ACTIVATION OF SODIUM AZIDE IN MAMMALIAN CELLS

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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.

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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 proportedly 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.

TABLE OF CONTENTS

Acknowledgements v

Abstract vi

List of Tables ix

List of Figures x

Introduction 1
- Sodium Azide 1
- Bacteria 1
- Plants 2
- Mammalian Cells 3
- Mutagenic Intermediate 5

Materials and Methods 10
- Cell Lines 10
- Cell Free Extract 10
  - Barley Extracts 10
  - Salmonella Extracts 11
  - Chinese Hamster Cells 11
- Assay for O-acetylserine(thio)-lyase 12
- Mutagenicity Assay 12
- Unscheduled DNA Synthesis 13
- Inhibition DNA Polymerase 14
- Chemosynthesis of Azidoalanine 15
- Biosynthesis of Putative Mutagenic Metabolite . . 17
- Detection of a DNA Adduct by HPLC 17

Results 19
- Detection of O-acetylserine(thio)-lyase 19
- Mutagenicity of Crude V-79 Cell Extracts 21
- Unscheduled DNA Synthesis Induced by Azidoalanine 21
- Inhibition of DNA Polymerase by Azidoalanine . . . 26
- Detection of a DNA Adduct Induced by Azidoalanine or Sodium Azide 26

Discussion 33

Bibliography 39

Curriculum Vitae 43

LIST OF TABLES

Table I O-acetylserine(thio)-lyase Activity 20

Table II. Induction of Unscheduled DNA Synthesis . . . 27

LIST OF FIGURES

Figure 1 Mutagenicity of Cell Extracts 22

Figure 2 Mutagenicity of Chemically Synthesized Azidoalanine. Salmonella 24

Figure 3 Inhibition of Polymerase by Azidoalanine . . 29

Figure 4 Elution Times of Standard Bases and Calf Thymus DNA incubated with Azidoalanine . . . 31