Società Chimica Italiana
Divisione di Spettrometria di Massa

IMSF
international mass spectrometry foundation

IMSC 2018 FLORENCE

XXII International Mass Spectrometry Conference

Florence (Italy) - August 26-31, 2018

ABSTRACT BOOK

Centre for Integrative Biology (CIBIO), University of Trento, Trento, Italy (1) - Center Agriculture Food Environment (C3A), University of Trento, Trento, Italy (2)

Keywords: metabolomics, microbial metabolites, gut microbiota, cancer, organoids

Introduction
Currently, colorectal cancer (CRC) is the second cause of death in EU[1]. In EU, the Czech Republic and Slovakia showed the highest rates. By contrast, Greece presented the lowest rates across Europe[2, 3]. This incidence is postulated to reflect risk factors associated to socioeconomic status, including poor dietary habits and obesity. However, emerging evidence also implicates gut microbiota as an important effector in the relationship among diet, human health and cancer[4].

Methods
A novel integrative strategy to deeper understanding of CRC is vital. To accomplish this, a real-life scenario is needed. In this context, colon organoids/tumoroids will be established. Afterwards, an apple will be digested/fermented in vitro using a batch culture colonic model inoculated with feces from lean/obese healthy donors. In the end, such polyphenol metabolites will be tested in colon organoids/tumoroids and the mechanisms of action will be revealed by metabolomics and organoids assays.

Results
In summary, the results from TRIANGLE through the integration of polyphenols (diet), gut microbiota and colon organoids (host), will be highly multidisciplinary, and will undoubtedly set the stage towards the identification of mechanisms contributing to CRC understanding and will ultimately pave the way to phytochemical treatment and prevention. First, it is still unknown how apple phytochemicals are affected by lean and obese microbiotas, and it must be understood in order to comprehend chemopreventive efficacy of polyphenols and to be able to give nutritional recommendations related to functional-group class therein. Secondly, tumor organoids (tumoroids) and organoids can bridge the gap between human 2D cancer cell lines and animal-based models. Lastly, metabolomics analysis and 3D cell assays of colon organoids/tumoroids will provide valuable new insights into the mechanisms by which nutrient-gene interaction influences colon stem cell niche and CRC, and will open up new possibilities for CRC understanding and prevention.

Conclusions
TRIANGLE will provide novel insights towards CRC prevention by (1) using a new in vitro model based on colon organoids, (2) considering both gut microbiota composition and microbial metabolites, and (3) applying novel techniques. By implementing this, colon organoids will clearly mimic human real-life scenario. Secondly, the manner how polyphenols are affected by microbiotas will reveal the type and quantity of polyphenol metabolites, which could be correlated to the chemoprevention of CRC.

Novel Aspect
Metabolomics will provide a holistic signature in organoids and, together with organoid assay data can generate new hypotheses regarding underlying the mechanisms by which polyphenol-gene interaction influences CRC.

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TP-233 / INDOLOME ANALYSIS FOR NUTRACEUTICAL AND PHYSIOLOGICAL STUDIES

Federico Maria Rubino [(1)] - ***Michele Dei Cas*** [(1)] - ***Jessica Rizzo*** [(1)] - ***Andrea Penoni*** [(2)] - ***Marcello Iriti*** [(3)] - ***Rita Clara Paroni*** [(1)]

Universita degli Studi di Milano, Dipartimento di Scienze della Salute, Milano (1) - Università dell'Insubria, Dipartimento di Scienza e Alta Tecnologia, Como (2) - Università degli Studi di Milano, Dipartimento di Scienze Agrarie e Ambientali - Produzione, Territorio, Agroenergia, Milano (3)
Indolome analysis for nutraceutical and physiological studies.

Keywords: isotope dilution, liquid chromatography, melatonin, tandem mass spectrometry, tryptophan ethyl ester

Introduction
Biotransformation products of tryptophan are gaining an increasing multi-faceted interest as nutritional supplements to cope with environmental and lifestyle related stressors. Their identification and measurement in nutritional and biological matrices mandates for flexible, yet accurate and precise analytical methods based on mass spectrometry and adapted to studies with stable isotopic labels. Fragmentation studies are necessary to fulfil this aim.

Methods
An API3000 LTQ LC-MS system is used for extensive tandem MS fragmentation studies on 3 tryptophan amino-acids, 4 tryptamines and 3 *N*-acetyl-tryptamines. A stable-isotope analogue of melatonin is custom synthesized. LC separation and quantification parameters are optimized for the detection by MRM of 8 analytes and 3 internal standards in four different biological and food matrices.

Results
Spectroscopic studies highlight key fragmentation pathways for the identification and measurement of 8 target analytes. The study of the fragmentation pattern [1] allowed designing and synthesizing[2] an under-considered isotope-labelled form of melatonin [3], to improve quantification by ID-MS-MS, with respect to previously employed isotopologues. Furthermore, the discrimination of the critical pair of isobaric melatonin and isomeric tryptophan ethyl ester, that also yield very similar fragmentation, could be accomplished with a scan function that addresses a triplet of consecutive fragments, only a pair of which are specific for each compound. With this method, the levels of melatonin and of its metabolic pathway are measured in human fluids from several unique conditions, as well as from nutraceutical and pharmaceutical formulations and food matrices.

Conclusions
Accurate fragmentation studies of biological indole compounds supply information to design a new internal standard for isotope dilution measurement of melatonin, and identification and quantification methods suitable for the measurement of the indolome in different natural matrices of interest for biological and technological applications.

Novel Aspect
An innovative internal standard to measure melatonin by ID-MS-MS and a method to discriminate isomers and isobars of melatonin are proposed.

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TP-234 / RAPID ANALYSIS OF NCI60 PANEL METABOLIC AND LIPID PROFILES WITH AN AUTOMATIC WELL PLATE READER USING LASER ASSISTED REIMS

Richárd Schäffer [(1)] - ***Julia Balog*** [(1)] - ***Daniel Simon*** [(1)] - ***Nora Kucsma*** [(2)] - ***Anna Lovrics*** [(2)] - ***Gergely Szakacs*** [(2)] - ***Steven Pringle*** [(3)] - ***Zoltán Takáts*** [(4)]