3rd International Conference on

Lipid Science and Technology

December 11-12, 2017 | Rome, Italy

Development and use of advanced mass spectrometry techniques for the characterization of cellular lipidome profile of fibroblasts in early on-set Parkinson's disease patients

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Parkinson's disease (PD) is a progressive neurodegenerative disease involving the nigrostriatal pathway; patients' manifest motor symptoms dysfunction when more than 50% of neurons are lost. Though it is well recognized that alterations of lipid signaling, and metabolism plays a significant role in many human diseases, little is known about the role of lipids during this specific disease. Recently, it has been reported that altered lipid pathways in the primary visual cortex and the anterior cingulate are possible in neurological disorders such as PD by analyzing post-mortem tissues from patients in advanced neuronal degeneration stage. Such an approach, however, hinders the identification of the first neuronal changes. Thus, understanding the mechanisms of PD and recognizing neuronal changes in the early phase of PD represents a crucial task. According to their polygenic predisposition and environmental etiopathology skin fibroblasts are today widely recognized as a useful model of primary human cells, capable of reflecting the chronological and biological aging of the patients. A lipidomics study of easily accessible primary human fibroblasts is presented here based on hydrophilic interaction liquid chromatography coupled to electrospray ionization-Fourier transform mass spectrometry, using both positive and negative polarities. Phospholipids (PL) from dermal fibroblasts of two unrelated PD patients with different parkin mutations and two controls were characterized by recurring to single and tandem MS measurements on a hybrid quadrupole-Orbitrap mass spectrometer. This untargeted approach enabled the identification of various PL classes as phosphatidylethanolamines (PE), phosphatidylcholines (PC), sphingomyelins, lysoPC, lysoPE, phosphatidylinositols, phosphatidylserines, mono-, di- and tri-hexosylceramides and ganglioside GM1, GM2 and GM3. To identify the main lipids involved in the pathological condition of PD, lipidomics data on a higher number of samples need to be collected and processed by multivariate statistical analyses. In this communication, an interesting set of preliminary findings will be reported and discussed.
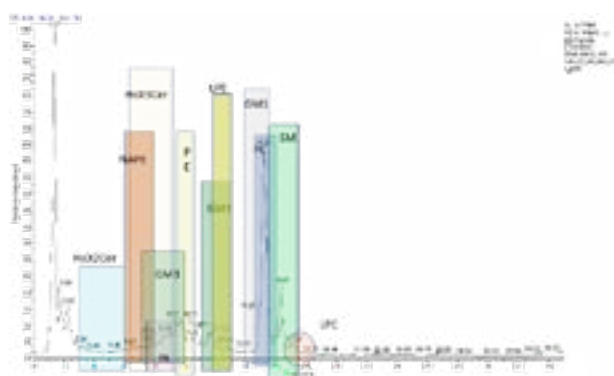

Figure 1: *HILIC-ESI (+) MS total ion current chromatogram of a lipid extract from human fibroblasts.*

Recent Publications:

1. M M Wiest et al. (2007) Full text biomarker discovery using high-dimensional lipid analysis. Current Opinion in Lipidology 18(2): 181-6.

2. T Klockgether (2004) Parkinson's disease: clinical aspects. Cell and Tissue Research 318:115–120.

Bioenergetics, an open access journal
ISSN: 2167-7662

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3. K Farmer et al. (2015) Major alterations of phosphatidylcholine and lysophosphotidylcholine lipids in the substantia nigra using an early stage model of parkinson's disease. International Journal of Molecular Science 16(8):18865-18877.

4. J Romaní-Aumedes et al. (2014) Parkin loss of function contributes to RTP801 elevation and neurodegeneration in Parkinson's disease. Cell Death and Disease 5: e1364.

5. S Granafei et al. (2015) Identification of isobaric lyso-phosphatidylcholines in lipid extracts of gilthead sea bream (*Sparus aurata*) fillets by hydrophilic interaction liquid chromatography coupled to high-resolution Fourier-transform mass spectrometry. Anal Bioanal. Chem 407:6391-6404.

Biography

Calvano Cosima Damiana is currently working as Assistant Professor at University of Bari in Department of Chemistry and she received the eligibility to become Associate Professor in Analytical Chemistry. She graduated in Chemistry at the University of Bari in 2003. In 2007, she accomplished her PhD studies in Microbiology, Health and Food Chemistry. In 2012, she received the Best Young Researcher Award from the Analytical Chemistry Division of the Italian Chemical Society (SCI). Her research interests focus on the development of new analytical protocols for biomolecules study, on the use of mass spectrometry in proteomics and lipidomics fields for applications in molecular science, food, clinical and cultural heritage. Her scientific activity is documented by 75 papers divided as peer-to-peer reviewing publications in international journals, book chapters and conference proceedings. She is r author/co-author of more than 100 communications to national/international conferences.

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ISSN: 2167-7662

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