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**Boyd E. Haley, Ph.D.**  
**Curriculum Vitae**

## CURRICULUM VITAE

**BOYD E. HALEY, Ph.D.** Born 22-09-40 Greensburg, Indiana

ADDRESS: Advanced Science Technology Commercialization Center, ASTeCC  
Room A057  
University of Kentucky  
Lexington, KY 40506-0286  
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### EDUCATION:

| <u>Institution</u>             | <u>Year</u> | <u>Degree/Area</u>           |
|--------------------------------|-------------|------------------------------|
| Franklin College               | 1963        | B.A./Chemistry-Physics       |
| University of Idaho            | 1967        | M.S./Organic Chemistry       |
| Washington State University    | 1971        | Ph.D./Chemistry-Biochemistry |
| Yale University Medical Center | 1971-74     | Postdoctoral Fellow          |

### RESEARCH AND PROFESSIONAL EXPERIENCE:

|              |  |
|--------------|--|
| 1963-1964    | Research Scholar, Food and Drug Administration.  |
| 1964-1966    | U.S. Army Medic  |
| 1966-1967    | Graduate Student, University of Idaho  |
| 1967-1971    | Graduate Student, Washington State University  |
| 1971-1974    | Postdoctoral Scholar, Yale University  |
| 1974-1979    | Assistant Professor, Department of Biochemistry, University of Wyoming, Laramie, W   |
| 1979-1981    | Associate Professor, Department of Biochemistry, University of Wyoming, Laramie, W   |
| 1981-1985    | Professor, Department of Biochemistry, University of Wyoming, Laramie, WY  |
| 1985-1997    | Professor of Medicinal Chemistry, College of Pharmacy, University of Kentucky, with joint appointments in Biochemistry & Chemistry |
| 1997-present | Chairman & Professor, Department of Chemistry with joint appointment in College of Pharmacy  |

### PROFESSIONAL ORGANIZATIONS, SOCIETIES, HONORS AND RESPONSIBILITIES

|      |  |
|------|--|
| 1959 | President's Scholarship, Franklin College, Indiana   |
| 1962 | Chi Beta Phi, Franklin College   |
| 1962 | James M. Sprague Award - \$400 award to outstanding undergraduate junior majoring in science.              |
| 1963 | Kennedy Scholar, Food and Drug Administration, Washington, D.C.  |
| 1970 | Sigma Xi   |
| 1975 | Dreyfus Foundation Visiting Researcher, Enzyme Institute University of Wisconsin                           |
| 1977 | American Society of Biological Chemists  |
| 1981 | Biophysical Society  |
| 1981 | Served on NIH Physiological Chemistry Study Section  |
| 1981 | Research was presented as a "highlight" in NIH report on "Cellular and Molecular Basis of Disease Program" |
| 1984 | "TOP" Professor Award, University of Wyoming   |
| 1982 | Served on NIH Physiological Chemistry Study Section  |
| 1983 | Served on NIH Physiological Chemistry Study Section  |
| 1985 | Permanent member NIH Biomedical Sciences, Study Section  |
| 1991 | Honorary Doctorate in Arts & Sciences, Franklin College  |
| 1992 | Society for Neuroscience   |

## GRANT SUPPORT

- 1975 - 1978 National Institutes of Health, "Application of Photoaffinity Nucleotide Analogs", \$82,000, Principal Investigator
- 1975 Research Coordination Committee, University of Wyoming \$1,800
- 1978 - 1981 National Institutes of Health, "Application of Photoaffinity Nucleotide Analogs", \$183,696, Principal Investigator
- 1978 - 1981 Eleanor Roosevelt Cancer Institute Grant, \$11,400
- 1979 - 1983 PHS Research Career Development Award, \$185,000
- 1981 - 1986 National Institutes of Health, "Application of Photoaffinity Nucleotide Analogs", \$434,000, Principal Investigator
- 1982 ASBC Travel Award to attend 12th IVB Congress, Perth, Australia
- 1983 - 1984 National Science Foundation, "Melatonin Photoaffinity Probe", \$84,000, Co-Principal Investigator
- 1983 - 1985 National Institutes of Health, "Epididymal Sperm Nucleotide Binding proteins", \$190,000, Co-Principal Investigator
- 1985 - 1988 U.S. Army Mycotoxin Photoprobes, \$390,000, Co-Principal Investigator
- 1986 - 1989 NIH, "Forskolin Photoaffinity Probes", \$170,000, Co-Principal Investigator
- 1986 - 1991 NIH, "Application of Photoaffinity Nucleotide Analogs" \$781,661, Principal Investigator
- 1989 - 1994 NIH, "Nucleotide-Tubulin Interactions in Alzheimer's Disease", \$405,259, Co-Principal Investigator
- 1990 - 1996 Lexington Clinic Foundation For Medical Education and Research, "Inhibition of Neoplastic C Proliferation Through Utilization of Photoactive DNA & RNA Synthesis, \$100,000, P.I.
- 1990 - 1993 Eli Lilly, "Development of a Diagnostic Test for Alzheimer's Disease, \$378,000, P.I.
- 1995 - 1997 Wallace Research Foundation, "Development of Diagnostic Tests Using Nucleotide Photoaffinity Probes". \$109,000 for two years.
- 1997-1998 Wallace Research Foundation, "Development of Diagnostic Tests Using Nucleotide Photoaffinity Probes". \$74,344.
- 1997-2000 NIH, "Application of Photoaffinity Nucleotide Analogs", \$378,081, P.I.
- 1997-1998 Isosent, Inc. "Photoattachment of <sup>32</sup>P to angioplastic ballon catheters" \$52,000.
- Pending NIH, "Identification of CSF proteins Related to ALS"  
NIH, "Photomodification of Antibodies for Diagnostic and Therapeutic Applications".

## TEACHING EXPERIENCE

Introductory Comparative Biochemistry  
General Biochemistry  
Problems and Topics in Biochemistry  
Mercury Toxicity: Chemistry and Biochemistry Involved  
Advanced Problems and Topics in Biochemistry  
Nucleic Acids and Protein Biosynthesis  
Nucleotides in Regulation of Biological Phenomena  
Bioenergetics  
Medicinal Chemistry  
Natural Products and Bio-organics  
Graduate level Biochemistry, Protein Chemistry

## INVITED LECTURES:

1975 - Sloan Kettering Memorial Cancer Institute, New York  
thru Colorado State University (3)  
1979 Albert Einstein University, New York  
Hoffman-LaRoche Research Institute, Nutley, New Jersey  
University of Colorado Medical School Denver (3)  
University of Colorado, Boulder (2)  
Yale University Medical School (2)  
The Salk Institute, San Diego  
University of California, Davis  
Stanford University Medical School  
University of California, San Diego  
University of Washington, Seattle  
Washington State University  
Kansas State University  
1979 Symposium Speaker, ASBC Meeting, Dallas, Texas  
1979 Symposium Speaker, New York Academy of Sciences Meeting, New York  
Department of Molecular Biology, National Jewish Hospital, Denver  
University of California, Riverside  
Workshop Speaker, ICN-UCLA Conference on Adenylyl Cyclase  
1982 Symposium Speaker, 1982 FASEB Meeting, New Orleans  
1982 Guest Lecturer and Scientist, German Cancer Research Center,  
Institute of Cell and Tumor Biology, Heidelberg, West Germany,  
May  
1982 Centre National De La Recherche Scientifique, Laboratoire  
D'Enzymologie, Gif Sur Yvette, France, June  
1982 Workshop Speaker, ASBC Meeting in New Orleans (Photoprobe  
utilization, sponsored by Schwarz-Mann)  
1982 Symposium Speaker, Society for the Study of Reproduction, Madison  
Wisconsin, August  
1982 Department of Biochemistry, University of Wisconsin, November  
1982 Department of Chemistry, New Mexico State University, November  
1982 Department of Chemistry, University of Colorado, December  
1983 Institute of Infectious Diseases, U.S. Army Medical Research  
Institute, Ft. Detrick, Michigan, January  
1983 Department of Biochemistry and Biophysics, Oregon State University  
1983 Department of Biochemistry, Texas Health Science Center, San Antonio, TX  
1983 Department of Biochemistry, University of Mississippi Medical Center  
1984 Department of Biochemistry, University of Kentucky, Lexington, KY  
1985 Department of Physiology and Biophysics, Northwestern University  
Medical School, Chicago, Illinois  
1985 Department of Chemistry, University of Southern California, Los  
Angeles, California

1985 Department of Physiology, University of Illinois at Chicago,  
Chicago, Illinois

1985 Department of Biochemistry, Ohio State University, Columbus, Ohio

1985 Department of Physiology, Yale University Medical School, New  
Haven, Connecticut

1986 Department of Biochemistry, Case Western University, School of  
Medicine, Cleveland, Ohio

1986 Department of Biochemistry, Indiana University, School of Medicine, Indianapolis, Indiana

1986 Department of Biochemistry, Washington University, School of  
Medicine, St. Louis, Missouri

1987 Division Fermentation Products Research Division, Eli Lilly  
Research Laboratories, Indianapolis, Indiana

1987 Department of Chemistry, University of South Florida, Tampa, Florida

1987 Department of Molecular Biology and Biochemistry, University of  
Wyoming, Laramie, Wyoming

1988 Worcester Foundation, Shrewsbury, Massachusetts

1988 Department of Biochemistry, University of Colorado, Denver, Colorado

1988 Department of Biochemistry, University of Delaware, Newark, Delaware

1989 University of California at San Diego

1989 University of California at Los Angeles

1989 Texas College of Osteopathic Medicine, Fort Worth, Texas

1990 Wright State University, Dayton, Ohio

1990 Athena Neurosciences, S. San Francisco, California

1990 Eli Lilly & Co., Indianapolis, Indiana

1990 Connaught Laboratories, Toronto, Canada

1990 University of East Carolina Medical School, Greenville, North Carolina

1990 Hoffman-LaRoche Research Center, Nutley, New Jersey

1991 Eli Lilly & Co., Indianapolis, Indiana

1991 City University of New York, New York, New York

1991 University of Cincinnati, Cincinnati, Ohio

1991 University of Colorado, Boulder, Colorado

1991 University of Missouri at Kansas, Kansas City, Missouri

1992 Williams College at Williamsburg, Massachusetts

1992 Centre College at Danville, Kentucky

1992 University of Colorado, Boulder, Colorado

1992 Eli Lilly & Co., Indianapolis, Indiana

1992 Merck Laboratories, West Point, Pennsylvania

1993 NIH Rocky Mountain Laboratory, Hamilton, MT

1993 Intern. Acad. Oral & Medical Toxicology, Chicago, IL

1993 Univ. Tenn. at Memphis, Memphis, TN

1993 Penn State University, College Station, PN

1993 University California, Riverside, Riverside, CA

1993 Mayo Clinic, Jacksonville, FL

1993 Washington University, St. Louis, MO

1993 University of Arkansas, Little Rock, AR

1994 European Academy of Science, Otzenhausen, Germany

1994 Intern. Acad. Oral & Medical Toxicology, London, England.

1994 Great Lakes College for Advancement of Medicine, Cincinnati, OH

1995 American College for the Advancement of Medicine, Colorado Springs, CO.

1995 Pfizer Pharmaceuticals, Groton, CN

1995 Ohio State University, Dept., Chemistry, Columbus, OH

1996 Intern. Acad. Oral & Medical Toxicology, Tuscon, AZ

1996 University of Wyoming, Laramie WY

1996 American College for the Advancement of Medicine, Colorado Springs, CO.

1997 American Academy Biological Dentistry, Carmel, CA March 7-9.

1997 International Academy of Oral and Medical Toxicology, Louisville, KY March 14-16

1997 Washington State University, Dept. of Chemistry and Biophysics, Pullman, WA, March 27-30.

1997 American Society of Biochemistry and Molecular Biology, Symposium talk, August 24-28.

1997 Canadian Academy Oral and Medical Toxicology, Toronto, Canada. September 19-21.

1997 Capital University of Integrative Medicine, Washington, DC, October 16-18

1997  
1997

American Academy Environmental Medicine, San Diego, CA, October 24-26.  
University of Missouri at Kansas City, Dept. Biology & Biophysics, November 20-22.

SERVICE TO DEPARTMENT, COLLEGE AND UNIVERSITY:

1975-1979 Faculty Senate  
Biological Interdepartmental Seminar Committee  
University Grievance Procedure Committee  
College of Agriculture Teaching Improvement Committee  
College of Agriculture Academic Planning Committee  
Faculty Senate Nominating Committee  
Division of Biochemistry Undergraduate Teaching Committee  
Division of Biochemistry Graduate Program Committee  
University Research Coordination Committee  
Chairman of the Graduate Committee, Biochemistry Department

1979-1982 College of Agriculture Tenure and Promotion Committee  
1979 College of Agriculture Dean Search Committee  
1981 Vice-President for Research Search Committee  
1981 College of Human Medicine Evaluation Committee  
1981-1982 Biomedical Research Funding Committee  
1982 Chairman, Department of Zoology and Physiology Review Committee  
1986 Research Committee College of Medicine  
Ad Hoc Committee to Review Center on Aging  
Ad Hoc Medical Center Research Advisory Committee  
Working Group for Biotechnology Center  
Center for Pharmaceutical Science and Technology Advisory Committee  
College of Pharmacy Graduate Program  
College of Pharmacy Research and Seminar

1987 Markey Cancer Center Internal Advisory Committee  
College of Medicine Research Committee  
Tobacco and Health Advisory Committee

1988 College of Pharmacy BRSB Committee, Tenure and Promotion  
1989 Chairman, College of Medicine BRSB Committee  
Member, Tobacco & Health Advisory Committee  
Member, Markey Cancer Center Advisory Committee

1990 Chairman, College of Medicine BRSB Committee  
1991-1992 Member, Intellectual Properties Committee  
Member, Search Committee Cancer Center Director  
Member, Cancer Center Advisory Committee  
Member, Search Committee Diagnostic Radiology Chair  
Member, Academic Area Committee, Biological Sciences

1993-1995 Chair, Research and Seminar Committee  
Member, Appointment, Tenure and Promotion Committee

1996-1997 Chair, Graduate Program task force, College of Pharmacy  
Chair, Physical Plant section, College of Pharmacy self-study  
University Chemical Safety Committee  
College of Medicine Academic Council  
College of Pharmacy Tenure and Promotion Committee

## PUBLICATIONS (REFEREED JOURNALS)

1. Haley, B. and Yount, R. Gamma-fluoradenosine Triphosphate.Synthesis, Properties and Interaction with Myosin and Heavy Meromyosin. Biochemistry II, 2863-2871 (1972).
2. Haley, B., Yount and Hoffman, J. Selective Inhibition of Divalent Metal Ion Requiring ATPase Activity Human Red Cell Ghost by an Analog of ATP. The Physiologist 16, 333-334 (1973).
3. Haley, B. and Hoffman, J. Interactions of Photo-Affinity ATP Analog with Cation-Stimulated ATPase Activities of Human Red Cell Ghost. Proc. Natl. Acad. Sci. 71, 3367-3371 (1974).
4. Staros, J.V., Haley, B. and Richards, F.M. Human Erythrocytes and Resealed Ghost: A Comparison of Membrane Topology. J. Biol. Chem. 249, 5004-5007 (1974).
5. Pomerantz, A., Rudolph, S.A., Haley, B. and Greengard, P. Photoaffinity Labeling of a Protein Kinase from Bovine Brain with 8-Azido-adenosine-3', 5'-monophosphate. Biochemistry 14, 3852-3857 (1975).
6. Haley, B. Photoaffinity Labeling of cAMP Binding Sites of Human Red Blood Cell Membranes. Biochemistry 14, 3852-3857 (1975).
7. Staros, J.V., Richards, F.M. and Haley, B. Photochemical Labeling of the Cytoplasmic Surface of the Membranes of Intact Human Erythrocytes. J. Biol. Chem. 250, 8174-8178 (1975).
8. Malkinson, A.M., Krueger, B.V., Rudolph, S.A., Casnelli, J.E., Haley, B. and Greengard, P. Widespread Occurrence of a Specific Protein in Vertebrate Tissues and Regulation by cAMP of its Endogenous Phosphorylation and Dephosphorylation. Metabolism 24, 331-341 (1975).
9. Haley, B. Photoaffinity Labeling of Adenosine 3', 5'-Cyclic Monophosphate Binding Sites. Methods in Enzymology, Jacoby and Wilchek, Editors. V 46, pp. 339-346 (1976).
10. Owens, J.R. and Haley, B.E. A Study of Adenosine 3', 5'-Cyclic Monophosphate Binding Sites of Human Erythrocyte Membranes Using 8-Azido-adenosine-3'-5' Cyclic Monophosphate. J. Supra. Mole. Structure 5, 91-102 (1976).
11. Skare, K., Black, J.L., Pancoe, W.L. and Haley, B. Determination of the Cellular Location of Cyclic Nucleotide Binding Sites Using 8-Azido-adenosine-3', 5'-monophosphate, A Photoaffinity Probe. Arch. Biochem. Biophys. 180, 409-415 (1977).
12. Lau, E., Haley, B. and Barden, R. Interactions of a Photoaffinity Analog of CoA with CoA Enzymes. Biochemistry 16, 2581-2585 (1977).
13. Owens, J.R. and Haley, B. A Study of Adenosine 3', 5'-Cyclic Nucleotide Binding Sites of Human Erythrocyte Membranes Using 8-Azido-adenosine 3'-5'-Cyclic Monophosphate. Cell Shape and Surface Architecture: Progress in Clinical and Biological Research 17, 65-76 (1977)
14. Lau, E.P., Haley, B. and Barden, R. The 8-Azidoadenine Analog of S-Benzoyl (3'-dephospho) Coenzyme A-A Photoaffinity Label for Acyl CoA; Glycine N-Acyltransferase. Biochem. Biophys. Res. Commun 76 843-849 (1977).
15. Geahlen, R.T. and Haley, B. Interactions of a Photoaffinity Analog of GTP with the Proteins of Microtubules. Proc. Natl. Acad. Sci. 74, 4375-4377 (1977).
16. Owens, J.R. and Haley, B. Use of Photoaffinity Nucleotide Analogs to Determine the Mechanism of ATF Regulation of a Membrane Bound, cAMP Activated Protein Kinase. J. Supra. Mole. Structure 9, 57-68 (1978).

17. Czarnecki, J., Geahlen, R.T. and Haley, B. Synthesis and Use of Azido Photoaffinity Analogs of Adenine and Guanine Nucleotides. Methods in Enzymology **56**, 642-653 (1979).
18. Marcus, F. and Haley, B. Inhibition of Fructose 1,6-biphosphatase by the Photoreactive AMP Analog, 8-Azido-AMP. J. Biol. Chem. **254**, 259-261 (1979).
19. Geahlen, R., Haley, B. and Krebs, E.G. Synthesis and Use of 8-azidoguanosine 3', 5'-cyclic Monophosphate as a Photoaffinity Label for Cyclic GMP-dependent Protein Kinase. Proc. Natl. Acad. Sci. **76**, 2213-2217 (1979).
20. Geahlen, R. and Haley, B. Use of GTP Photoaffinity Probe to Resolve Aspects of the Mechanism of Tubulin Polymerization. J. Biol. Chem. **254**, 11982-11987 (1979).
21. Haley, B. Application of Photoaffinity Nucleotide Analogs to Biological Membrane Research. Selected Aspects of Cancer-Related Protein, Carbohydrate, Lipid and other Biochemistry, International Cancer Research Data Bank, p. 87 (1979).
22. Owens, J. and Haley, B. Mechanism of MgATP Regulation of Membrane Bound Type I cAMP Activated Protein Kinase. Transmembrane Signaling. Alan R. Liss, Inc. New York, New York, pp. 149-160 (1979).
23. Forrester, I.T., P.K. Schoff, B.E. Haley and R.G. Atherton. Determination of Protein Kinase Activity in Intact Mammalian Sperm. J. of Andrology **1**, 70 (1980).
24. Briggs, F. Norman, Al-Jumaily, Walid and Haley, Boyd. Photoaffinity Labeling of the (Ca<sup>+</sup>Mg) ATPase of Skeletal and Cardiac Sarcoplasmic Reticulum with [<sup>32</sup>P]-8-Azido ATP. Cell Calcium **1**, 205-215 (1980).
25. Hoyer, P., Owens, J.R. and Haley, B.E. Use of Nucleotide Photoaffinity Probes to Elucidate Molecular Mechanisms of Nucleotide Regulated Phenomena. Annals of New York Academy of Science **346**, 280-301 (1980).
26. Takemoto, D.J., B.E. Haley, J. Hanse, P. Pinbett and L.J. Takemoto. GTPase from Rod Outer Segments: Characterization by Photoaffinity Labeling and Tryptic Peptide Mapping. Biochem. Biophys. Res. Commun. **102**, 341-347 (1981).
27. Leichtling, B.H., Coffman, D.S., Yaeger, E.S., Rickenberg, H.V., Al-Jumaily, W. and Haley, B.E. Occurrence of the Adenylate Cyclase "G-Protein" in Membranes of Dictyostelium discoidium, Biochem. Biophys. Res. Commun. **102**, 1187-1195 (1981).
28. Schoff, P.K., Forester, I.T., Haley, B.E. and Atherton, R. A Study of cAMP Binding Proteins on Intact and Distrupted Sperm Cells Using 8-Azidoadenosine-3', 5'-Cyclic Monophosphate. J. Supra. Molecular Structure **19**, 1-15 (1982).
29. King, M.M., Carlson, G. and Haley, B.E. Photoaffinity-Labeling of the Subunit of Phosphorylase Kinase by 8-Azidoadenosine-5'-Triphosphate and its 2', 3' -Dialdehyde Derivative. J. Biol. Chem. **257**, 14058-14065 (1982).
30. Potter, R. and Haley, B.E. Photoaffinity Labeling of Nucleotide Binding Sites with 8-Azidopurine Analogs. Meth. Enzymol. **91**, 613-633 (1982).
31. Hoyer, P.B. and Haley, B.E. Utilization of Nucleotide Photoaffinity Probes to Study Protein-Nucleotide Interactions in Cell Fractions. J. Cellular Biochemistry, submitted. (1983)
32. Haley, Boyd. Development and Utilization of 8-Azidopurine Nucleotide Photoaffinity Probes. Federation Proceedings **42**, 2831-2836 (1983).
33. Khatoon, S., Atherton, R. Al-Jumaily, W. and Haley, B.E. Use of Nucleotide Photoaffinity Probes to Study Hormone Action. Biology of Reproduction **28**, 61-73 (1983).

34. Kaiser, I.I., Kladianos, D.M., Van Kirk, E.A., and Haley, B.E. Photoaffinity Labeling of catechol-o-methyltransferase with 8'-Azido-S-adenosylmethionine. *J. Biol. Chem.* **258**, 1747-1751 (1983).
35. Abraham, K., Haley, B. and Modak, M. Biochemistry of Terminal Deoxynucleotidyl Transferase: 8-Azido ATP as A Substrate Binding Site-Directed Photoaffinity Labeling Prob. *Biochemistry* **22**, 4197-4203 (1983).
36. Haley, B.E., Ponstingl, H. and Doenges, K.H. Photoaffinity Labeling of Pure Tubulin Using 8-Azidoguanosine triphosphate at the  $\beta$ -Subunit. *Hoppe-Sevlers J. Physiol. Chem.* **364**, 1137 (1983).
37. Woody, A.M., Vader, C.R., Woody, R.W. and Haley, B.E. Photoaffinity Labeling of DNA-dependent RNA polymerase from *E. coli* with 8-azidoadenosine-5'-triphosphate. *Biochemistry* **23**, 2843-2848 (1984).
38. Owens, J.R. and Haley, B.E. Synthesis and Utilization of [5'-<sup>32</sup>P]-8-Azidoguanosine-3'-phosphate-5'-phosphate: Photoaffinity Studies on Cytosolic Proteins of *E. coli*. *J. Biol. Chem.* **259**, 14843-14848 (1984).
39. Pfister, K.K., Haley, B.E. and Witman, G.B. The Photoaffinity Probe 8-azidoadenosine-5'-triphosphate. Selectivity Labels the Heavy Chain of Chlamydomonas 12S Dynein. *J. Biol. Chem.* **259**, 8499-8504 (1984).
40. Atherton, R.W., Khatoon, S., Schoff, P.K. and Haley, B.E. A Study of Rat Epididymal Sperm Adenosine-3', 5'-monophosphate-dependent Protein Kinase: Maturation Differences and Cellular Location. *Biol. of Reproduction* **32**, 155-172 (1985).
41. McMurray, M.M., Hansen, J.S., Haley, B.E., Takemoto, D.J. and Takemoto, L.J. Interspecies Conservation of Retinal Guanosine-5'-triphosphatase: Characterization by Photoaffinity Labeling and Tryptic Peptide Mapping. *Biochemical Journal* **225**, 227-232 (1985).
42. Khatoon, S., Haley, B.E. and Atherton, R.W. A Comparative Analysis of cAMP-dependent Protein Kinase Regulatory Subunits in Sea Urchin and Rat Sperm. *J. Andrology* **6**, 251-260 (1985).
43. DeBortoli, M.E., Issa, H.A., Haley, B.E. and Cho-Chung, Y.S. Elevated Levels of p21 *ras* Protein in Hormone-Dependent Mammary Carcinomas of Humans and Rodents. *Bioch. Biophys. Res. Commun.* **127**, 699-709 (1985).
44. Evans, R., Haley, B. and Roth, D. Photoaffinity Labeling of a Viral Induced Protein from Tobacco. *J. Biol. Chem.* **260**, 7800-7804 (1985).
45. Nunamaker, R.A., Wilson, W.T. and Haley, B.E. Electrophoretic Detection of Africanized Honey Bees (*Apis mellifera scutellata*) in Guatemala and Mexico Based on Malate Dehydrogenase Allozyme Patterns. *Journal of the Entomological Society* **57**, 622-631 (1985).
46. Pfister, K.K., Haley, B.E. and Witman, G.B. Labeling of Chlamydomonas 18S Dynein Polypeptides by 8-Azidoadenosine 5'-Triphosphate, a Photoaffinity Analog of ATP. *J. Biol. Chem.* **260**, 12844-12850 (1985).
47. Hoyer, P.B., Fletcher, P. and Haley, B.E. Synthesis of 2', 3'-O-(2,4,6-trinitrocyclohexadienylidene) guanosine 5'-Triphosphate and study of its Inhibitory Properties with Adenylate Cyclase. *Arch. Biochem. Biophys.* **245**, 368-378 (1986).
48. Evans, R.K., Johnson, J.D. and Haley, B.E. 5'-Azido-2'-deoxyuridine-5'-triphosphate: A Novel Photoaffinity Labeling Reagent and Tool for the Enzymatic Synthesis of Photoactive DNA. *Proc. Natl. Acad. Sci. USA.* **83**, pp. 5382-5386 (1986).
49. Jeganathan, A., Richardson, S.K., Mani, R.S., Haley, B.E. and Watt, D.S. Selective Reactions of Azide-substituted  $\alpha$ -Diazoamides with Olefins and Alcohols Using Rhodium (II) Catalysts. *J. Org. Chem.* **51**, 5362-5367 (1986).

50. Malkinson, A.M., Haley, B.E., Macintyre, B.E. and Buthy, M.S. Changes in Pulmonary Adenosine Triphosphate Binding Proteins Detected by Nucleotide Photoaffinity Labeling Following Treatment of Mice with the Tumor-Modulatory Agent Butylated Hydroxytoluene. Cancer Res. **46**, 4626-4630 (1986).
51. Evans, R.K. and Haley, B.E. Synthesis and Biological Properties of 5-Azido-2'-deoxyuridine-5'-triphosphate: A Photoactive Nucleotide Suitable for Making Light Sensitive DNA. Biochemistry **26**, 269-276 (1987).
52. Richardson, S.K., Jeganathan, A., Mani, R.S., Haley, B.E. and Watt, D.S. Synthesis and Biological Activity of C-4 and C-15 Aryl Azide Derivatives of Anguidine. Tetrahedron Letters **43**, 2925 (1987).
53. Droms, K.A., Haley, B.E. and Malkinson, A.M. Decreased Incorporation of the Photoaffinity Probe [ $\gamma$ - $^{32}$ P]-8N<sub>3</sub> GTP into a 45KD Protein in Lung Tumors. Bioch. Biophys. Res. Commun. **144**, 591-597 (1987).
54. Karpel, R.L., Levin, V.Y. and Haley, B.E. Photoaffinity Labeling of T4 Bacteriophage 32Protein. J.Biol.Chem. **262**, 9359-66 (1987).
55. Suhadolnik, R.J., Li, Shi Wu, Sobol, Jr. R.W., and Haley, B.E. 2- and 8-Azido Photoaffinity Probes. II. Studies on the Binding Process of 2-5A Synthetase. Biochemistry **27**, 8846-8851 (1988).
56. Suhadolnik, R.J., Kariko, K., Sobol, Jr., R.W., Shi Wu, Richenbach, N.L. and Haley, B.E. 2- and 8-Azido Photoaffinity Probes. I. Enzymatic Synthesis, Characterization and Biological Properties of 2- and 8-Azido Photoprobes of 2-5A & Photolabeling of 2-5A Binding Proteins. Biochemistry **27**, 8840-8846 (1988).
57. Droms, K.A., Haley, B.E., Smith, G.J. and Malkinson, A.M. Decreased Photolabeling of G<sub>s</sub> $\alpha$  With [ $\alpha$ - $^{32}$ P]8N<sub>3</sub>-GTP in Tumorigenic Lung Epithelial Cell Lines: Association with Decreased Hormone Responsiveness and Loss of Contact-Inhibited Growth. Experimental Cell Research **182**, 330-339 (1989).
58. Francis, B., Overmeyer, J., John, W., Marshall, E. and Haley, B. Prevalence of Nucleoside Diphosphate Kinase Autophosphorylation in Human Colon Carcinoma versus Normal Colon Homogenates. Molecular Carcinogenesis **2**, 168-178 (1989).
59. King, S.M., Haley, B.E. and Witman, G.B. Structure of the  $\alpha$  and  $\beta$  Heavy Chains of the Outer Arm Dynein from Chlamydomonas Flagella. J. Biol. Chem. **264**, 10210-10218 (1989).
60. Khatoon, S., Campbell, S.R., Haley, B.E. and Slevin, J.T. Aberrant GTP  $\beta$ -Tubulin Interaction in Alzheimer's Disease. Annals of Neurology **26**, 210-215 (1989).
61. Lawson, S.G., Mason, T.L., Sabin, R.D., Sloan, M.E., Drake, R.R., Haley, B.E. and Wasserman, B.P. UDP-Glucose: (1,3)- $\beta$ -Glucan Synthase from Daucas carota L.: Characterization, Photoaffinity Labeling and Solubilization. Journal of Plant Physiology **90**, 101-108 (1989).
62. Lewis, C.T., Haley, B.E. and Carlson, G.M. Formation of an Intramolecular Cystine Disulfide During the Reaction of 8-Azido-GTP with Cytosolic Phosphoenolpyruvate Carboxykinase (GTP) Causes Inactivation without Photolabeling. Biochemistry **28**, 9248-9255 (1989).
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CURRICULUM VITAE

The basic research interest of our laboratory centers on biochemical and biomedical problems involving control at the molecular level. Specifically, we are most interested in biological systems regulated by protein-nucleotide interactions where the bioenergetics involved are expressed through site-specific nucleotide binding of high affinity or through protein substrate phosphorylation. Our approach to the study of this general phenomenon is to synthesize novel nucleotide analogs that are photoactive or fluorescent, or both. The analogs are then used to study various aspects of protein-nucleotide interactions which regulate enzyme activity. Analogs used may be modifications of the commonly known nucleotides such as ATP, cAMP, GTP, dUTP, NAD<sup>+</sup>, UDP-Glc, etc. or probes of the more unusual nucleotides such as the proposed alarmones guanosine-3'-phosphate-5'phosphate (magic spot compounds) and diadenosine-P<sup>1</sup>, P<sup>4</sup>-tetraphosphate.

These nucleotide analogs are used to study a wide variety of enzymes that either use or are regulated by nucleotides including cyclases, kinases, and polymerases. Certain of these probes have proven useful in the study of the differences between normal and diseased tissues as observed through changes in nucleotide binding proteins. Alzheimer's disease, Amyotrophic Lateral Sclerosis and Multiple Sclerosis are some of the diseases we are currently investigating. I am currently interested in the several low molecular weight nucleotide binding proteins that we have detected in human cerebrospinal fluid that seem to vary in presence and concentration with various disease states. One of these is aFGF (binds ATP) and another is myelin basic protein (binds GTP, is phosphorylated and ADP-ribosylated).

We have also done studies that implicate low levels of Hg as being capable of being involved in certain neurological diseases. This is based on our observation that Hg<sup>2+</sup> chelated with EDTA is a more potent inhibitor of tubulin polymerization than is free Hg<sup>2+</sup>. Addition of Hg-EDTA complex to non-demented human brain homogenates renders the photolabeling profile to be identical to that of Alzheimer's diseased brain homogenates. Further, exposure of rats to low level mercury vapor causes a great increase in rat brain mercury levels and a marked decrease in brain tubulin photolabeling as is observed in Alzheimer's diseased brain. These results support the contention that mercury vapor would exacerbate the symptoms associated with Alzheimer's disease. This is a major concern since substantial levels of mercury vapor is known to be released from dental amalgams and EDTA is a common food additive.

Additionally, we have found that several of the large polypeptide hormones (or biological response modifiers) have nucleotide binding sites. These include GM-CSF, aFGF, IL-1, IL-2, Interferon-alpha, TNF (tumor necrosis factor), glucagon and GH (growth hormone). We therefore feel that the transmembrane signaling effected by these proteins may, at least be expressed partially by an activity associated with the "hormone" itself. This is supported by the observation that IL-1 and IL-2 also autophosphorylate using ATP.