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Effects of 'high' fat diet on intestinal carcinogenesis, cell proliferation and apoptosis in ApcMin/+ mice

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The risk of colorectal cancer, the commonest cancer of the alimentary tract, is increased by obesity, but may be modified by dietary fatty acid composition[1]. We investigated the effects of 'high' fat diets with different fatty acids on tumour development, cell proliferation and apoptosis in the $APC^{min/+}$ mouse model of intestinal cancer[2].

Sixteen $APC^{min/+}$ mice and 16 wild-type mice were allocated to either a fish oil, palm oil or corn oil diet (25% energy as fat – normal rodent diet is 12.5% energy as fat) for 10 weeks from weaning. The diet also contained levels of antioxidant vitamins and selenium which were considered adequate but not optimal so as to better emulate the human diet. After sacrifice the small intestines (SI) and large intestines were removed for analysis of tumour number and size. Also, intestinal biopsies were taken from the distal small intestine, for morphological analyses of crypt cell proliferation and apoptosis.

No tumours were found in the wild-type mice and fish oil tended to decrease mitosis and increase apoptosis in a similar pattern to that described previously[3]. In $APC^{min/+}$ mice, the total tumour numbers were higher in the proximal SI in mice fed fish oil (204) compared to corn oil (170), $P = 0.01$ and in the mid SI the number of tumours was higher with fish oil (431) than with the palm oil (431 *v.* 378, $P = 0.03$). On the other hand, total tumour area was approx. 30% lower in the distal SI in mice fed fish oil compared to those fed corn oil or palm oil ($P < 0.05$). The $APC^{min/+}$ mice fed the corn oil diet had a significantly higher level of apoptosis (4.2 ± 3.3 apoptotic cells/crypt) compared to either fish oil (2.8 ± 3.0) or palm oil diets (1.5 ± 1.9), $P = 0.03$. The corn oil diet was also associated with significantly higher numbers of mitotic cells/crypt compared to either fish or palm oil ($P = 0.01$) so that the ratio of apoptosis: mitosis was not affected by diet ($P = 0.09$; CO>PO).

In conclusion, fish oil fed post weaning, when pre-neoplastic lesion are already present, does not suppress the number of tumours in this model but does reduce tumour size, thus even at this early stage in life fish oil does not appear to suppress initiation but instead inhibits progression. The results suggest that the protective effects of fish oil reported in the literature in relation to reduction in tumour development post-initiation involves mechanisms other than cell proliferation and apoptosis, possibly angiogenesis[4].

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