ABSTRACT PRESENTATION 25.01.2019

[TITLE] IRONing the mitochondria: insights into iron metabolism and mitochondria

Overview of the PhD work done in collaboration with Oroboros, Instrument

Chiara Volani

OLD AFFILIATION
Department of Internal Medicine II (Infectious Diseases, Immunology, Rheumatology and Pneumology), Medical University of Innsbruck, Innsbruck, Austria.
** Collaboration with Oroboros Instruments, Innsbruck, Austria

NEW AFFILIATION
EURAC, Institute for Biomedicine, Bolzano/Bozen, Italy

Introduction Iron is an essential co-factor for several metabolic processes, including the Krebs cycle and mitochondrial respiration. Specifically, it supports the activity of mitochondrial I-IV complexes and regulates the Krebs cycle by modulating mitochondrial aconitase. In this way, iron influences the overall metabolism, reason why its homeostasis should be tightly regulated, as an imbalance can lead to insufficient energy production and reactive oxygen species (ROS) formation. For instance, patients suffering from iron overload disorders often complain of fatigue, suggesting an energetic deficit. Nevertheless, the underlying mechanisms affecting tissue mitochondrial activity and the systemic metabolism are poorly understood. **Aim** Therefore, the PhD work aimed to investigate the impact of iron imbalance on tissue mitochondrial respiratory capacity as well as on the systemic metabolism. **Results** Dietary iron loading caused a significant impairment in mitochondrial oxidative phosphorylation, possibly due to an increment in ROS production. Augmented oxidative stress was also found to be present in the periphery. In addition, metabolomics analysis revealed a metabolic re-programming involving glucose homeostasis. **Conclusion** Altogether, iron imbalance affected several central metabolic circuits. Hence, investigating mitochondrial and metabolic signatures of iron imbalances represents an important issue for monitoring the health of patients suffering both from anemia and iron overload.

Materials&Methods To investigate the effects of iron imbalance, mitochondrial function was studied by means of high resolution respirometry (OROBOROS Instruments) in liver samples from FVB and C57BL/6N mice (10 weeks old), receiving either normal (180 mg/kg) or high-iron (25 g/kg) diet two weeks before being sacrificed. Mitochondrial respiratory capacity was also assessed in peripheral blood mononuclear cells (PBMCs) in controls and patients showing lower iron stores. In addition, metabolic profiling was performed to assess the impact of iron imbalance on the systemic metabolism. Metabolomics was assessed in peripheral blood that was collected by means of volumetric absorptive microsampling (VAMS). Extracted blood metabolites were analyzed by liquid chromatography combined to high resolution mass spectrometry.