BREATH®
BIOPSY

Welcome to the:

Breath Biopsy Conference 2021

12th - 13th OCTOBER

#BBCon21

DAY 1
Tuesday 12th October 2021

TIME (BST)	EVENT
10:00-10:15	**Welcome to the Breath Biopsy Conference**
10:15-12:15	**Keynote Talk**
	Patrick Bossuyt, University of Amsterdam *From biomarkers to medical tests: About pitfalls and peaks*
	Session 1: Early Detection
	Yury Kistenev, Tomsk State University *Acute myocardial infarction diagnostics through exhaled air volatile markers analysis by machine learning and laser optical-acoustic spectroscopy*
	Guido Verbeck, University of North Texas *The determination of breath biomarkers and metabolites for disease and health constituents using non-invasive direct inject mass spectrometry*
12:15-13:00	**Break**
13:00-14:00	**Session 2: Precision Medicine**
	Graham Clarke, AstraZeneca *Addressing the utility of breathomics in drug discovery and development*
	Fereshteh Jahanbani, Stanford Center for Genomics and Personalized Medicine *Breath Biopsy® for empowering multi-omics and precision medicine to unravel the biology of complex chronic conditions*
14:00-14:30	**Break**
14:30-16:30	**Early Careers Presentations**
	Ramji Kalidoss, Bharath Institute of Higher Education and Research *Heater and substrate profile optimization for low power portable breathalyzer*
	Robert van Vorstenbosch, Maastricht University *The detection of colorectal cancer via exhaled breath analysis, where we stand and where we go*
	Arafat Mahmood, City University of London *Metal oxide based chemiresistive sensors for detecting and management of diabetes from exhaled breath*
	Keynote Talk
	Sam Janes, University College London *Screening for lung cancer: The SUMMIT study and biomarker integration*
16:30-17:15	**Breakout Discussions (limited spaces, separate sign-up required)**

DAY 2

Wednesday 13th October 2021

TIME (BST)	EVENT
10:00-10:15	**Welcome to Day 2**
10:15-12:00	**Session 3: Sampling and Analysis**
	Morad Nakhleh, Owlstone Medical (sponsored by ThermoFisher) *Towards standardization: Breath Biopsy® OMNI Assay for enhanced biomarker discovery*
	Orna Barash, NanoScent Labs *Outcomes and conclusions from clinical performance evaluation of using VOCID™ for the detection of COVID-19 in exhaled breath*
	Ivneet Kaur Banga, University of Texas at Dallas *Passive breathomics for ultrasensitive characterization of acute and chronic respiratory diseases using electrochemical transduction mechanism*
	Jolanda Palmisani, University of Bari (sponsored by Markes International) *Breath analysis for early detection of oncologic diseases: Outcomes, challenges and future perspectives*
12:00-13:00	**Break**
13:00-14:30	**Session 4: Induced Volatomics and EVOC® Probes**
	Pauline Poinot, University of Poitiers *Off-on VOC-based probe for cancer diagnosis and prognosis*
	Melodi Anahtar, Massachusetts Institute of Technology *Engineering synthetic breath biomarkers for respiratory disease*
	Giuseppe Ferrandino, Owlstone Medical *Chronic liver disease detection using Exogenous Volatile Organic Compound (EVOC®) Probe approaches*
14:30-15:00	**Break**
15:00-17:00	**Poster Presentations & Panel Session**
	Poster Presentations *5 minute presentations of selected conference posters*
	Panel Discussion *Standardization in the breath research field: How as a community we could benefit from each other's data*
17:00-17:15	**End of Conference**

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DAY 1

Keynote

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Patrick Bossuyt, University of Amsterdam

Biography:

Patrick M. Bossuyt is the professor of Clinical Epidemiology at the University of Amsterdam and acts as Chair of the Division of Public Health & Clinical Methods in the Academic Medical Center. His scientific work spans a broad range of topics in clinical research, developed in close collaboration with clinical departments in the Academic Medical Center, with an emphasis on studies of the effectiveness of clinical interventions to guide clinical recommendations and coverage decisions.

Dr Bossuyt leads the Biomarker and Test Evaluation Research program in Amsterdam. The BiTE Program aims to appraise and develop methods for evaluating medical tests and biomarkers, and to apply these methods in relevant clinical studies. In doing so, the program wants to strengthen the evidence-base for rational decision-making about the use of tests and test strategies in healthcare. Bossuyt spearheaded the STARD initiative for the improved reporting of diagnostic test accuracy studies.

Dr Bossuyt has authored and co-authored several hundred publications in peer reviewed journals and serves on the editorial board of a number of these, including Radiology and Clinical Chemistry. He is a member of several national and international advisory committees. He chairs the Scientific Advisory Committee of the Dutch Health Insurance Board, overseeing the national healthcare benefits package.

Talk Title:

From biomarkers to medical tests: About pitfalls and peaks

Talk Abstract:

Progress in unraveling the molecular basis of diseases and biomarkers in many diseases and advances in technology have fueled the search for novel biomarkers in many diseases. There is hope that biomarkers will improve our ability to identify, manage, or prevent a wide range of conditions that jeopardize health. Despite enthusiasm and high prospects for biomarkers, the massive investment has not yet resulted into tangible health benefits for a large number of patients and citizens.

This failure has led to scrutiny. Some have pointed to analytical capacity and limitations of existing measurement methods or the difficulty in finding laboratory professionals with sufficient expertise in applying these laboratory methods. This led to calls for the investment of even more resources into biomarker research and development.

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We argue that other, additional explanations, beyond technical caveats, can also account for the current failures to deliver that plague biomarker research. Some of these are not unique for biomarker studies, but apply to biomedical and clinical research in general.

In this presentation, we will discuss the major challenges and hurdles in biomarker research. We will highlight these with examples from the published literature and will discuss how research and development into biomarkers as future tests can be further improved.

Session 1: Early Detection

Yury Kistenev, Tomsk State University

Biography:

Yury V. Kistenev is a professor at Tomsk State University, Russia. He received his PhD in optics in 1987 and his doctorate degree in physics and mathematics in 1997. He is the author of more than 140 journal papers and has written four book chapters. His current research interests include laser molecular imaging, IR and terahertz laser spectroscopy, and machine learning.

Talk Title:

Acute myocardial infarction diagnostics through exhaled air volatile markers analysis by machine learning and laser optical-acoustic spectroscopy

Talk Abstract:

Our work demonstrates the abilities of exhaled air volatile marker analysis by machine learning and laser optical-acoustic spectroscopy for acute myocardial infarction diagnostics. The target group included 30 patients with primary myocardial infarction, which had been recruited in the Cardiology Research Institute, Tomsk, Russia. The control group included 42 healthy volunteers. The interval in hours between the AMI case and sampling time was 15.75 (the mean value). We have used and compared the pattern-recognition-based approach and chemical-composition-based approach. The predictive model was based on using support vector machine combined with principal component analysis. The created predictive model based on the pattern-recognition technique provided 0.86 of the mean values of both the sensitivity and specificity. The created predictive model based on the chemical analytical-based detection using six volatile markers (C_5H_{12}, N_2O, NO_2, C_2H_4, CO, CO_2) provided 0.82 and 0.93 of the mean values of the sensitivity and specificity, respectively. The research was carried out with the support of a grant under the Decree of the Government of the Russian Federation No. 220 of 09 April 2010.

Guido Verbeck, University of North Texas

Biography:

Dr Guido F. Verbeck, Professor of Chemistry and Biochemistry, is an expert is mass spectrometry, specifically instrument design and development. Guido Verbeck received his PhD as a Proctor & Gamble fellow in chemistry at Texas A&M University. Dr Verbeck has developed mass spectrometers over the past 20 years, and has been a member of the analytical community for 25 years. His appointment is at the University of North Texas where he continues to design novel ion optical devices for miniaturization, preparative, and analytical mass spectrometry, and is the Director for the Laboratory of Imaging Mass Spectrometry. In this appointment Dr Verbeck has received $5M in external funding, 85 peer reviewed publications, 10 awarded patents and 8 applications, and graduated 20 graduate students in instrument development. Guido Verbeck was awarded a Young Investigator Award from the Air Force Office of Scientific Research and the University of North Texas Early Career Award for Research Creativity. Dr Verbeck continues to develop new mass spectrometers specifically for single-cell analysis for cancer biomarkers, nanoparticle development for pharmaceutical and toxicological biochemical effects, and determining the biological mechanisms for biomolecular condensates.

Talk Title:

The determination of breath biomarkers and metabolites for disease and health constituents using non-invasive direct inject mass spectrometry

Talk Abstract:

Breath capture chemistry is a rising method of examining physiological information as a means to discover and track biomarkers and metabolites for clinical applications. Previous studies have highlighted the ability of breath samples to indicate presence of respiratory viral infections, such as Influenza A, MERS, SARS-CoV-1, and in our group SARS-CoV-2, through the detection of volatile chemical markers via mass spectrometry, typically with solid phase substrates. Due to its noninvasive sample collection and unlimited supply, further exploration of this volatile chemistry in the breath for a more detailed understanding of its connection to disease, diet, and general lifestyle is incredibly beneficial for the medical field, among others. Here we will present a rapid non-invasive breath capture techniques using the Teslin substrate for direct analysis with mass spectrometry. We then coupled this data with the analytics of partial-least squared discriminant analysis and K-nearest neighbor, and check with K-fold cross validation to confirm chemical assignments. These experiments are designed to exact the chemistry of the breath biomarker and metabolites, and help train more portable instruments on the chemicals of interest. Previous research will be shown as to the efficacy of this direct inlet mass spectrometry technique. For disease states, presence of drug metabolites, and lifestyle biomarkers, limits of detection and mass accuracy of this direct inject mass spectrometry will be presented.

DAY 1

Session 2: Precision Medicine

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Graham Clarke, AstraZeneca

Biography:

Graham Clarke is the Head of Translational Science and Experimental Medicine Operations for Early Respiratory & Immunology at AstraZeneca. His role is to develop and evolve the operating infrastructures to enable the precision medicine strategy across the Early R&I portfolio. Graham has a PhD from King's College London, UK, in Respiratory Pharmacology and Physiology. He comes with 20 years of clinical operation and clinical model development experience, with specific focus on inhaled challenge models of inflammation and non-invasive methods of measuring airway inflammation. Prior to joining AZ, Graham held increasing levels of responsibility at Quintiles Drug Research Unit, latterly leading the Respiratory early clinical development group first in man and first in patient drug trials, and more recently at Hvivo Ltd. as Head of Clinical Operations and virus challenge model development. Graham is the AZ lead for the 3TR-IMI consortium, a Pan-European cross-disease research consortium aimed at improving personalized biological treatment of asthma and COPD. He also leads the 3TR Breathomics working group to critically evaluate its utility and incorporation in 3TR sponsored clinical trials and its broader adoption in drug discovery research.

Talk Title:

Addressing the utility of breathomics in drug discovery and development

Talk Abstract:

The number of breath biomarker discovery trials has increased in recent years with the discovery of potential breath volatile biomarkers across multiple studies. The adoption of breath into large scale studies such as U-BIOPRED, EMBER and most recently 3TR-IMI confirms the interest of the respiratory research community, including pharma, in this technology. However we are now at a critical stage. To date the mounting evidence supports breath VOC biomarkers at the proof-of-concept level, but no tests have yet penetrated through to clinical practice. A number of key elements need to be addressed to develop confidence in this technology, notably amongst others; reproducibility, pre-analytical competencies, VOC stability, the robustness of data and its synergy with more established 'omic' approaches. The path for adoption in drug discovery and development modalities are manifold, but the presentation will continue to address its utility as a tool for target-candidate identification and progressively

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to inform diagnosis, early detection and phenotyping of disease. This puts breath analysis at an exciting time where it is at the cusp of having true impact in clinic. The presentation further explores requirements for the next decade of breath research.

Fereshteh Jahanbani, Stanford Center for Genomics and Personalized Medicine

Biography:

Fereshteh Jahanbani received her PharmD from Tehran University of Medical Sciences (TUMS) and her PhD in pharmacology from Iran University of Medical Sciences (IUMS). She also received 6 years postdoctoral degree from Case Western Reserve University (CWRU) and University of California Santa Cruz (UCSC). She has been working in the Stanford Center for Genomics and Personalized Medicine since June 2012. Combining family and population studies and using the power of multi-omics and precision medicine to understand the genetic and epigenetics risk factors associated with chronic complex diseases is the main focus of her research. Currently she is working on the pathological cross talk between EDS, ME/CFS, PANS/PANDAS and Lyme using an array of cutting edge technologies including Breath Biopsy®.

Talk Title:

Breath Biopsy® for empowering multi-omics and precision medicine to unravel the biology of complex chronic conditions

Talk Abstract:

Myalgic encephalomyelitis, chronic fatigue syndrome (ME/CFS), is a prototypical example of complex, debilitating disease characterized by extreme fatigue that is not improved by rest and often gets worse after any activity. Other symptoms include cognitive impairments, headaches, muscle and joint pain, sore throat, tender lymph nodes, GI issues, chills and nightsweats, multi chemicalsensitivity, shortness of breath, irregular heartbeat, sleep disturbance, pain, and orthostatic intolerance. CFS has a prevalence of 0.1–2.5% and affects people of all age. Genetic variations and environmental stressors such as infection, trauma and toxin exposure contribute to ME/CFS etiology. However, the exact underlying molecular basis of ME/CFS is not yet well understood and diagnostic biomarkers and FDAapproved drugs are lacking.

To better understand the etiology of ME/CFS, longitudinal analysis using both population and family approaches is of high priority. To this end we conducted a pilot multi-omics study on ME/CFS patients, their unaffected family members and unrelated healthy controls. Exhaled breath contains valuable biomarkers including hundreds of volatile organic compounds (VOCs) reflecting the metabolic condition of an individual. Integrating Breath Biopsy® with Omics data can help us to generate a more holistic pictures of ME/CFS pathophysiology. We collaborated with Owlstone Medical to measure sulfur-containing VOCs. Our results show that people with genetics and epigenetic predisposition can be in higher risk to develop chronic health conditions due to the build-up of the toxic compound in their body and can be used for the development of novel diagnostics and therapeutics strategies.

DAY 1

Keynote

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Sam Janes, University College London

Biography:

Sam won an MRC Training Fellowship to perform a PhD and then a post-doctoral period working in the Cancer Research UK Lincoln's Inn Fields Institute with Fiona Watt working on lung cancer biology. He then moved as an MRC Clinician Scientist to UCL leading a group interested in the role of stem cells in lung cancer pathogenesis and treatment of lung disease using cell therapies. He was awarded a Wellcome Trust Senior Clinical Fellowship in October 2010 to work on novel cell therapies for lung cancers resulting in a DPFS first-in-man award and in 2015 won his Wellcome Senior Fellowship renewal to study the genetic and cellular changes lung cancer pathogenesis. He is the lead of four academic lead randomised clinical trials and most notably recently launched the SUMMIT study, a 12000 participant London-based study examining CT and blood screening for lung and other cancers.

He works as a respiratory consultant at UCLH with a particular interest in lung cancer, mesothelioma, interventional and diagnostic bronchoscopy and early lung cancer detection. He is Head of the Respiratory Research Department at UCL, Vice-Chair of the National 'Clinical Expert Group' on Lung Cancer.

Talk Title:

Screening for lung cancer: The SUMMIT study and biomarker integration

Talk Abstract:

In the UK, only 12.9% of those diagnosed with lung cancer are alive after five years due to 68% of lung cancers being diagnosed at stage III or IV which infers incurable, advanced disease. One-year survival by stage ranges from around 71% for stage I disease to around 14% for stage IV. Early detection is therefore key to improving lung cancer survival.

The SUMMIT study is a clinical trial run in partnership between UCL, UCLH and an American biotech company (GRAIL Inc). It will help to build the evidence base for a screening programme in the UK. The aim for the US company is to develop a blood test (cfDNA) to detect cancer early before symptoms appear. In my talk I will discuss the challenges in delivering a study like SUMMIT. I'll examine the evidence for CT screening and the difficulties in delivering it at a population level. I'll then examine the potential for biomarkers to improve the landscape of lung cancer screening.

DAY 2

Session 3: Sampling and Analysis

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Morad Nakhleh, Owlstone Medical

Biography:

Morad K. Nakhleh Joined Owlstone Medical in 2018, in his role as Lead Biomarker Discovery Scientist he leads the scientific and technical development of the biomarker discovery platforms and solutions for exhaled VOCs sampling and analysis. Morad has more than 11 years of experience in biomarker discovery and exhaled breath analysis. He holds a degree in Emergency medicine, Master's degree in medical sciences and PhD in Nano-biotechnology. Prior to joining Owlstone, as part of his post-doctoral research, Morad focused on understanding the origins and biochemistry of VOCs, mainly in respiratory diseases.

Talk Title:

Towards standardization: Breath Biopsy® OMNI Assay for enhanced biomarker discovery

Talk Abstract:

Exhaled Volatile Organic Compounds (VOCs) hold the potential to be effective non-invasive biomarkers for diagnostics and precision medicine. The success of biomarker discovery studies in the field heavily relies on optimized sample acquisition and analysis. That includes, but is not limited to, maximizing the number of biologically relevant compounds detectable by the analytical platform, and reducing process variability.

Developing a fit for purpose end-to-end breath sampling and analysis platform remains a significant challenge, particularly due to the complex nature of the breath matrix and external sources of VOCs contaminating the samples.

This presentation aims to provide data-driven insights, gained through the development of the OMNI Assay, towards enhancement of global biomarker discovery capabilities and data quality. We will focus on the optimization of approaches for sample acquisition, analysis and quality control.

Finally, we will share and recommend standardized key metrics, that not only allow decision making and monitoring of the platform's performance, but also have the potential to drive the future of standardized scientific reporting and communication within the breath analysis community.

Orna Barash, NanoScent Labs

Biography:

Orna Barash works as VP Clinics at NanoScent. She previously worked as a researcher and teacher assistant at Technion, Israel Institute of Technology, and as a research assistant at the Marie Curie Excellence Center for Artificial Olfactory Systems. Orna has a PhD from the Laboratory for Nanomaterial-based Devices (LNBD), Department of Chemical Engineering, Technion – Israel Institute of Technology.

Talk Title:

Outcomes and conclusions from clinical performance evaluation of using VOCID™ for the detection of COVID-19 in exhaled breath

Talk Abstract:

The mitigation of the COVID-19 pandemic greatly depends on early detection of asymptomatic and symptomatic infected individuals. Thus, there is a rising demand for quick, easy to use, point-of-care tests. A potential tool for such rapid screening is based on Volatile Organic Compounds (VOCs) measurement and analysis comprising NanoScent's VOCID™ breath test. NanoScent's breath test was designed to identify a 'fingerprint' of disease-specific VOCs for COVID-19 in less than one minute. The core of NanoScent's technology is based on proprietary chemoresistor nanoparticle sensors that react differently to distinct VOC fingerprints, allowing for the individual identification of diseases such as COVID-19, as well as other health-related states of interest. While there are several considerable challenges to portable scent recognition technology, mostly due to environmental effects and sensor drift, the VOCID™ breath test was successfully deployed in a major hospital in Israel. This feasibility study, including 152 individuals (45 PCR-positive and 107 PCR-negative patients), resulted in 76% sensitivity and 75% specificity for identification of SARS-CoV-2. We also explored three breath sampling methods for their effectiveness, as well as the timeframe necessary between breath collection and before exposure to the sensor. This study proved that the VOCID™ test has a potential for mass screening of COVID-19 and helped shape future development plans for improving the NanoScent system as a fast, reliable and sensitive tool for upper respiratory tract viral infections.

Ivneet Kaur Banga, University of Texas at Dallas

Biography:

Ivneet is a PhD student at the Department of Bioengineering, University of Texas at Dallas. She joined the doctoral program at the Biomedical Microdevices and Nanotechnology Laboratory under the supervision of Dr Shalini Prasad in 2019. The primary focus of her research is to develop wearable platforms using the principles of micro and nanotechnology for breathomics based technology. Ivneet has published work on the use of RTIL based technology for gas sensing interface. In the past year, Ivneet's research group have filed three patents in association with a company for the development of these devices. Ivneet has published three papers as part of her PhD on the development of the electrochemical sensors for disease diagnosis and monitoring. She has also presented at prestigious national conferences such as Pittcon 2021, ECS 2021, BMES 2020 and 2019. Ivneet completed her master's in technology from Amity University (India). She published her research work on the development of immunoassays for detection of opiate drugs as part of her graduate degree.

Talk Title:

Passive breathomics for ultrasensitive characterization of acute and chronic respiratory diseases using electrochemical transduction mechanism

Talk Abstract:

There are thousands of volatile organic compounds (VOCs) present in the exhaled air that can provide insights into respiratory diseases such as asthma and chronic obstructive pulmonary disease. Noninvasive disease diagnosis primarily using breath to monitor metabolites, is fast emerging as an area of interest. The technologies being currently used to develop sensors for field monitoring are based on resistance change, before and after the exposure to the target. A drawback of such sensors is that they measure electrical resistance, which lacks both sensitivity as well as specificity. They have low reproducibility, narrow range of sensing, and need high operating temperature. However, if the electrochemical sensors are integrated onto an Internet of Things (IoT)-based platform, they can be used *in-situ* and do not need prior sample preparation. We have earlier reported the development of an electrochemical sensor for the detection of endogenously and exogenously produced methanol vapors, ammonia, and isopentane. We now demonstrate the proof of concept of an electrochemical sensor, specific and sensitive for the detection of endogenously produced VOCs, toward developing a handheld breath analyzer for onsite applicability.

Jolanda Palmisani, University of Bari

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Biography:

Jolanda Palmisani is an Environmental Chemistry researcher at the Department of Biology, University of Bari (Italy). Jolanda graduated in Chemistry in 2011 and obtained a PhD in Chemical Sciences in 2015. Her research activities focus on: atmospheric pollution (chemical characterization of air samples, high temporal resolution monitoring of target pollutants, source apportionment, pollutant emissions impact evaluations); indoor air quality (determination of VOCs and particles concentration, real-time air quality monitoring, identification of indoor sources, evaluation of VOCs and particle emissions from materials and consumer products, ozone-initiated chemistry and secondary organic aerosol formation, exposure scenario evaluations); development of innovative methodological approaches for high temporal resolution monitoring of outdoor/indoor pollutants; and breath analysis for the early diagnosis of oncologic diseases. Jolanda has been involved as an early-career scientist in research projects and presented at several national and international conferences on the topics above. She is a Management Committee Substitute Member (Italy Representative) and leader of Working Group 3 for the Cost Action CA 17136 'Indoor air network' and is also an European Commission public sector expert. Jolanda is first author or co-author of 33 papers in peer-reviewed scientific journals and books.

Talk Title:

Breath analysis for early detection of oncologic diseases: Outcomes, challenges and future perspectives

Talk Abstract:

Chemical characterization of Volatile Organic Compounds (VOCs) in human breath and the identification of a characteristic metabolite pattern is to date recognized as non-invasive and promising methodological approach alternative to traditional diagnostic exams for early detection and follow-up of oncologic diseases. VOC composition in exhaled breath reflects the volatile composition of the bloodstream and airways, therefore able to provide information about human metabolic status allowing a discrimination between healthy and sick clinical conditions due to an instantaneous equilibrium established between the bloodstream and the alveoli air in the lung. Despite the promising outcomes obtained by the scientific community over the last decades, breath analysis is still far from being applied as a routine clinical technique. This it due to the lack of standardized procedures for sampling and analysis that guarantee good repeatability and comparability of experimental results at all the methodology-levels. For decades the most applied methodology was based on the collection of human samples through polymeric bags but nowadays innovative devices (e.g., Mistral) for the automatic collection of exhaled breath-VOCs directly onto sorbent tubes have been developed and launched onto the market. The excursus of the promising outcomes obtained in terms of identification of breath VOCs pattern for the discrimination between patients affected by oncologic diseases (i.e., lung cancer, malignant pleural mesothelioma and colorectal cancer) and healthy controls is herein explored, highlighting the achievements on the methodological approach and data treatment and underlying the limitations to overcome as well as challenges for the future.

DAY 2

Session 4: Induced Volatomics and EVOC® Probes

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Pauline Poinot, University of Poitiers

Biography:

Pauline Poinot is a transdisciplinary researcher at IC2MP, Institute of Chemistry, University of Poitiers, France. After obtaining a master's degree in Molecular Biochemistry, she graduated from a French Engineering School and then started a PhD on Flavor Chemistry and Sensory Analysis in Nantes. In 2010, she joined the French Alternative Energies and Atomic Energy Commission, Orsay, where she was trained to Proteomics with the investigation of protein biomarkers for Alzheimer's disease in patient cerebrospinal fluid.

Pauline then joined the Institute of Chemistry of Poitiers where she has initiated a novel research group whose major objective is to develop Chemistry toolboxes for Biology. Thanks to her multidisciplinary background, she investigates Chemical and Biochemical strategies combining diverse "Omics" approaches with the aim to highlight and monitor relevant biomarkers involved either in the origin or the basic processes of any living system.

A recent illustration of her program is the development of a VOC-based probe that allows solid cancers diagnosis and prognosis *in vivo* in real time

Talk Title:

Off-on VOC-based probe for cancer diagnosis and prognosis

Talk Abstract:

Volatolomics allows us to elucidate cell metabolic processes in real time. In particular, a volatile organic compound (VOC) excreted from our bodies may be specific for a certain disease, such that measuring this VOC may afford a simple, fast, accessible and safe diagnostic approach. Yet, finding the optimal endogenous volatile marker specific to a pathology is nontrivial because of interlaboratory disparities in sample preparation and analysis, as well as high interindividual variability. These limit the sensitivity and specificity of volatolomics and its applications in biological and clinical fields but have motivated the development of induced volatolomics. In this context, we have recently proposed a new strategy, that we've called "Induced Volatolomics", that relies on the use of an off-on VOC-based probe which is converted into an exogenous volatile compound through a metabolic-specific enzymatic metabolism.

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In this communication, an off-on VOC-based probe and its *in vivo* use to diagnose tumour-bearing animals will be described. Next, the interest of employing such a VOC-based probe as a companion tool to predict, survey and improve the efficacy of novel chemotherapeutic agents will be shown. Finally, the scientific and clinical perspectives of off-on VOC-based probe will be presented.

Melodi Anahtar, Massachusetts Institute of Technology

Biography:

Melodi Anahtar is a PhD candidate in Medical Engineering and Medical Physics through the Harvard-MIT Health Sciences and Technology program. She is conducting her doctoral research under Dr Sangeeta Bhatia at MIT as an NSF Graduate Research Fellow. Her PhD is focused on creating diagnostic tools for infectious disease. After completing her degree, she hopes to work at the intersection of climate change and health.

Talk Title:

Engineering synthetic breath biomarkers for respiratory disease

Talk Abstract:

Historically, breath tests have relied on endogenous volatile organic compounds (VOCs) to differentiate and diagnose disease. However, hurdles such as the presence of confounding environmental VOCs, subject variability, overall low VOC concentrations, and a lack of method standardization have prevented breath-based tests from being widely utilized as a reliable and accurate diagnostic tool. To overcome these challenges, our lab has leveraged our prior experience in creating synthetic biomarkers to develop volatile releasing nanoparticles that can generate exogenous, specific breath-based signatures of disease. These nanoparticles, which we have termed volatile activity-based nanosensors (vABNs), produce these synthetic volatile biomarkers in response to dysregulated protease activity in the lungs. The power of this system lies in our ability to select which VOC will be detected, thereby optimizing our signal-to-noise ratio in a way that cannot be done when relying on endogenous breath biomarkers. We have demonstrated that vABNs can be used to non-invasively detect aberrant protease activity in the lungs within 10 minutes after sensor administration, and can be repeatedly administered to monitor changes in protease activity over time, thus enabling a novel means of diagnosing and monitoring disease via breath.

Giuseppe Ferrandino, Owlstone Medical

Biography:

Giuseppe's keen interest in the study of NAFLD arose during his post-doctoral experience at Yale School of Medicine in the USA, where he contributed to discovering the link between hypothyroidism and NAFLD. He provided significant support to several other research projects ranging from ion transport to the characterization of a new drug for thyroid cancer treatment.

Giuseppe then moved to Dresden, Germany, where he joined the Max Planck Institute of Molecular Cell Biology and Genetics as a post-doctoral scientist. His research there focused on the identification of a signalling pathway that promotes lipid accumulation in the liver. This pathway may underlie the pathogenesis of non-alcoholic fatty liver disease (NAFLD), a metabolic disorder aecting 25% of the European population.

Despite advanced new technologies, liver biopsy remains the gold standard to diagnose NAFLD and other liver conditions. At Owlstone Medical, Giuseppe contributes to replacing this invasive diagnostic procedure with a simple Breath Biopsy, aiming to promote early diagnosis, when most liver diseases are easily defeated.

On a personal note, Giuseppe enjoys his favorite hobby, cooking, with an able company. He had the opportunity to train at a professional level in his homeland, Ischia, a beautiful island immersed in the blue of the Gulf of Naples in Italy. A place where Giuseppe loves to admire colorful sunsets by the sea.

Talk Title:

Chronic liver disease detection using Exogenous Volatile Organic Compound (EVOC®) Probe approaches

Talk Abstract:

The last three decades have seen a ~30% death toll rise caused by liver cirrhosis, and a ~100% increase in the prevalence of decompensated cirrhosis, with more than 50% of cases diagnosed at advanced stages. These numbers express the pressing need of less invasive diagnostic tests effective at earlier stages.

Limonene, a generally recognized as safe (GRAS) compound used as a flavouring agent, was found elevated in breath of cirrhosis patients, and correlated with blood metrics of liver function, thus representing a candidate biomarker for a non-invasive breath test. Yet, the inability to control limonene intake in the general population complicates the definition of on-breath threshold values for the identification of subjects with liver dysfunction. To overcome this limitation, we established the exogenous volatile organic compound (EVOC) probe approach, where random dietary contribution is reduced by overnight fasting followed by standardized oral limonene exposure.

We found that the range of breath limonene in fasted healthy subjects was similar to that of the ambient background. Hence, administration of limonene produced a spike on breath after 30 minutes, followed by a reduction after 60 minutes. A similar profile was observed also for other GRAS compounds. These data suggest that the EVOC

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approach could be used to detect liver dysfunction, which is expresses as delayed on-breath EVOC reduction after administration, due to impaired hepatic clearance.

We aim to test the EVOC approach in patients with cirrhosis and earlier stages liver diseases, to identify time point and EVOC dose that provide the best discriminatory performance from healthy controls.

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