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Peroxisome Proliferator Activated Receptor- α (PPAR- α) may regulate tumour formation in APC^{Min/+} mice

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Background: Peroxisome proliferator-activated receptor-alpha (PPAR-alpha) is expressed at low levels in colon tumours. APC^{Min/+} mice fed with methylclofenapate (a PPAR-alpha ligand) have significantly less polyp area in the small intestine and colon¹. It is not certain that this response is PPAR-alpha specific. We investigated the hypothesis that PPAR-alpha activation in the colon can prevent colon cancer. Before studying the effect of pharmacological PPAR α ligand methylclofenapate on colon carcinogenesis, we examined the role of PPAR-alpha in colon carcinogenesis using APC^{Min/+} PPAR-alpha^{-/-} mice.

Aim: To establish if PPAR-alpha has a tumour suppressive function in APC(Min)/+ mice.

Method: Once weaned C57BL/6J APC^{Min/+} mice and C57BL/6J APC^{Min/+} PPAR- α ^{-/-} mice were fed standard chow (Rat & mouse standard diet, BEEKAY, Humberside) throughout the study. Mice were weighed weekly and until mice showed signs of anaemia or lost >20% of weight at which time they were sacrificed by cervical dislocation. The primary endpoints to be compared in both groups were number, location of tumours.

Result: APC^{Min/+} PPAR- α ^{-/-} mice have significantly greater number of tumours in the colon. They also have more tumours in the small intestine. The mean number of polyps in the colon was 2.43 (SE 0.31) in APC^{Min/+} PPAR- α ^{-/-} mice and 0.75 (0.25) in APC^{Min/+} (Min) p<0001. In the small intestine the mean numbers of tumours were 18.00 (2.26) and 15.92 (1.7) respectively (p=ns).

Conclusions: PPAR- α has a role in the formation of tumours in APC^{Min/+} mice.