

complementary to DNA. It is interesting to note that of the two A10 hydrolysis products, the known natural product phenylacetylglutamine (2) does not fit into the DNA as well as phenylacetylisoglutamine, which to date has not been detected in humans. Future studies of the antineoplastic activity of this compound appear warranted.

As has been observed previously (5), portions of the A10 molecule are related in structure to two experimental anticancer agents, PCNU and 5-cinnamoyl-6-aminouracil. Using this methodology, both agents could be accommodated within the helix; 5-cinnamoyl-6-aminouracil had been shown previously to interact with DNA *in vitro* (12). Neither of these experimental agents, however, appeared to fit as well as A10.

It is important to note that the fit of A10 into DNA involves stereospecific, albeit weak, interactions with the double helix. If A10 bound to DNA in this manner, there would be no undue strain on the DNA and the complexes formed should be easily reversible. Because A10 does not possess chemically reactive moieties (e.g., epoxides), in contrast to many known intercalating carcinogens, covalent linkages of A10 with DNA would be unlikely. Indeed, Lehner *et al.* (3) demonstrated that A10 does not form covalent linkages even upon heating with DNA *in vitro*. Thus it is predicted that A10 would have low toxicity and few untoward side-effects, as is the case with other molecules with such properties.

In conclusion, the ability of A10 to insert into DNA and to form stereospecific hydrogen bonds led to the authors' prediction that A10 may: (i) interact with DNA in a rapidly reversible manner; (ii) compete with certain carcinogens which covalently bind to DNA and cause mutations; and (iii) prevent tumour formation (1). The present findings confirm that A10 can fit into DNA with some sequence preference. Muldoon *et al.* (14) further demonstrate that A10 can delay appearance of spontaneous mammary tumours in mice infected with the mammary tumour virus.

References

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