ABSTRACT

Fatty acid esters of hydroxy fatty acids (FAHFAs) are a recently discovered group of lipokines consisting of a fatty acid attached to a hydroxy fatty acid with an ester bond resulting in a diverse group of compounds with many different biological activities. Antidiabetic and anti-inflammatory activities are the most studied.

The thesis aimed to study this group of bioactive lipids to elucidate the metabolism of FAHFAs and describe the role of antioxidant defense, namely peroxiredoxin 6 (Prdx6), in their biosynthesis with the help of isotopic labeling together with in vitro and in vivo experiments. All the samples, including white adipose tissue, liver, and even human breast milk, were subjected to untargeted or targeted lipidomic and metabolomics analysis using LC-MS/MS.

We used the data from isotopically labeled experiments to describe the role of 5-PAHSA in glucose uptake and to show which specific pathways are stimulated by 5-PAHSA administration and which by insulin to compare the effect of both antidiabetic agents. In our samples, we analyzed TAG estolides, which function as intracellular reservoirs of FAHFAs, and managed to describe the role of specific lipases in their metabolism. We reported the role of Prdx6 and the specific enzymatic activity involved in synthesizing precursors that could be utilized for FAHFA biosynthesis. At last, we investigated if any changes in human breast milk metabolome of FAHFA levels were caused by timing, mode of delivery, or lactation stage.

The findings mentioned in this dissertation thesis provide insight into the metabolism of FAHFAs and TAG estolides and can be used in further research.

Key words: antioxidant defense, FAHFAs, lipokines, metabolic pathways, peroxiredoxin 6, TAG estolides, white adipose tissue