2DCOS Analysis of Metabolic Processes Associated to Friedreich Ataxia.

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Friedreichs's Ataxia (FRDA) is a pathology associated with spinocerebellar ataxia, progressive neurodegeneration, sensory loss, and hypertrophic cardiomyopathy. At the molecular level the pathology arises from faults in the process of iron-sulfur (FeS) cluster biogenesis which in turn arise from the silencing of the gene for the protein Frataxin (FXN). The resulting oxidative stress, iron accumulation and malfunction of the mitochondrial machinery are reflected in changes of metabolic pathways in eukaryotic cells. To study the onset of FRDA at the molecular level, the laboratory of Annalisa Pastore has produced an engineered cellular model (T-REx293-cFXN) that allows regulation of FXN expression at will [1, 2].

We present the possibility to use 2DCOS analysis to describe metabolic processes in this cellular system. We use a workflow based on micro-FTIR spectroscopy and 2DCOS, which we called Correlated Cellular Spectromicroscopy (CSM) [3]. The approach allows us to identify small molecule metabolites and other molecules that are turned over in living T-REx293-cFXN cells. We do that at different levels of expression of the Frataxin gene. Molecular identification is followed up by analysis of the kinetic traces of selected metabolites, to quantify the variation in turnover at different levels of expression of frataxin. The work tests the capabilities of the CSM, in terms of both sensitivity and spectral resolution. In this context, we discuss different options for data processing that allow us to optimize these parameters.

The authors acknowledge Diamond Light Source for beamtime allocation at the MIRIAM beamline, B22, (proposal SM15664-1) and support, which contributed to the results presented here. Part of this research has also been performed using equipment purchased in frame of the project co-funded by the Malopolska Regional Operational Program Measure 5.1 Krakow Metropolitan Area as an important hub of the European Research Area for 2007-2013. Project No. 2014/15/B/ST4/04839.

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