

Effect of dietary omega-3 fatty acids on tumor-associated macrophages and prostate cancer progression

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Background. Preclinical and clinical studies suggest that a fish oil-based diet may play a role in delaying the progression of prostate cancer through a number of different mechanisms involving inflammatory pathways. Given the importance of tumor-associated macrophages (TAMs) in carcinogenesis, we hypothesized that a fish oil-based diet will inhibit TAM infiltration and delay the growth of prostate cancer.

Methods. Two mouse studies were performed growing androgen sensitive mouse prostate cancer (MycCaP) allograft tumors in fully immunocompetent FVB mice fed a high-fat fish oil (omega-3) or corn oil (omega-6) diet. In exp. 1 gene expression of markers for immune cell populations, cytokines, chemokines and signaling pathways were determined by real-time PCR and western blot in tumor tissue. In exp. 2 immune cells were enumerated in tumor tissue using flow cytometry.

Results. Tumor weight and volumes were significantly smaller in mice in ω -3 vs the ω -6 group in both experiments ($p=0.005$; $p=0.048$). In tumor tissue TAMs primarily had M2 characteristics. The number of M2 macrophages was decreased and M1 macrophages increased significantly in tumor tissue from mice fed the ω -3 diet compared to the ω -6 diet. In tumor tissue gene expression of markers for total macrophages and M2 macrophages (F4/80, ARG1), associated cytokines (IL-6, TNF alpha, IL-10) and the chemokine CCL-2 were lower in the ω -3 group compared to the ω -6 group. Feeding the ω -3 diet reduced protein expression of transcription factors in the nuclear factor kappa B pathway.

Conclusions. These findings underscore the potential of fish oil in modulating the clinical course of human prostate cancer through the immune system. Further preclinical and clinical studies are warranted evaluating fish oil-based therapies for inhibiting the recruitment and function of M1 and M2 tumor infiltrating macrophages.

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