

SYMPOSIA SERIES No. 42

BIOCHEMISTRY OF THE CELL NUCLEUS

Edited by **P. B. Garland** and **A. P. Mathias**
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The articles of this Symposium deal with aspects of the structure and function of the cell nucleus, at several levels of molecular and biological organization. Although much is already known of the way in which the genetic information of eukaryotic cells is stored, replicated, transcribed and processed, the scale and intricacy of the operation is immense in comparison with the simpler and more amenable bacterial systems. Accordingly our knowledge of the more highly evolved eukaryotic systems is far from complete, both in concept and detail. The articles not only review present knowledge; no less importantly they identify areas where mystery is more obvious than mechanism, and they pose some of the central questions that future research will have to answer.

Biochemistry of the Cell Nucleus will be timely reading for those in life or medical sciences who, either by their teaching or research, or just general intellectual curiosity, desire to deepen their understanding of how the nucleus masterminds the incredibly complex but beautifully co-ordinated activities of the cell.

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Multiplicity of Animal Cell Deoxyribonucleic Acid Polymerases by **G. Brun & F. Chapeville.**

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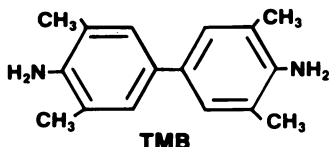
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Tetramethylbenzidine

A reported noncarcinogenic analog of benzidine



For many years benzidine has been used as a sensitive and specific reagent for the detection of blood.¹ However, its extreme carcinogenicity has curtailed its use in recent years. In fact, in 1974, the Occupational Safety and Health Administration banned its manufacture and use in the United States.²

Several chemical transformations are thought to be responsible for the carcinogenicity of aromatic amines. An early hypothesis involved possible *ortho*-hydroxylation.³ Later views suggested that *N*-oxidation is important. Since *o*-tolidine (3,3'-dimethylbenzidine) retains the sensitivity in the detection of blood, it seemed likely that 3,3',5,5'-tetramethylbenzidine (TMB) (in which *ortho*-hydroxylation is impossible) might also be an effective but *safe* substitute for benzidine.⁴ Indeed, it was found that subcutaneous injection of TMB into rats "produced no tumors specifically attributable to it, in doses greater than those in which benzidine or *o*-tolidine cause a high yield of neoplasms."⁴

The simple *Salmonella*/microsome microbial test (Ames test)⁵ for the detection of mutagenic activity showed TMB to be nonmutagenic.^{6,7} Results of these studies suggest that TMB is also noncarcinogenic.

Garner *et al.*⁸ have recently evaluated the use of TMB as a presumptive test for blood in forensic work. As might be expected from its structural similarity to benzidine, TMB, in various concentrations of glacial acetic acid, reacted with blood in the presence of hydrogen peroxide to form a colored product. Comparative studies with benzidine showed TMB to be equally sensitive in the detection of blood.

The specificity of TMB and its tendency to give a false positive reaction with substances known to in-

terfere with the benzidine test for blood were examined using various vegetables and applying several methods of testing.⁸ The results indicate that TMB is as specific as benzidine. Also, TMB and benzidine reacted similarly to chemical oxidants and catalysts before addition of hydrogen peroxide.⁸

Pinkus and Goldman have also studied the utility of TMB as a presumptive blood-test reagent.⁹

Since benzidine in solution is well known to lose its sensitivity with storage, the effects of time, light and heat on TMB solutions were studied.⁸ Results indicate that the stability of TMB is the same as that of benzidine.

The only significant difference observed between TMB and benzidine was in their solubilities in glacial acetic acid. The concentration of a saturated solution of TMB approaches 0.2M, while that for benzidine ranges between 0.7 and 1.0M.

Thus, the sensitivity, specificity, stability and apparent noncarcinogenicity of TMB are very important criteria in determining the usefulness of TMB as a substitute for benzidine in the detection of blood.

The use of TMB as the chromogenic reducing agent in a sensitive and accurate assay for plasma hemoglobin has been reported.¹⁰

References:

- 1) B.J. Culliford and L.C. Nickolls, *J. Forensic Sci.*, **9**, 175 (1974).
- 2) (a) Occupational Safety and Health Administration (OSHA), *Federal Register*, **39**, 3779 (1974). (b) Department of Labor, Code of Federal Regulations (CFR), OSHA, Title 29, Section 1910.1010 (annual publication).
- 3) E.C. Miller, J.A. Miller, and H.A. Hartmann, *Cancer Res.*, **21**, 815 (1961).
- 4) V.R. Holland, B.C. Saunders, F.L. Rose, and A.L. Walpole, *Tetrahedron*, **30**, 3299 (1974).
- 5) B.N. Ames, W.E. Durston, E. Yamasaki, and F.D. Lee, *Proc. Nat. Acad. Sci. U.S.A.*, **70**, 2281 (1973).
- 6) R.C. Garner, A.L. Walpole, and F.L. Rose, *Cancer Lett.*, **1**, 39 (1975).
- 7) J. McCann, E. Choi, E. Yamasaki, and B.N. Ames, *Proc. Nat. Acad. Sci. U.S.A.*, **72**, 5135 (1975); J. McCann and B.N. Ames, *ibid.*, **73**, 950 (1976).
- 8) D.D. Garner, K.M. Cano, R.S. Peimer, and T.E. Yeshion, *J. Forensic Sci.*, **21**, 816 (1976).
- 9) J.L. Pinkus and L.S. Goldman, *J. Chem. Educ.*, **54**, 380 (1977).
- 10) J.C. Standefer and D. Vanderjagt, *Clin. Chem.*, **23**, 749 (1977).

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