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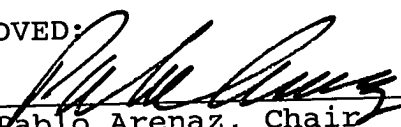
PREVIEW


ACTIVATION OF SODIUM AZIDE IN MAMMALIAN CELLS


LANCE M. HALLBERG

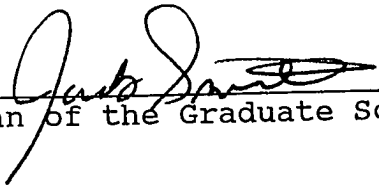
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DEDICATION

During the last four years, my life has dramatically changed. I wish to dedicate this work to the people that made this paper possible.

I want to thank my sons Michael, Sean, and Andrew who were patient with me on those Saturdays when I had work to complete my experiments and who gave me a great amount of joy in the rough times. To Julie, though we have changed and grown apart, I am sorry for all I have put you through and still love you. Thank you for putting up with me. I love you all very much.

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and became my friends and family, I love you. To Jesus, who changed my life and gave me the courage to carry on and to whom I run when ever the going gets tough.

ACTIVATION OF SODIUM AZIDE IN MAMMALIAN CELLS

by

LANCE M. HALLBERG, BS

THESIS

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ABSTRACT

Sodium azide has been prevalent in the environment for decades. The high mutagenicity of azide in both plants and bacteria is well documented. Sodium azide mutagenesis is mediated through a metabolic intermediate in bacteria and plants. However, very little is known about the interaction of this intermediate with nucleic acids, its genotoxic potential, or its mechanism of action, especially in mammalian cells. Research on the effects of azide and its putative mutagenic intermediate, on mammalian cells, has yielded conflicting results. Sodium azide appears to be non to weakly mutagenic in mammalian cells. Consequently, cell free extracts from Chinese hamster cells were analyzed for the presence of O-acetylserine(thio)-lyase, which is capable of converting azide to its putative mutagenic intermediate. Chinese Hamster cells demonstrated O-acetylserine(thio)-lyase activity comparable to that found in Salmonella extracts. Chinese hamster cells or their cell free extracts, were treated with azide and tested for mutagenicity using the plate incorporation assay. Neither Chinese Hamster cells nor cell extracts treated with sodium azide were able to induce a mutagenic response. In addition, incubation of calf thymus DNA with azidoalanine did not induce DNA repair as

measured by unscheduled DNA synthesis, nor did azidoalanine inhibit the activity of DNA polymerase. However, analysis of this DNA, by HPLC, revealed the presence of a suspected DNA adduct, which is as yet unconfirmed. Although mammalian cells possess the enzyme activity purportedly responsible for the conversion of azide to azidoalanine, the putative mutagenic intermediate, they appear incapable of converting azide into a mutagenic metabolite. These data suggest that azide may be modified in mammalian cells to a non mutagenic byproduct or may produce damage which is unique and undetectable to the repair mechanism of the cell.

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