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N-ACETYL TRANSFERASE ACTIVITY (NAT) IN NORMAL AND NEOPLASTIC HUMAN COLON

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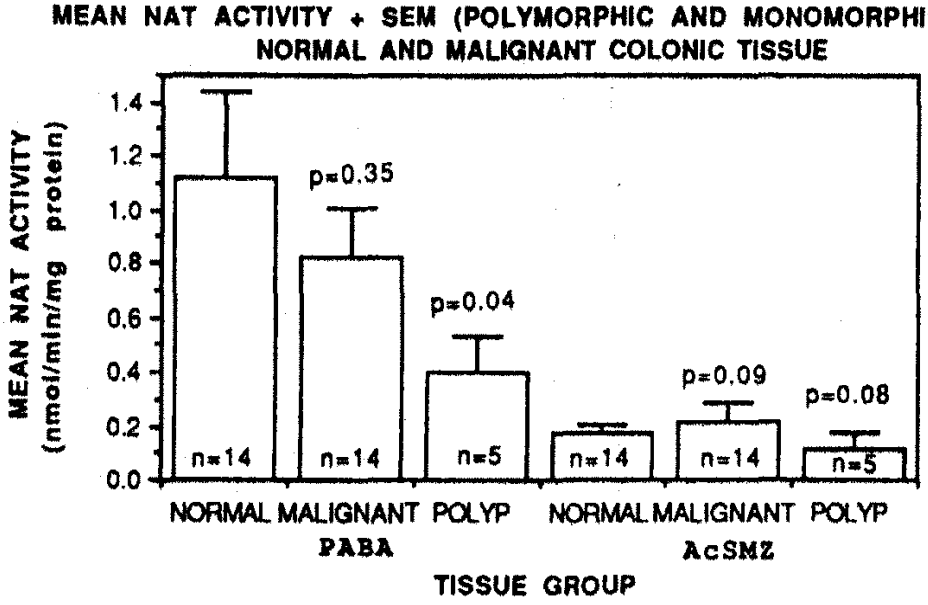
Heterocyclic arylamines have been identified in cooked fish and meat products and in pyrolsates of proteins and amino acids. These xenobiotic (foreign) compounds can be activated by acetyltransferases to intermediates that may act as proximate carcinogens. N-Acetyl T ransferase catalyses the acetyl CoA-dependent acetylation of arylamines. Different isoenzymes of NAT have varying specificities for particular arylamines. One NAT is influenced by genetic polymorphism for fast and slow rates of acetylation, and is present in greatest activity in the liver; a monomorphic form accounts for most extra-hepatic activity. Individuals classified as fast acetylators by virtue of hepatic acetylation of test drugs have been shown to be predisposed to colorectal cancer. However, it is unclear to what extent colonic NAT activities may influence local carcinogen activation. In this study, we compared polymorphic and monomorphic NAT activity in normal, adenomatous, and malignant colorectal tissues. Specimens were obtained from patients (17 male and 8 female, aged 50-75 years) by endoscopic biopsy or surgical resection. Mucosal tissue was homogenised, centrifuged (20,000g for 20 minutes) and assayed for polymorphic and monomorphic activity by high performance liquid chromatography utilising the rates of substrate acetylation for sulphamethazine (AcSMZ)and para-aminobenzoic acid (PABA), respectively.



Results were expressed as nmol/min/mg protein (mean±SEM). Polymorphic NAT activity was not significantly different (P>0.10) between normal mucosa (0.177±0.03; n=14), adenomas (polyp) (0.115±0.06; n=5), or carcinomas (0.211±0.078; n=14) . Monomorphic NAT activity was significantly different (P<0.05) between normal mucosa (1.124±0.318; n=14) and adenomas (0.400±0.138; n=5) but not when compared to carcinomas (0.825±0.186; n=14). Monomorphic NAT activity was significantly higher (5-fold; P<0.001) than polymorphic NAT activity in all specimens. We conclude that there is no difference in NAT activity between normal and malignant colorectal tissues for the polymorphic or monomorphic forms of the enzyme however preliminary data suggests that there may be a difference in monomorphic activity in adenomas. Substantially greater target tissue activity for monomorphic NAT brings into question the relative importance of effects of genetic polymorphism versus environmental factors (transit time, pH, redox state) in the local activation of potential colonic carcinogens.

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