

## CURRICULUM VITAE

Name: Herbert T. Nagasawa

Place of Birth: Hilo, Hawaii

### Education:

B.S.	1950	Western Reserve University, Cleveland, OH Major: Chemistry Minor: Mathematics Honors: Phi Society (Honorary Scholastic)
Ph.D.	1955	University of Minnesota, Minneapolis, MN Major: Organic Chemistry Minor: Analytical Inorganic and Physical Chemistry Honors: Phi Lambda Upsilon (Chemistry Scholastic)
Post-Doctoral Fellow	1955- 1957	Department of Biochemistry, University of Minnesota, Minneapolis, MN Honors: Sigma Xi (Scientific Research)

### Military Service:

1945 - 1947 Military Intelligence Service, U.S. Army

### Positions Held:

1951 - 1954	Teaching Assistant, Department of Chemistry, University of Minnesota, Minneapolis, MN
1954 - 1955	Pre-doctoral Fellow, Allied Chemical & Dye Corp., Department of Chemistry, University of Minnesota, Minneapolis, MN
1955 - 1957	Post-doctoral Fellow, Department of Biochemistry, University of Minnesota, Minneapolis, MN
1957-1961	Senior Chemist, Radioisotope Service Research Laboratory, Veterans Administration Medical Center, Minneapolis, MN
1961-1978	Senior Scientist, Laboratory for Cancer Research, Veterans Administration Medical Center, Minneapolis, MN
1961 - 1976	Principal Scientist, General Medical Research, Veterans Administration Medical Center, Minneapolis, MN
1961 - 1981	Member and Basic Science Representative, Research and Education Committee, Veterans Administration Medical Center, Minneapolis, MN
1978 - 2002	Senior Research Career Scientist, Veterans Administration Medical Center, Minneapolis, MN
2002 - 2004	Senior Medical Research Scientist, Veterans Administration Medical Center, Minneapolis, MN

1959 - 1963	Assistant Professor, Pharmaceutical Chemistry, University of Minnesota, Minneapolis, MN
1963 - 1972	Associate Professor, Medicinal Chemistry, University of Minnesota, Minneapolis, MN
1973 - 2004	Professor, Medicinal Chemistry, University of Minnesota, Minneapolis, MN (Officially retired 6/04)
1987 - 1995	Professor, Pharmacology, University of Minnesota, Minneapolis, MN
1990 - 2004	Professor, Toxicology, University of Minnesota, Duluth, MN (Officially retired 6/04)
2004-2007	Member, Center for Drug Design, Academic Health Center, University of Minnesota
2007-to date	Adjunct Professor, Center for Drug Design, Academic Health Center, University of Minnesota
1972 - 1984	Associate Editor, <u>Journal of Medicinal Chemistry</u> , American Chemical Society (Acting Editor: 8/73 to 6/74)
1985 - 2004	Senior Editor, <u>Journal of Medicinal Chemistry</u> , American Chemical Society (Retired 6/04)
1974 - 1977	Member, Health Sciences Policy and Review Council, University of Minnesota Graduate School, Minneapolis, MN
1976 - 1978	Chairperson, Biomedical Research Committee, Alcohol and Other Drug Abuse Program (AODAP), University of Minnesota, Minneapolis, MN
1983 - 1984	AODAP Biomedical Grants Review Committee, University of Minnesota, Minneapolis, MN
1980 - 1981	Ad Hoc Member, Initial Review Group (IRG), Biomedical Research Review Committee, Alcohol, Drug Abuse and Mental Health Administration (ADAMHA)
1984 - 1985	Member, Special Review Committee, "National Cooperative Drug Discovery Group (NCDDG)", National Cancer Institute, National Institutes of Health (NIH)
1985	Judge, Third Annual Graduate Student Awards, Mechanisms Section, Society of Toxicology
1990	Visiting Professor, College of Pharmacy, Washington State University, Pullman, WA (March 24-31)
1990 - 1997	Editorial Board, <u>Bioconjugate Chemistry</u> , American Chemical Society

Professional Societies:

American Academy of Anti-Aging Medicine (A<sup>4</sup>M)  
 American Chemical Society (ACS)  
 American Society for Pharmacology and Experimental Therapeutics (ASPET)  
 American Association for Cancer Research (AACR)  
 American Association for the Advancement of Science (AAAS)

International Society for Biomedical Research on Alcoholism (ISBRA)  
International Society for the Study of Xenobiotics (ISSX)  
New York Academy of Sciences (NYAS): Elected as Fellow, 1983  
Research Society on Alcoholism (RSA)  
Society of Toxicology (SOT)  
Nitric Oxide Society  
Listed: American Men and Women of Science; Who's Who in the Midwest

Graduate Faculty Appointment:

Medicinal Chemistry: B Appointment (Full Member)  
Pharmacology: A Appointment (Associate Member)  
Toxicology: B Appointment (Full Member)

Research Interests: Design and synthesis of a) trapping agents for the detoxification of xenobiotic substances that are activated to toxic metabolites in vivo, b) latentiated (prodrug) forms of biologically active substances such as nitroxyl (HNO), c) prodrugs of cysteine and glutathione as protective agents for cellular oxidative stress, and d) cyanide antidotes based on  $\beta$ -mercaptopyruvate.

## Publications

Nagasawa, H. T. Ph.D. Thesis, Studies in Polypeptide Synthesis: Some Polyglycyl Derivatives of Desoxyephedrine. University of Minnesota **1955**.

Nagasawa, H. T.; Gutmann, H. R. On the Acylation of the Carcinogen, 2-Aminofluorene, by Rat Liver *In Vitro*. *Biochim. Biophys. Acta* **1957**, *24*, 631-632.

Nagasawa, H. T.; Gutmann, H. R. A Note on the Deacylation of the Carcinogen, 2-Acetamidofluorene and Related Compounds by Rat Liver and Intestine. *Biochim. Biophys. Acta* **1957**, *25*, 186-189.

Gutmann, H. R.; Burtle, J. G.; Nagasawa, H. T. Protein Binding of Model Quinone Imides. I. The Synthesis of Some Fluorenoquinone Imides. *J. Am. Chem. Soc.* **1958**, *80*, 5551-5555.

Nagasawa, H. T.; Morgan, M. A.; Gutmann, H. R. The Enzymatic Oxidation of *o*-Aminophenols. *Biochim. Biophys. Acta* **1958**, *28*, 665-666.

Nagasawa, H. T.; Gutmann, H. R. Preparation and Properties of S-Acetyl-N-benzoylcysteamine. *J. Org. Chem.* **1958**, *23*, 487.

Nagasawa, H. T.; Gutmann, H. R. The Oxidation of *o*-Aminophenols by Cytochrome *c* and Cytochrome Oxidase. I. Enzymatic Oxidations and Binding of Oxidation Products to Bovine Serum Albumin. *J. Biol. Chem.* **1959**, *234*, 1593-1599.

Nagasawa, H. T.; Gutmann, H. R. The Oxidation of *o*-Aminophenols by Cytochrome *c* and Cytochrome Oxidase. III. 2,3-Fluorenoquinone from 2-Amino-3-fluoreneol and Binding of Quinonoid Oxidation Products to Bovine Serum Albumin. *J. Biol. Chem.* **1960**, *235*, 3466-3471.

Alexander, C. S.; Nagasawa, H. T.; Filbin, D. Distribution and Excretion of Aminonucleoside-8-C<sup>14</sup> in Normal and Nephrotic Rats. *Proc. Soc. Exp. Biol. Med.* **1962**, *111*, 521-526.

Alexander, C. S.; Hunt, V. R.; Nagasawa, H. T. Dose-Response Relationship in Aminonucleoside Nephrosis. *Proc. Soc. Exp. Biol. Med.* **1963**, *112*, 506-510.

Alexander, C. S.; Nagasawa, H. T. Aminonucleoside of Puromycin: Elimination of Nephrotoxicity by Acetylation of the Aminoribose Moiety. *Biochem. Pharmacol.* **1964**, *13*, 548-551.

Nagasawa, H. T.; Osteras, A. J. The Biological Arylation of Proteins *In Vitro* by a Metabolite of the Carcinogen, N-2-Fluorenylacetylamide. *Biochem. Pharmacol.* **1964**, *13*, 713-723.

Dickie, N.; Alexander, C. S.; Nagasawa, H. T. Inhibition of Nucleic Acid Synthesis in Escherichia coli B by Puromycin Aminonucleoside. *Biochim. Biophys.* **1965**, *95*, 156-169.

Derr, R. F.; Alexander, C. S.; Nagasawa, H. T. An Interaction Between Aminopurines, Aminopyrimidines and Fluorescent Thin-Layer Plates. *J. Chromatogr.* **1966**, *21*, 146-147.

Dickie, N.; Norton, L. F.; Derr, R. F.; Alexander, C. S.; Nagasawa, H. T. The Effect of Puromycin Aminonucleoside on the Incorporation of Labeled Precursors into Rat Kidney RNA. *Biochim. Biophys.* **1966**, *129*, 288-293.

Dickie, N.; Norton, L. F.; Derr, R. F.; Alexander, C. S.; Nagasawa, H. T. The Inhibition of Adenosine Deaminase by a Metabolite of the Nephrotoxic Drug, Puromycin Aminonucleoside. *Proc. Soc. Exp. Biol. Med.* **1966**, *123*, 421-423.

Nagasawa, H. T.; Gutmann, H. R. Ortho-methoxy Derivatives of the Carcinogen, N-2-Fluorenylacetamide: Latent Biological Arylating Agents. *J. Med. Chem.* **1966**, *9*, 719-725.

Nagasawa, H. T.; Elberling, J. A. Synthesis of Ring Homologs of Proline by the Favorskii Rearrangement of  $\alpha$ -Halolactams. *Tetrahedron Lett.* **1966**, *44*, 5393-5399.

Alexander, C. S.; Swingle, K. F.; Nagasawa, H. T. Tetratogenic Effect of Puromycin Aminonucleoside on Rat Kidney. *Nephron* **1966**, *3*, 344-351.

Nagasawa, H. T.; Swingle, K. F.; Alexander, C. S. Metabolism of Aminonucleoside-8-C<sup>14</sup> in the Rat and Guinea Pig. *Biochem. Pharmacol.* **1967**, *16*, 2211-2219.

Derr, R. F.; Alexander, C. S.; Nagasawa, H. T. The Metabolism of Puromycin Aminonucleoside in the Normal, "Pre-nephrotic" and Nephrotic Rat. *Proc. Soc. Exp. Biol. Med.* **1967**, *125*, 248-252.

Nagasawa, H. T.; Alexander, C. S.; Swingle, K. F. Inhibition of Aminonucleoside Nephrosis in Rats. The Lack of Effect of Hepatic Drug Metabolizing Enzyme Inhibitors and Stimulators on Nephrotoxicity. *Toxicol. Appl.* **1967**, *11*, 336-345.

Derr, R. F.; Loechler, D. K.; Alexander, C. S.; Nagasawa, H. T. Inhibition of Rat Liver Microsomal N-Demethylase by  $\alpha$ -Naphthylisothiocyanate: Studies with Puromycin Aminonucleoside. *Proc. Soc. Exp. Biol. Med.* **1967**, *126*, 844-845.

Derr, R. F.; Loechler, D. K.; Alexander, C. S.; Nagasawa, H. T. Metabolism of Aminonucleoside-8-C<sup>14</sup> in the Mouse. The Relationship Between Metabolism and Experimental Nephrosis. *Biochem. Pharmacol.* **1968**, *17*, 265-268.

Derr, R. F.; Loechler, D. K.; Alexander, C. S.; Nagasawa, H. T. Inhibition of Aminonucleoside Nephrosis in Rats. IV. Prevention of N<sup>6</sup>-Methyladenosine. *J. Lab. Clin. Med.* **1968**, *72*, 363-369.

Nagasawa, H. T.; Fraser, P. S.; Elberling, J. A. Chromatographic Properties of Some Cyclic  $\beta$ -Imino Acids Homologous to Proline, and their DNP-, DNS- AND PTH-derivatives. *J. Chromatogr.* **1969**, *44*, 300-306.

Nagasawa, H. T.; Alexander, C. S.; Shirota, F. N.; Ghobrial, H.; Swingle, K. F.; Derr, R. F. Metabolic Basis for the Lack of Nephrotoxicity of Acetylated Puromycin Aminonucleoside in Rats. *Toxicol. Appl. Pharmacol.* **1970**, *16*, 1-9.

Derr, R. F.; Aaker, A.; Alexander, C. S.; Nagasawa, H. T. Synergism Between Cobalt and Ethanol on Rat Growth Rate. *J. Nutr.* **1970**, *100*, 521-524.

Nagasawa, H. T.; Elberling, J. A.; Fraser, P. S.; Mizuno, N. S. Medium Ring Homologs of Proline as Potential Amino Acid Antimetabolites. *J. Med. Chem.* **1971**, *14*, 501-508.

Nagasawa, H. T.; Shirota, F. N.; Alexander, C. S. Identification and Synthesis of the Major Nucleoside Metabolite in Rabbit Urine After Administration of Puromycin Aminonucleoside. *J. Med. Chem.* **1972**, *15*, 177-181.

Nagasawa, H. T.; Fraser, P. S.; Elberling, J. A. N-Phenyl-2-thio-1,2-azetidene-carboximide, the Phenylthioglydantoin of Azetidene-2-carboxylic Acid. *J. Org. Chem.* **1972**, *37*, 516-519.

Nagasawa, H. T.; Shirota, F. N.; Matsumoto, H. Decomposition of Methylazoxylmethanol, the Agycone of Cycasin, in D<sub>2</sub>O. *Nature* **1972**, *236*, 234-235.

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Nagasawa, H. T.; Kohlhof, J. G.; Fraser, P. S.; Mikhail, A. A. Synthesis of 1-Hydroxy-L-proline and Related Cyclic N-Hydroxyamino Acids. Metabolic Disposition of <sup>14</sup>C-Labeled 1-Hydroxy-L-proline in Rodents. *J. Med. Chem.* **1972**, *15*, 483-486.

Nagasawa, H. T.; Thompson, J. A. Reactions of Interest in Medicinal Chemistry. In *Annual Reports in Medicinal Chemistry*, Chapter 25, Vol. 7; Heinzelman, R., Ed.; Academic Press: New York, NY, **1972**, pp. 269-279.

Nagasawa, H. T.; Fraser, P. S.; Yuzon, D. L. A New Method for Nitrosation of Proline and Related Secondary- $\beta$ -Amino Acids to N-Nitrosamine with Possible Oncogenic Activity. *J. Med. Chem.* **1973**, *16*, 583-585.

Nagasawa, H. T.; Elberling, J. A.; Shiota, F. N. 2-Aminoadamantane-2-carboxylic Acid, A Rigid, Achiral, Tricyclic  $\alpha$ -Amino Acid with Transport Inhibitor Properties. *J. Med. Chem.* **1973**, *16*, 823-826.

Forsyth, G. W.; Nagasawa, H. T.; Alexander, C. S. Acetaldehyde Metabolism by the Rat Heart. *Proc. Soc. Exp. Biol. Med.* **1973**, *144*, 498-500.

Nagasawa, H. T.; Fullerton, D. S. Reactions of Interest in Medicinal Chemistry. In *Annual Reports in Medicinal Chemistry*, Chapter 31, Vol. 8; Heinzelman, R., Ed.; Academic Press: New York, NY, **1973**, pp. 303-312.

Nagasawa, H. T.; Shiota, F. N.; Mizuno, N. S. The Mechanisms of Alkylation of DNA by 5-(3-Methyl-1-triazeno)imidazole-4-carboxamide (MIC), a Metabolite of DIC (NSC-45388). Non-involvement of Diazomethane. *Chem. Biol. Interact.* **1974**, *8*, 403-413.

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Shiota, F. N.; Nagasawa, H. T. Synthesis of Ethambutol-<sup>14</sup>C Dihydrochloride [(+)-N,N'-bis(1-Hydroxy-2-butyl)ethylene-U-<sup>14</sup>C-diamine Dihydrochloride]. *J. Labelled Compd.* **1975**, *11*, 457-459.

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Nagasawa, H. T.; Goon, D. J. W.; Constantino, N. V.; Alexander, C. S. Diversion of Ethanol Metabolism by Sulfhydryl Amino Acids. D-Penicillamine-directed Excretion of 2,5,5-Trimethyl-D-thiazolidine-4-carboxylic Acid in the Urine of Rats after Ethanol Administration. *Life Sci.* **1975**, *17*, 707-713.

Nagasawa, H. T.; Kuo, T. H.; Shiota, F. N.; Alexander, C. S. An Intestinal Arylamidase that Selectively Hydrolyzes Certain Aromatic Amides. *Biochem. Pharmacol.* **1976**, *25*, 855-858.

Jenne, J. W.; Nagasawa, H. T.; Thompson, R. D. The Relationship of Urine Metabolites of Theophylline to Serum Theophylline Levels. *Clin. Pharmacol. Ther.* **1976**, *19*, 375-381.

Vince, R.; Almquist, R. G.; Ritter, C. L.; Shiota, F. N.; Nagasawa, H. T. An Active Puromycin Analog Derived from a Non-nephrotoxic Aminonucleoside. *Life Sci.* **1976**, *18*, 345-350.

Forsyth, G. W.; Nagasawa, H. T.; Alexander, C. S. Ethanol Metabolism by the Rat Heart and Alcohol Dehydrogenase Activity. *Can. J. Biochem.* **1976**, *54*, 539-545.

Alexander, C. S.; Forsyth, G. W.; Nagasawa, H. T.; Kohloff, J. G. Alcoholic Cardiomyopathy in Mice. Myocardial Glycogen, Lipids and Certain Enzymes. *J. Mol. Cell. Cardiol.* **1977**, *9*, 235-245.

Alexander, C. S.; Sekhri, K. K.; Nagasawa, H. T. Alcoholic Cardiomyopathy in Mice. Electron Microscopic Observations. *J. Mol. Cell. Cardiol.* **1977**, *9*, 247-254.

Nagasawa, H. T.; Goon, D. J. W.; DeMaster, E. G.; Alexander, C. S. Lowering of Ethanol-Derived Circulating Blood Acetaldehyde in Rats by D-Penicillamine. *Life Sci.* **1977**, *20*, 187-194.

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Shiota, F. N.; Nagasawa, H. T.; Elberling, J. A. Potential Inhibitors of Collagen Biosynthesis. 4,4-Difluoro-L-proline and 4,4-Dimethyl-DL-proline and Their Activation by Prolyl-t-RNA Ligase. *J. Med. Chem.* **1977**, *20*, 1176-1181.

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Shiota, F. N.; Nagasawa, H. T.; Elberling, J. A. Potential Inhibitors of Collagen Biosynthesis. 5,5-Difluorolysine and 5,5-Dimethyllysine and Their Activation by Lysyl-t-RNA Ligase. *J. Med. Chem.* **1977**, *20*, 1623-1627.

Nagasawa, H. T.; Muldoon, W. P.; Shiota, F. N. Nitramino Acids. Synthesis and Biological Evaluation of 1-Nitroproline, 1-Nitropipecolic Acid and N-nitrosarcosine. *J. Med. Chem.* **1977**, *20*, 1588-1591.

Nagasawa, H. T.; Alexander, C. S.; Goon, D. J. W.; DeMaster, E. G. Lowering of Blood Acetaldehyde Levels as a Therapeutic Approach to Alcoholism. In *Alcohol and Aldehyde Metabolizing Systems*, Vol. III; Thurman, R. G., Williamson, J. R., Pratt, H., Chance, B., Eds.; Academic Press: New York, NY, **1978**, pp 529-536.

Alexander, C. S.; Nagasawa, H. T.; DeMaster, E. G. Lowering of Blood Acetaldehyde Levels--A Possible Approach to Prevention of Alcoholic Cardiomyopathy. In *Recent Advances in Studies on Cardiac Structures and Metabolism*, Vol. 12, Cardiac



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DeMaster, E. G.; Nagasawa, H. T. Isoprene, an Endogenous Constituent of Human Alveolar Air with a Diurnal Pattern of Excretion. *Life Sci.* **1978**, *22*, 91-98.

DeMaster, E. G.; Nagasawa, H. T. Inhibition of Aldehyde Dehydrogenase by Propionaldehyde, a Possible Metabolite of Pargyline. *Res. Commun. Chem. Pathol. Pharmacol.* **1978**, *21*, 497-505.

Nagasawa, H. T.; Goon, D. J. W.; DeMaster, E. G. 2, 5,5-Trimethylthiazolidine-4-carboxylic Acid, a D(-)-Penicillamine-directed Pseudometabolite of Ethanol. Detoxication Mechanism for Acetaldehyde. *J. Med. Chem.* **1978**, *21*, 1274-1279.

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