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Impaired immune function in an animal model for cancer cachexia

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In general it is assumed that 50% of all patients with cancer have significant weight loss before treatment and many of them suffer from cachexia[1,2]. Malnutrition and inflammation occurring during cachexia directly affects the immune system. Thus, patients with cachexia have a higher susceptibility towards infections, which significantly influences survival [3].

Several preclinical studies show the cachectic features of the colon-26 tumour model in mice in which the pro-inflammatory cytokines IL-6 and TNFα are denoted as pivotal mediators[4]. In contrast, fewer studies have investigated the effects of cachexia and nutrition on immune function. The present study aims to develop a model to study nutritional effects on immune function in mice with cachexia.

Murine colon adenocarcinoma (C26) cells were inoculated in syngenic CD2F1 mice to induce cachexia. Body weight, skeletal-muscle weight and weight of adipose tissue were measured to assess the cachectic status of the mice. To investigate effects on the immune system contact hypersensitivity against oxazolone was determined, as an *in vivo* model for cellular (T-helper (Th) 1 dependent) immunity. In addition, plasma cytokines, concanavalin A (ConA)-induced splenocyte proliferation and cytokine production, and lipo-polysaccharide (LPS)-induced cytokine production in whole blood were measured.

Tumour inoculation resulted in a significant impairment of body weight and wasting of skeletal muscles and adipose tissue. In addition, pro-cachectic cytokines IL-6 and TNFα in plasma demonstrated a substantial increase, whereas the anti-cachectic cytokine IL-4 was significant lower in the tumour-bearing mice. Contact hypersensitivity showed a significant decrease in tumour-bearing animals, reflecting a reduced Th1 immune response.

Furthermore, proliferation capacity, but also Th1 and Th2 cytokine production after ConA stimulation by splenocytes demonstrated a significant reduction compared with the control group. Lower capacity of immune cells in whole blood to react on LPS was reflected in a decreased production of both IL-1β and TNFα in the tumour-bearing group while IL-6 remained unchanged.

Present findings demonstrate an impaired immune function in tumour-bearing mice suffering from cachexia. Thus, it is a useful model to study potential effects of nutritional interventions on immune function in cancer cachexia.

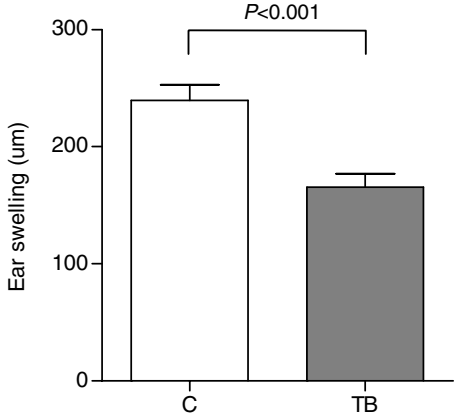

Fig. 1. Effect of tumour inoculation on contact hypersensitivity in a mouse model for cancer cachexia. Values are means (μm) with their standard errors represented by vertical bars for control (C) group ($n=10$) and tumour-bearing (TB) group ($n=20$).

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