HA.36 - Microbial metabolites reduce α-synuclein aggregation in a *Saccharomyces cerevisiae* model

Edlene Ribeiro Prudêncio de Souza [1], Rosane Nora Castro[2], Marcos Dias Pereira[3], Cristiano Jorge Riger[1]
[1]Department of Biochemistry, [2]Department of Organic Chemistry, Federal Rural University of Rio de Janeiro (RJ, Brazil), [3]Department of Biochemistry, Federal University of Rio de Janeiro (RJ, Brazil)

Parkinson's disease (PD) is a progressive neurodegenerative disease associated mainly with aging. The current understanding of the pathophysiology of PD suggests a central role in the accumulation of the protein α-synuclein and several evidences have been directing that the initial site of this process would be the enteric nervous system. It is known that the intake of phenolic substances contributes to the redox balance of the organism, however its bioactivities are highly impacted by microbial biotransformation that occur in the intestinal lumen. The objective of this work was to evaluate the influence of phenolic compounds and probiotic microorganisms on the aggregation of α-synuclein protein expressed in the yeast *Saccharomyces cerevisiae*. A pre-inoculum was prepared in SC-GLU at 160rpm/30°C, and after 24 h of growth, cells were transferred to SC-GAL medium supplemented with caffeic acid phenethyl ester (CAPE) or mangiferin; CAPE and mangiferin fermented by probiotic blend; medium fermented by probiotic blend; and control with only SC-GAL. CAPE and mangiferin concentrations were 0.1 mM and cell suspensions were incubated at 160rpm/30°C for 35h. Yeast growth was kinetically monitored by measuring the OD600 and also submitted to fluorescence microscopy, spot plating and detection of metabolites by HPLC-Q-TOF-MS. Results showed that CAPE and mangiferin without fermentation did not inhibit protein aggregation, but fermentation was able to reduce this aggregation by about 50%. Inhibition of α-synuclein aggregation was correlated with the presence of fermented metabolites. The detection of 3-hydroxyphenylpropionic acid (3-HPPA), a microbial metabolite associated with the reduction of α-sin toxicity converges with recent theories that the microbiota influences the etiology of PD. Therefore, our studies suggest that interactions between the microbiome and certain dietary factors may support new therapeutic strategies to modulate the onset and/or progression of synucleinopathies.
Keywords: Parkinson's disease, phenolic compounds, probiotics. **Supported by:** FAPERJ, CNPq and CAPES

HA.37 - An integrated study of transcriptome, lipidome and proteome in search of new therapeutic targets for pathological angiogenesis

Lilian Cristina Costa Alecrim de Oliveira [1], Alex Inague[1], Jhonatas Sirino Monteiro[1], Marcos Yoshinaga[1], João Carlos Setubal[1], Sayuri Miyamoto[1], Ricardo José Giordano[1]
[1]Bioquímica, Instituto de Química - Universidade de São Paulo (SP, Brasil)

Angiogenesis, the formation of new blood vessels from pre-existing ones, is essential in physiology and pathology. Cancer and retinopathy are examples of diseases for which anti-angiogenic drugs are already available. Despite its success, we need to better understand the molecular mechanisms driving angiogenesis in order to develop a new generation of anti-angiogenesis drugs for these patients. Recently, using RNA-seq from an angiogenesis *in vivo* animal model (OIR, oxygen-induced retinopathy), our group has shown that differentially expressed genes in the retina of these animals could be used as a prognostic tool for a human angiogenesis dependent disease. We will expand these studies by characterizing the lipidome and proteome of mice retinas under pathological angiogenesis to integrate with the transcriptome data. Samples were collected at different postnatal days (P12, P12.5, P15, and P17) from mouse pups under pathological (OIR model from day 7 to day 12) and physiological development. Total lipid extracts were analyzed through non-targeted lipidomics by HPLC coupled to high-resolution mass spectrometry. For proteome, samples were collected in the same conditions and are being prepared for analysis. We identified and quantified 301 lipid species. PCA analysis revealed alterations in retinal lipidome mainly according to time, but also to the condition, physiological or pathological angiogenesis. The most significantly altered lipids in pathological angiogenesis correspond to storage lipids (CE and TAG) and membrane lipids (phospholipids). A preliminary integration of these results with transcriptome shows a cholesterol metabolism enzyme as a possible new marker for pathological angiogenesis. Lipidomic analysis suggests that pathological angiogenesis leads to intense remodeling of membrane and storage lipids. Proteomic analysis is ongoing and will provide, along with transcriptome and lipidome data, a better understanding of the different pathways associated with pathological angiogenesis.
Keywords: Angiogenesis, Retinopathy, Oxygen-Induced Retinopathy. **Supported by:** CAPES, FAPESP and CNPq