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Aspirin induces activation of NF κ B signalling and apoptosis in rectal cancer patients

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Introduction: Aspirin protects against colorectal cancer (CRC), but the molecular mechanism of action is unclear. We have previously shown that aspirin induces apoptosis in CRC cells *in vitro* via NF κ B signalling. The aim here was to investigate whether aspirin modulates NF κ B signalling *in vivo*, in tumour biopsies from CRC patients.

Methods: Rectal cancer patients (n=6) were given aspirin (600mg QDS) for 1 week and biopsies taken before and after treatment. I κ B α phosphorylation and degradation, and NF κ B nuclear translocation were analysed in normal mucosa and tumour extracts by immunoblotting. Apoptosis was assessed by counting apoptotic bodies. To study the kinetics of the response, patients (n=9) were given aspirin (75mg OD, 600mg OD, 600mg QDS) and biopsies taken at 2 hrs, 4hrs 24 hrs and 7 days. All studies had ethical approval.

Results: Aspirin (600mg QDS) induced I κ B α phosphorylation, degradation, and NF κ B nuclear translocation in rectal tumours and normal mucosa. Furthermore, this response was associated with the induction of apoptosis. Studies on the kinetics of the response show that aspirin induces a time-dependent increase in I κ B α phosphorylation and nuclear NF κ B within 4 hours in 5 of 9 patients on low-dose aspirin (75 and 600mg OD).

Conclusion: This is the first study to examine the *in vivo* effects of aspirin on NF κ B signalling in patients. The results show that aspirin induces I κ B α phosphorylation and degradation, NF κ B nuclear translocation and induces apoptosis in CRC patients. This work indicates that the previously identified *in vitro* mechanism of action does translate into NF κ B modulation in patients.