INTRODUCTION

Low-grade systemic inflammation (LGSI) is a state of chronic sub-clinical inflammation, characterized by slightly but perpetually elevated levels of inflammatory markers in the blood[1]. Metabolic syndrome (MS) is a condition consisting of central obesity, dyslipidaemia, dysglycaemia, and hypertension; all of which are common risk factors for development of lifestyle diseases[2]. LGSI may be the mechanistic link between obesity and development of lifestyle diseases, such as type 2 diabetes. LGSI is usually assessed by measuring a number of circulating inflammatory markers, such as interleukin (IL)6, tumour necrosis factor (TNF)α, and C-reactive protein (CRP)[1]. Recently, the acute phase protein Pentraxin 3 (PTX3) has been identified as a novel marker for cardiovascular disease (CVD) severity and as PTX3 can be induced in many cell types as a result of circulating inflammatory markers, it may serve as a marker for LGSI as well. *Ex vivo* production of cytokines from stimulated whole blood, or isolated cell sub-populations, can be used as an indication of immune capacity[3], however, the clinical significance of this measure, as well as how it reflects circulating cytokine levels in the context of LGSI is virtually unanswered in the literature. LGSI can be detected concomitantly with several inflammatory conditions, including obesity, allergic asthma, inflammatory bowel disease, and rheumatoid arthritis[4]. The aetiology behind LGSI, in the context of obesity, is thought to be release of pro-inflammatory adipokines and cytokines from especially visceral adipose tissue; either directly from adipose cells or from infiltrating macrophages[5]. LGSI may be counteracted through life-style alterations, such as diet changes, manipulation of the gut microbiota, increased physical exercise, and/or reduction of emotional stress reduction[4]. Whole grain (WG) intake has been associated with reductions in both body-mass index (BMI)[6; 7; 8] and fat-percentage[9], and consumption of WG may therefore influence LGSI through an effect on visceral adiposity. Changes in gut microbiota composition has also been suggested to occur as a result of WG intake, as WGs contain high amounts of dietary fibres, which can serve as a significant source of sustenance for beneficial subpopulations of the gut microbiota[10]. Concurrently, provision of gut microbes with dietary fibres, enables fermentation of these and thus production of short-chain fatty acids, which can diffuse into the blood stream, where they can be bound by specific receptors on leukocytes, such as the free fatty acid receptor 2 (FFAR2)[11]. FFAR2 is highly expressed on both human neutrophils and monocytes, and both these cell

types have been shown to reduce their production of pro-inflammatory compounds as a result of short chain fatty acids[12].

In this thesis, I will evaluate the potential for PTX3 and *ex vivo* production of IL6, TNFα, and IL1β after stimulation of whole blood with lipopolysaccharide (LPS) to serve as markers for MS-associated LGSI. Finally, I will investigate if a diet rich WG can reduce LGSI, and thus the risk of developing life-style diseases, compared to a diet rich in refined grain (RG).