

## CURRICULUM VITAE

Nom : Herbert T. Nagasawa

Lieu de naissance : Hilo, Hawaii

### Éducation :

B.S.	1950	Western Reserve University, Cleveland, OH Majeure : Chimie Mineure : Mathématiques Distinctions : Phi Society (Scolastique honoraire)
Ph.D.	1955	University of Minnesota, Minneapolis, MN Majeure : Chimie Organique Mineure : Spécialités en Chimie analytique inorganique et en Physique : Phi Lambda Upsilon (Scolastique en chimie)
Post-doctorat Boursier	1955- 1957	Département de biochimie, University of Minnesota, Minneapolis, MN Distinctions : Sigma Xi (Recherche scientifique)

### Service militaire :

1945 à 1947      Service d'intelligence militaire, United States Army

### Postes occupés :

1951 à 1954	Assistant à l'enseignement, Département de la chimie, University of Minnesota, Minneapolis, MN
1954 à 1955	Boursier de doctorat, Allied Chemical & Dye Corp., Département de chimie, University of Minnesota, Minneapolis, MN
1955 à 1957	Boursier de doctorat, Département de biochimie, Université of Minnesota, Minneapolis, MN
1957 à 1961	Chimiste principal, Laboratoire de recherche en service de radio-isotopes, Veterans Administration Medical Center, Minneapolis, MN
1961 à 1978	Chercheur principal, Laboratoire pour la recherche sur le cancer, Veterans Administration Medical Center, Minneapolis, MN
1961 à 1976	Chercheur principal, Recherche médicale générale, Veterans Administration Medical Center, Minneapolis, MN
1961 à 1981	Membre et représentant en science de base, comité de recherche et éducation, Veterans Administration Medical Center, Minneapolis, MN
1978 à 2002	Chercheur de carrière principal, Veterans Administration Medical Center, Minneapolis, MN
2002 à 2004	Chercheur médical principal, Veterans Administration Medical Center, Minneapolis, MN

1959 à 1963	Chargé de cours senior, Chimie pharmaceutique, University of Minnesota, Minneapolis, MN
1963 à 1972	Professeur agrégé, Chimie médicale, University of Minnesota, Minneapolis, MN
1973 à 2004	Professeur, Chimie médicale, University of Minnesota, Minneapolis, MN (Officiellement retraité 6/04)
1987 à 1995	Professeur, Pharmacologie, University of Minnesota, Minneapolis, MN
1990 à 2004	Professeur, Toxicologie, University of Minnesota, Duluth, MN (Officiellement retraité 6/04)
2004 à -2007	Membre, Center for Drug Design (Centre de conception de médicaments), Academic Health Center, University of Minnesota
2007 à aujourd'hui	Professeur auxiliaire, Center for Drug Design (Centre de conception de médicaments), Academic Health Center, University of Minnesota
1972 à 1984	Corédacteur, <u>Journal of Medicinal Chemistry</u> , American Chemical Society (Rédacteur intérimaire : 8/73 à 6/74)
1985 à 2004	Rédacteur principal, <u>Journal of Medicinal Chemistry</u> , American Chemical Society (Retraité 6/04)
1974 à 1977	Membre, Health Sciences and Review Council (Conseil de politiques et de révision des sciences de la santé), University of Minnesota Graduate School, Minneapolis, MN
1976 à 1978	Membre du conseil d'administration, comité de recherche biomédicale, Alcohol and Other Drug Abuse Program (Programme en matière d'abus et autres drogues [AODAP]), University of Minnesota, Minneapolis, MN
1983 à 1984	Comité de révision de l'AODAP pour subventions biomédicales, University of Minnesota, Minneapolis, MN
1980 à 1981	Membre ad hoc, Initial Review Group (Groupe de révision initiale [IRG]), Comité de révision de recherche biomédicale, Alcohol, Drug Abuse and Mental Health Administration (Administration en matière d'abus d'alcool, de drogue et de santé mentale [ADAMHA])
1984 à 1985	Membre, Comité de révision spécial, « National Cooperative Drug Discovery Group (NCDDG) », National Cancer Institute, National Institutes of Health (NIH)
1985	Juge, Troisième concours annuel d'attribution de bourses pour études supérieures, Mechanisms Sections, Society of Toxicology
1990	Professeur invité, College of Pharmacy (École de pharmacie), Washington State University, Pullman, WA (24 au 31 mars)
1990 à 1997	Comité de rédaction, <u>Bioconjugate Chemistry</u> , American Chemical Society

#### Organismes professionnels :

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)

Société internationale de recherches biomédicales sur l'alcoolisme  
International Society for the Study of Xenobiotics (ISSX)  
New York Academy of Sciences (NYAS) : Élu en tant que boursier, 1983  
Research Society on Alcoholism (RSA)  
Society of Toxicology (Société de toxicologie [SOT])  
Nitric Oxide Society (Société Oxide Citrique)  
Nommé dans : Hommes et femmes Américains de sciences; les personnes importantes dans le Midwest

Nomination à la faculté d'études supérieures :

Chimie médicale : Nomination B (Membre à part entière)  
Pharmacologie : Nomination A (Membre associé)  
Toxicologie : Nomination B (Membre à part entière)

Intérêts de recherche : Conception et synthèse de a) agents de piégeage pour la détoxification des substances xénobiotiques activées en métabolites toxiques *in vivo*, b) formes latentes (promédicaments) de substances biologiquement actives telles que l'acide nitrique (HNO), c) promédicaments de la cystéine et le glutathion en tant qu'agents de protection contre le stress de l'oxydation cellulaire, et d) antidotes de cyanure basés sur  $\beta$ -mercaptopyruvate.

## Publications

Nagasawa, H. T. Ph.D. Thèse, Études en synthèse de polypeptide : 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.; Osteraas, 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- $C^{14}$  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- $C^{14}$  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  $\alpha$ -Amino 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-azetidine-carboximide, the Phenylthioglydantoin of Azetidine-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- $\alpha$ -Amino Acids to N-Nitrosamine with Possible Oncogenic Activity. *J. Med. Chem.* **1973**, *16*, 583-585.

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

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Nagasawa, H. T.; Elberling, J. A.; Shirota, F. N. Potential Latentiation Forms of Biologically-Active Compounds Based on Action of Leucine Aminopeptidase. Dipeptide Derivatives of the Tricycloaliphatic -Amino Acid, Adamantanine. *J. Med. Chem.* **1975**, *18*, 826-830.

Shirota, 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.

Jenne, J. W.; Nagasawa, H. T.; McHugh, R.; MacDonald, F.; Wyse, E. Decreased Theophylline Half-life in Cigarette Smokers. *Life Sci.* **1975**, *17*, 195-198.

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.; Shirota, 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.

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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.

Goon, D. J. W.; Nagasawa, H. T. A Simple, Rapid and Semi-Automated Method for the Determination of Expired <sup>14</sup>CO<sub>2</sub> in Metabolism Studies with Laboratory Animals. *Res. Commun. Chem. Pathol. Pharmacol.* **1977**, *16*, 745-748.

Shirota, 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.

DeMaster, E. G.; Nagasawa, H. T. Disulfiram-induced Acetonemia in the Rat and Man. *Res. Commun. Chem. Pathol. Pharmacol.* **1977**, *18*, 361-364.

Shirota, 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.; Shirota, 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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Nagasawa, H. T.; Elberling, J. A.; DeMaster, E. G. Structural Requirements for the Sequestration of Metabolically-generated Acetaldehyde. *J. Med. Chem.* **1980**, *23*, 140-143.

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Nagasawa, H. T.; Elberling, J. A.; Shirota, F. N. Latentiated Forms of the Transport Inhibitory -Amino Acid, Adamantanine. *J. Pharm. Sci.* **1980**, *69*, 1022-1025.

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Zera, R. T.; Nagasawa, H. T. N-Acetyl-DL-penicillamine and Acetaminophen Toxicity in Mice. *J. Pharm. Sci.* **1980**, *69*, 1005-1006.

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