**Publishable summary**

Chronic inflammatory diseases are rapidly developing in industrialized countries and it is hypothesized that this can in part be explained by changes in our diet. Major changes that occurred in recent years include the reduced intake of fibers and altered intake of omega 3 and 6 fatty acids. These are important changes as for example omega 6 fatty acids, which are nowadays much more abundantly present in our diet, are an important precursor for the formation of pro-inflammatory molecules. In contrast, the relative dietary intake of omega 3 fatty acids has been reduced, which is important because these serve as precursors for anti-inflammatory molecules. There is thus an important link between these dietary fatty acids and inflammation. Also dietary fibers are important in the context of inflammation, as they are converted by gut microbiota to fatty acids that mainly have anti-inflammatory properties. In this proposal we aimed to investigate if these fatty acids play a role in cigarette smoke-induced inflammation in chronic obstructive pulmonary disease (COPD). We have shown that cigarette smoke negatively affects airway epithelial cell differentiation and thereby the presence of antimicrobial molecules that are produced by the airway epithelium. Sodium butyrate, a fiber-derived fatty acid, could not prevent cigarette smoke-induced effects on airway epithelium differentiation. Butyrate did however improve the barrier function of the epithelium, reduce endoplasmic reticulum (ER) stress and reduce pro-inflammatory mediator production. We also investigated if and how butyrate affects monocyte-macrophage differentiation in the presence or not of cigarette smoke extract. Here we observed clear effects of butyrate on macrophage morphology and on cytokine production by macrophages. We also observed important effects of vitamin D, another lifestyle related factor, on airway epithelial cell function, showing an important role of epithelial inflammation on the anti-inflammatory and host defense-enhancing actions of vitamin D. This work was also part of an on-going project of a PhD-student in the laboratory of the Dept. of Pulmonology of the LUMC.

We furthermore investigated whether smoking - the main risk factor for the development of the chronic lung disease COPD - disrupted the absorption and conversion of omega 3 and -6 fatty acids. We examined whether there was a difference in the types of fatty acids present in the cell membranes of airway epithelial cells (e.g. saturated vs unsaturated), and investigated the conversion of these fatty acids in cells from patients with COPD compared to (ex) smokers with a normal lung function. We found only few differences between fatty acids in the membranes of COPD patients compared to healthy controls. Importantly, we did find that cigarette smoke inhibits the conversion of fatty acids to anti-inflammatory lipid mediators. This conversion was however not different between cells derived from COPD patients and those of controls. Furthermore, we have successfully measured the content of pro-inflammatory and anti-inflammatory lipid mediators in the sputum of COPD patients before, during and after an exacerbation, and we will compare this to those found in the sputum of healthy controls. These data will allow us to understand if lipid mediator production in the lungs is different between COPD patients and healthy controls, and reveal the differences in lipid mediator levels before and after an exacerbation.

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