**Final Publishable Summary Report**

The consumption of fruit and vegetables as well as fish is associated with beneficial effects on human health. It is assumed that polyphenols and n3-polyunsaturated fatty acids (n3-PUFA) play a key role in this process. Several studies suggest an anti-inflammatory effect of polyphenols mediated by a modulation of the formation of endogenous signaling molecules. Oxylipins - oxidation products of fatty acids - represent one of the most potent classes of endogenous cellular mediators. The overall aim of the project was to investigate the effects of nutrition on endogenous oxylipin levels and their impact on the regulation of inflammation.

We have developed new instrumental analytical methods based on liquid chromatography mass spectrometry (LC-MS) for the quantification of oxylipins in biological samples. The developed techniques are superior to earlier described methods with respect to sensitivity and chromatographic resolution. The methods have been used successfully to characterize baseline levels of oxylipins in blood samples of human subjects on different diets as well as of animal models of colitis and sepsis. In these studies we only detected moderate changes in oxylipin levels during inflammation, but found out that an n3-PUFA-rich nutrition distinctly modulates the oxylipin pattern. Most significantly, that change directly correlated with the nutrition status of their precursor PUFA. With respect to polyphenols we focused on the investigation of effects on oxylipins formed by the enzyme cyclooxygenase-2 (COX-2). This enzyme is the target of common drugs such as aspirin or acetaminophen used for the treatment of pain and fever. For this purpose, a specific rapid method was developed allowing to omit laborious sample preparation. With this approach the COX products thromboxane B2, prostaglandin E2 and prostaglandin D2 were simultaneously quantified. By applying this method, the effects of selected polyphenols on COX-2 were investigated in three different *in vitro* test systems: (i) an enzyme assay, (ii) a cancer cell line, and (iii) lipopolysaccharide (LPS)-stimulated primary human monocytes (white blood cells). Finally, the *in vivo* relevance of the COX-2 activity modulation by polyphenols was investigated in murine sepsis (acute systemic inflammation, a major cause of death worldwide). The results of the experiments showed that despite a moderate *in vitro* activity the selected polyphenols were not able to reduce COX-2 activity *in vivo*. This discrepancy could be explained by a low bioavailability of polyphenols - demonstrated by evaluating their intestinal absorption in the Caco-2 cellular transwell system and their metabolic stability in microsomal incubations. Extrapolating from the animal model to humans, the results suggest that an effect of food polyphenols on COX-2 activity in acute inflammation is unlikely. The results of our project will assist in our understanding of a healthy diet: The limitation of the curative potential of polyphenols on the one hand and the massive effects of n3-PUFA on oxylipins on the other hand indicate that a major part of the beneficial health effects associated with these food ingredients is mediated via this pathway. This finding may help to improve the diet in Western countries.