SUMMARY IN ENGLISH

Type 2 diabetes (T2D) incidence and prevalence rates are increasing worldwide, which imposes human, social and economic costs. While the risk of T2D is determined by interplay of genetic and metabolic disorders, overweight and obesity are the predominant risk factors. The treatment of obesity today is primarily lifestyle modification, including moderately energy-reduced diets, increased physical activity and often behavioural strategies to facilitate adherence to the lifestyle changes. But other strategies exist too, such as pharmacotherapy and surgery. The various strategies may be used in combination. An increased dietary protein intake has been recommended in the treatment of obesity mainly due to the high satiating effect of protein compared with other macronutrients. Results from intervention studies have shown that diets rich in protein may result in larger weight loss. However, unwanted effects of an increased protein intake on kidney function and putative colorectal cancer risk markers as well as insulin sensitivity have also been suggested. Still, the literature to date in this regard is contradictory.

The overall objective of this PhD thesis was to investigate the effect of an increased protein intake, including the role of animal and plant protein in pre-diabetic, overweight or obese individuals on health outcomes: markers of kidney function and putative risk factors for colorectal cancer as well as insulin sensitivity and kidney function in healthy individuals.

The thesis is based on PREVIEW data from three European population studies; NQplus, Lifelines and the Young Finns Study (paper I) as well as the large international RCT (paper II and paper III).

In paper I, the aim of the study was to develop a protein diet score, based on both dietary protein quantity and source i.e. plant or animal protein. The score was used to investigate the relation to T2D-related adverse metabolic health events. A total of 76,777 healthy individuals were included in the analysis. We found that a higher total protein diet score (higher intake of total protein and plant to animal protein ratio) was associated with a lower concentration of HbA1c and an increase in eGFR after adjustments for potential confounders in Lifelines. However, this relationship was neither observed in NQplus nor in the Young Finns Study. In conclusion, the results indicate a beneficial effect of a higher protein intake, especially plant protein, on insulin sensitivity and kidney function.
In **paper II**, the aim of the study was to assess the effect after one year of a higher protein intake on kidney function, measured by in creatinine clearance. This was investigated in pre-diabetic older adults based on a sub-group of 310 pre-diabetic individuals included in the PREVIEW RCT. We found that a higher protein intake was associated with a significant increase in urea to creatinine ratio and serum urea after one year. There were no associations between increased protein intake and creatinine clearance, estimated glomerular filtration rate, albumin to creatinine ratio or serum creatinine. In conclusion, there was no indication of impaired kidney function after one year on a higher protein intake in pre-diabetic older adults.

In **paper III**, the aims were to investigate the association between a protein diet score (developed in **paper I**) and putative colorectal cancer risk markers. In addition, we wanted to examine the relation between intake of protein from red and processed meat and effects on putative colorectal cancer risk markers. Analyses were based on 3-day faecal samples collected at baseline and after one year in a sub-group of 94 pre-diabetic individuals included in the PREVIEW RCT. In conclusion, we found no associations between a higher total protein intake or protein intake from red and processed meat on putative colorectal risk markers after one year of intervention.

In summary, our results indicate, that a higher protein score is associated with lower HbA1c values and an increased eGFR in healthy individuals, and provide evidence, that both quantity and source of proteins (plant and animal) are determining factors on the effects on HbA1c and eGFR (paper I). We found no evidence that a higher protein intake was associated with a decrease in kidney function after one year (paper II), and no indications that a higher protein intake as well as higher plant to animal protein ratio are associated with a change in putative colorectal cancer risk markers. In addition, we found no indication that red and processed meat causes detrimental changes on putative colorectal cancer risk markers (paper III) in pre-diabetic individuals after one year of intervention.