clinical and personal monitoring will be discussed.

[I] Sukul P, Trefz P, Schubert JK, Miekisch W. Immediate effects of breath holding maneuvers onto composition of exhaled breath. J Breath Res. 2014

[II] Sukul P, Trefz P, Kamysek S, Schubert JK, Miekisch W. Instant effects of changing body positions on compositions of exhaled breath. J Breath Res. 2015

[III] Fischer S, Bergmann A, Steffens M, Trefz P, Ziller M, Miekisch W, Schubert JS, Köhler H, Reinhold P. Impact of food intake on in vivo VOC concentrations in exhaled breath assessed in a caprine animal model. J Breath Res. 2015

[IV] Obermeier J, Trefz P, Wex K, Sabel B, Schubert JK, Miekisch W. Electrochemical sensor system for breath analysis of aldehydes, CO and NO. J Breath Res. 2015

[V] Bergmann A, Trefz P, Fischer S, Walter G, Steffens M, Ziller M, Reinhold P, Schubert JK, Köhler H, Miekisch W. PLoS One. 20

15:45

Hands-on-Workshop 1:

“Data interpretation of complex volatomic data”

Tuesday, 07.06.2016

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11:00	Coffee break	
11:30	**"Charactrization of saliva volatiles as potential biomarkers for cancer diagnosis – preliminary studies with breast and lung cancers"** *Jorge Pereira (Madeira, Portugal)*	18
12:15	**Hands-on-Workshop_3 - organized by MedSurv:** **Conferee Networking "Blood – Breath – Saliva – What do we need for diagnostic applications?"**	19
13:00	Lunch	
14:15	**"Real time MS – Basics & Applications"** *Jens Herbig (Innsbruck, Austria)*	20
15:00	Coffee break	
15:30	**Panel discussion** "Perspectives for EU-Indian cooperations within NewIndigo and InnoIndigo-Projects"	
16:15	End	

9:05

VOC-Measurements from cell cultures

Wojciech Filipiak

Breath Research Institute at the Leopold Franzens University of Innsbruck,
Innrain 66, A-6020 Innsbruck, Austria
Uni-Clinic for Anesthesia and Intensive Medicine, Medical University Innsbruck, Austria.

Volatile organic compounds (VOCs) offer unique insights into ongoing biochemical processes in healthy and diseased humans. Yet, their diagnostic use is hampered by the limited understanding of their biochemical or cellular origin and their frequently unclear link to the underlying diseases. Bearing in mind that human beings are hosts for bacterial, fungal, or other cells of non-human origin, which outnumber the body's cells by far as well as numerous endogenous and exogenous factors that potentially affect human volatilome, the identification of those VOCs, which are really human cellderived becomes a formidable challenge. Also the diversity of analytical techniques available for gas analysis (GC-MS, PTR-MS, SIFT-MS, IMS, lasers, nanosensors, etc.) and related to them sample preparation procedures result in somewhat inconsistent results of exhaled VOCs determination. Major advancements are expected from the analyses of human primary cells, cell lines and cultures of microorganisms.

The results of *in vitro* studies focused on VOCs production by human cancer and nontransformed lung cell lines as well as microbial cultures are presented here to demonstrate the complexity of the human volatilome. Additionally, a database of reliably identified volatile organic compounds found in the analyses of the *human cell lines* is compiled. Even though more than 100 different volatile biomarkers for lung cancer have been proposed during the past 10 years the biochemical background of most of these compounds has not been elucidated. Here, a literature survey for potential biochemical processes underlying VOCs production is given, including activity of CYPoxidase, aldehyde dehydrogenase, cell death and immune activation.

Finally, the analytical challenges will be discussed focusing on technical issues affecting analysis of volatile metabolites in cell culture studies, and recommendations will be outlined for reliable identification and quantification of those analytes.

9:50

Hands-on-Workshop 2*:*

“How to measure volatile organic compounds in vitro over cultures?”

Characterization of saliva volatiles as potential biomarkers for cancer diagnosis - preliminary studies with breast and lung cancers -

11:30

Jorge A. M. Pereira[1], Carina Cavaco[1], Michael Caldeira[1], Fernando Aveiro[2], José S. Câmara[1,3]

1. *Analytical Chemistry and Enology Lab (ACE lab), Madeira Chemistry Research Centre, Universidade da Madeira, Campus Universitário da Penteada, 9000-390 Funchal, Portugal.*
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Human saliva is apparently a quite simple fluid mainly composed by water and very small amounts (less than 0.5%) of several compounds, notably the digestive enzymes involved in starches and fats degradation in the mouth. However, saliva also contains electrolytes, mucus, glycoproteins, antimicrobial agents as secretory IgA and lysozyme, and volatile organic metabolites (VOMs), that constitute a promising fingerprint to assess different conditions. Additionally, compared with blood, saliva contains less proteins, thus decreasing any potential risk of non-specific interference and hydrostatic interactions, and furthermore its sampling is easier and non-invasive and can be repeated without causing discomfort to the patient. Therefore, saliva volatomics holds a very interesting potential for the non-invasive disease diagnosis, notably breast and lung cancers. This was explored by using dynamic headspace solid phase microextraction (HS-SPME) followed by Gas Chromatography coupled to Mass Spectrometry (GC-MS).

The methodology was fully optimized (fibre, sample volume, ionic strength, time and temperature of extraction) and applied to breast and lung cancer patients. The data obtained was then processed using multivariate statistical analysis, namely Partial Least Square-Discriminant Analysis (PLS-DA) and Monte Carlo Cross Validation (MCCV) to obtain the preliminary saliva volatomes for breast and lung cancers. Several VOMs present considerable variations with an interesting discriminative potential that has to be further explored with more ambitious studies able to recruit a much larger number of subjects.

Acknowledgements: The authors acknowledge the financial support of the FP7 New INDIGO Partnership Programme through the HCV project (New-INDIGO/0003/2012 project, ERA- NET) and Fundação para a Ciência e a Tecnologia (FCT) with funds from the Portuguese Government (Project PEst-OE/QUI/UI0674/2011), the MS Portuguese Network (Rede/1508/RNEM/2011) and the fellowship SFRH / BPD / 66177 / 2009 given to Jorge Pereira.

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12:15

Workshop 3 - Conferee Networking:

"Blood – Breath – Saliva – What do we need for diagnostic applications?"

14:15

Real-time MS – basics and applications

Jens Herbig
IONICON Analytik GmbH,
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Monitor volatile organic compounds (VOCs) in real-time offers great advantages for numerous applications in trace gas analysis, especially for real-time breath analysis. We introduce the concepts, advantages, and requirements that are specific for real-time analysers and present lessons learned from clinical breath studies.

A central advantage of real-time, direct analysis is the reduced likelihood of sample adulteration through storage-induced artefacts, as is frequently encountered in off-line analysis of breath gas samples collected in bags. An analyser with a fast time response allows the continuous monitoring with breath-to-breath resolution. The relevant end-tidal concentrations can then be selected by a software algorithm and the inhaled concentrations, important parameters in breath studies, are acquired in the same process. In contrast, in offline analysis, the end-tidal (or alveolar) breath fractions have to be separated mechanically prior to sampling and inhaled concentrations are measured as a separate sample. The ability of real-time instruments, to analyse a large number of breath samples without significant additional effort facilitates new types of studies, such as the monitoring of fast haemodynamic or metabolic processes in the body or pharmacokinetics. We discuss the relation found in most real-time analysers that connects the sampling frequency and the achievable signal-to-noise ratio and present a setup for real-time breath analysis that to enhance this important constraint.

We exemplify the above using a real-time trace gas analyser based on Proton Transfer Reaction (PTR) ionization with a Time Of Flight (TOF) mass spectrometer (MS). This PTR-TOFMS allows the analysis of the volatolome in real-time with a sensitivity sufficient for ppt-level detection limits. The high mass-resolution TOF MS allows the separation of isobaric molecules and the identification of their chemical composition. Finally, we give an overview over the latest developments that have greatly increased the sensitivity and selectivity of PTR-TOFMS instruments.

Wednesday, 08.06.2016

Steam and Waves

07:30: Pickup Hotel Sportforum

08:00: Departure Rostock, Thierfelder Straße

08:35: Departure Steam Train to the Baltic Sea, Bad Doberan

10:00: Departure Ship from the sea bridge, Kühlungsborn

11:30: Arrival in Warnemünde

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Invited Speaker				
Dr. Wojciech Filipiak	A	Breath Research Institute at the Leopold Franzens University of Innsbruck, Austria		EE
Dr. Jens Herbig	A	IONICON Analytik, Innsbruck, Austria		EE

Venue: Hotel Sportforum

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Plan of public transportation service: