INTERACTIONS BETWEEN NUTRITION, OBESITY AND THE IMMUNE SYSTEM

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin vid Göteborgs Universitet kommer att försvaras offentligt i hörsal Arvid Carlsson, Academicum, Medicinaregatan 3, Göteborg, fredagen den 11 dec 2009, kl. 09:00.

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Avhandlingen baseras på följande delarbeten:

I Mice chronically fed high-fat diet have increased mortality and disturbed immune response in sepsis

II Septic mortality is lower in mice fed a diet rich in polyunsaturated compared with saturated fatty acids
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III Interleukin-1 system gene polymorphisms are associated with fat mass in young men
J Clin Endocrinol Metab 2006 Jul;91(7):2749-2754

IV IL6 and IL1B polymorphisms are associated with fat mass in older men: the MrOS Study Sweden
Obesity (Silver Spring) 2008 Mar;16(3):710-713
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ABSTRACT

There are several links between body fat and the immune system. For example, mice lacking activity of the pro-inflammatory interleukin-(IL)-1 and IL-6 develop obesity. Conversely, obesity is associated with adipose tissue inflammation and increased risk of infection. The aims of this thesis were to investigate (1) the effect of Western diet on Staphylococcus aureus (S. aureus)–induced mortality in mice; (2) if dietary fat composition affects mortality in S. aureus inoculated mice; and if IL-6 and IL-1 system gene polymorphisms, associated with expression, are associated with fat mass in (3) young and (4) elderly men.

The S. aureus-induced mortality was investigate in mice fed a lard-based high-fat diet (HFD) rich in saturated and monounsaturated fatty acids (HFD/S) or a low fat diet (LFD). After 8 weeks on these diets, the mice were intravenously inoculated with S. aureus. The obese HFD/S-fed mice had increased S. aureus-induced mortality compared with the lean LFD-fed mice. The HFD/S-fed mice showed signs of immune suppression as evident by increased bacterial load and decreased capacity to phagocytose bacteria. We then added a group of mice fed a HFD rich in polyunsaturated fatty acids (HFD/P) from fish. The HFD/P-fed mice displayed a degree obesity and glucose intolerance that was milder than in the HFD/S-fed mice, but higher than in LFD mice. However, the S. aureus-induced mortality and the bacterial load of HFD/P-fed mice were comparable with that of LFD-fed mice, and markedly lower than that of mice fed HFD/S.

Gene polymorphisms were investigated in two well-characterized population-based cohorts of young and elderly Swedish men. In young but not elderly men, we found that carriers of the T variant of the +3953 C>T IL1B polymorphism had lower total fat mass, compared with CC carriers. In elderly but not young men, the IL1B -31T>C polymorphism was associated with total fat mass. In young but not elderly men, we found that IL-1RN*2 carriers, with two repeats of the IL1RN 86 base pair variable number tandem repeat polymorphism, had increased total fat mass. Also, IL1RN*2 was associated with increased IL-1Ra production in vitro and enhanced serum IL-1Ra in vivo. We also confirmed earlier findings that the C variant of the -174G>C IL6 is associated with obesity in elderly men.

Thus, the present results indicate the S. aureus-induced mortality is associated with dietary fat consisting of saturated and monounsaturated fatty acids, but not polyunsaturated fatty acids. We also show that polymorphisms in the IL1B, IL1RN, and IL6 genes are associated with obesity. In conclusion, this thesis emphasize that there are reciprocal interactions between the immune system on one hand and obesity and nutrition on the other.

Keywords: obesity, nutrition, infection, polymorphisms, interleukin, fatty acids, fat mass, neutrophils, innate immunity, mortality