

Curriculum Vitae

THOMAS PATRICK HOPP, Ph.D.

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PROFESSIONAL EXPERIENCE

Summary: Broad experience in biotechnology research team leadership, recombinant protein product development, synthetic peptide chemistry, technical, medical, and popular writing. Isolated and patented Interleukin 1, invented the Flag epitope tag. Advised the team that created the blockbuster arthritis drug, ENBREL. Currently a consultant to the biotechnology industry.

POSITIONS

7/05-8/09 **CG Therapeutics, Inc.**, Seattle, Washington. A biotechnology company developing cancer vaccines and monoclonal antibodies.

Vice President, Research and Development. Responsible for collaborative monoclonal antibody research with the Hellstrom laboratory in Seattle, cancer vaccine studies with Ohio State University, and hCG vaccine clinical trial design.

- Lead writer for business plans, investigational new drug (IND) applications, technical publications, and small business innovation research (SBIR) grants.

11/88-6/05 **Protein Research Laboratories, Inc.**, Seattle, Washington and San Diego, California. A small biotechnology research and consulting company focused on recombinant protein production, purification, and crystallization.

Research Director. Planned, staffed, and equipped the fermentation, protein purification, and crystallization operations of a small biotechnology company.

- Developed protein purification and crystallization technology based on the Flag epitope tag, funded by an NIH Small Business Grant. Flag tagging is now one of the world's most widely used biotechnology techniques.
- Acted as consultant to several other biotechnology companies regarding cGMP protein production, purification, chemistry, and analysis.

2/96-6/97 **ImmunoTherapy Corporation**, Seattle, Washington. A biotechnology company created for clinical testing and development of anti-cancer vaccines.

Chief Scientific Officer. Provided scientific oversight of cancer vaccine development and clinical testing; Chairman of the company's Scientific Advisory Board.

- Responsible for reviewing and acting upon scientific issues arising during the development of the CTP-37 vaccine, planning in-house and extramural science including product development and testing collaborations.

- Wrote IND submission materials including the therapeutic rationale for CTP-37's demonstrated efficacy against colorectal and pancreatic cancer.

10/94-1/96

Burnham Institute, San Diego, California. Non-profit cancer research institute (formerly La Jolla Cancer Research Foundation) emphasizing the embryological aspects of the transformed state.

Visiting Scientist. Prepared recombinant integrins and anti-integrin antibodies for crystallography and NMR structural studies in Dr. Kay Ely's laboratory.

- Baculovirus protein expression, purification of affinity-tagged and non-tagged, native proteins from serum-containing and serum-free media.
- Solved problems of lipid contamination from serum-free cell culture media, isolated protein pure enough for crystallography studies.

9/92-1/96

Houghten Pharmaceuticals, Inc., San Diego, California. A biotechnology company established to develop pharmaceutical products based on combinatorial library analogs of alpha melanocyte stimulating hormone.

Consultant. Participated in group efforts to identify targets for α -MSH-related therapeutics; offered expertise in molecular biology of the immune system and biotechnology product development.

- Helped develop α -MSH peptide analogs that entered clinical trials.

9/92-1/96

Multiple Peptide Systems, San Diego, California. A biotechnology research and development company established to capitalize on proprietary combinatorial peptide synthesis technology.

Consultant. Offered guidance in synthetic peptide technology, purification and molecular biology techniques.

- Directed MPS's Technical Development Group, overseeing the production and purification of synthetic combinatorial libraries containing trillions of compounds for drug discovery screening.
- Acted as lead writer for grant applications, obtaining over \$10 million in U.S. government grant and contract funds.

9/82-11/88

Immunex Corporation, Seattle, Washington. A biotechnology company (now Amgen) with a focus on research, development, manufacture and marketing of immune system proteins as therapeutic products.

1/87-11/88

Vice President of New Research Evaluation. Identified and pursued new research opportunities and participated in the corporate Strategic Planning process.

- Brought Immunex's first directly marketed product, the Flag fusion-protein system for recombinant protein production and purification, from conception through pre-market testing and launch.

Immunex Corporation, continued

- Initiated new research projects in site-specific mutagenesis of IL-1, computer aided drug design, and transgenic animals.
- Advised the team that developed Immunex's blockbuster arthritis drug, ENBREL.

1/88-11/88 **Director, Transgenics Department.** Designed and oversaw construction of a fully functioning transgenics facility with the capacity to undertake both mouse and goat transgenics experimentation.

- Produced Interleukin-7-secreting embryonic stem cell lines and transgenic mice in the first year of operations.
- Cloned the genes necessary to produce human serum albumin in goat's milk, for an ongoing project at Immunex.

9/82-12/87 **Director, Protein Chemistry Department.** Established this department during the initial staffing and start-up of Immunex. Hired PhDs and technicians responsible for protein purification and analysis. Facilities included protein sequencers, amino acid analyzers, and a peptide synthesizer.

- Had a leading role in the discovery and development of many of Immunex's first generation of pharmaceutical product candidates, including Interleukin 1 α and β , the Interleukin 1 receptor, GM-CSF, and the Flag epitope.
- Headed a project team of 30 scientists that purified and cloned human Interleukin 1 α and β , as well as the T-cell Interleukin 1 receptor.
- Developed E coli production of recombinant Interleukin 1 α and β . Products were adopted as the international standards for IL-1. Scaled up purification methods for large scale GMP manufacturing.

9/80-9/82 **The New York Blood Center, New York.** One of the world's largest blood banks, with extensive research laboratories for blood and plasma related work.

Director, Protein Analysis Laboratory. Established a group to provide protein chemistry services at the Lindsley F. Kimball Research Institute of the Blood Center. These included protein sequencing, amino acid analysis, peptide synthesis, and HPLC analysis.

- Developed large-scale purification protocols for human interferons from blood plasma. Prepared α -Interferon for pre-clinical testing.
- Published a computerized method for analyzing protein antigenic sites (the Hopp and Woods algorithm) that found wide applications in molecular biology research.
- Visiting Investigator with Nobel Laureate R.B. Merrifield. Developed patented carriers for chemically synthesized peptide vaccines.

EDUCATION

- 9/96-6/00 **University of Washington**, Seattle. Writers' Program. Obtained certificates in Literature Writing, Commercial Writing and Advanced Commercial Writing.
- 2/77-9/80 **The Rockefeller University**, New York City. Nobel Laureate Dr. Gerald Edelman's laboratory. **Postdoctoral Fellow**. Studied molecular immunology, protein purification and sequencing.
- 9/72-2/77 **Cornell University Graduate School of Medical Sciences**, New York City, Biochemistry Department. Ph.D., 1977. **Graduate Fellow**. Studied protein chemistry and molecular evolution; taught medical school biochemistry.
- 9/68-6/72 **University of Washington**, Seattle. B.S. Biology 1972. Undergraduate research with Dr. Kenneth Walsh. Protein 3-D structure modeling.

PUBLICATIONS

Patents

1. Hopp, T.P. (1985) Identification and preparation of epitopes on antigens and allergens on the basis of hydrophilicity. United States Patent 4,554,101.
2. Hopp, T.P., Bektesh, S.L., Conlon, P.J., and March, C.J. (1987) Synthesis of protein with an identification peptide (vectors). United States Patent 4,703,004.
3. Hopp, T.P., Bektesh, S.L., Conlon, P.J. and March, C.J. (1988) Synthesis of protein with an identification peptide (proteins). United States Patent 4,782,137.
4. Hopp, T.P. and Prickett, K.S. (1989) Immunoaffinity purification system. United States Patent 4,851,341.
5. Hopp, T.P. and Prickett, K.S. (1991) Hybridoma and monoclonal antibody for use in an immunoaffinity purification system. United States Patent 5,011,912.
6. Hopp, T.P. (1991) Fatty acid carriers for synthetic peptides. United States Patent 5,019,383.
7. Conlon, P.J., Cosman, D.J., Grabstein, K.H., Hopp, T.P., Kronheim, S.R., Larson, A.D., March, C.J., Price, V.L., and Cerretti, D.P. (1992) Gene encoding biologically active interleukin 1. United States Patent 5,122,459.
8. Kronheim, S.R., March, C.J., Conlon, P.J., and Hopp, T.P. (1996) Homogeneous interleukin 1. United States Patent 5,484,887.
9. Brizzard, B., Bianca, D., Chubet, R., Vizard, D. and Hopp, T. (1998) A polypeptide surface marker for cells. United States Patent 5,731,425.
10. Brizzard, B., Bianca, D., Chubet, R., Vizard, D. and Hopp, T. (1999) Method of identifying cells with polypeptide surface marker. United States Patent 5,945,292.

Scientific Research Papers

1. Hopp, T.P. (1976) Identification of aqueous phase amino acid phenylthiohydantoins on polyamide sheets. *Analytical Biochemistry* 74, 683-640.
2. Hopp, T.P. (1977) Ph.D. Thesis: Immunochemistry of α -lactalbumin. Cornell University Medical College, New York, NY.
3. Hemperly, J.J., Hopp, T.P., Becker, J.W. and Cunningham, B.A. (1979) The chemical characterization of favin, a lectin isolated from *Vicia faba*. *J. Biol. Chem.* 254, 6803-6810.
4. Cunningham, B.A., Hemperly, J.J., Hopp, T.P. and Edelman, G.M. (1979) Favin versus concanavalin A: circularly permuted amino acid sequences. *Proc. Natl. Acad. Sci. USA* 76, 3218-3222.
5. Lingappa, V.R., Cunningham, B.A., Jazwinski, S.M., Hopp, T.P., Blobel, G. and Edelman, G.M. (1979) Cell-free synthesis and segregation of β 2-microglobulin. *Proc. Natl. Acad. Sci. USA* 76, 3651-3655.
6. Hopp, T.P. and Woods, K.R. (1979) Primary structure of rabbit α -lactalbumin. *Biochemistry* 18, 5182-5191.
7. Rothbard, J.B., Hopp, T.P. Edelman, G.M. and Cunningham, B.A. (1980) Structure of the heavy chain of the H-2K^k histocompatibility antigen. *Proc. Natl. Acad. Sci. USA* 77, 4239-4243.
8. Hopp, T.P. and Woods, K.R. (1981) Prediction of protein antigenic determinants from amino acid sequences. *Proc. Natl. Acad. Sci. USA* 78, 3824-3828.
9. Hopp, T.P. (1981) A synthetic peptide with hepatitis B surface antigen reactivity. *Molecular Immunology* 18, 869-872.
10. Prince, A.M., Ikram, H. and Hopp, T.P. (1982) Hepatitis B virus vaccine: Identification of HBsAg/a,d but not HBsAg/y subtype antigenic determinants on a synthetic immunogenic peptide. *Proc. Natl. Acad. Sci. USA* 79, 579-582.
11. Hopp, T.P., Hemperly, J.J. and Cunningham, B.A. (1982) Amino acid sequence and variant forms of favin, a lectin from *Vicia faba*. *J. Biol. Chem.* 257, 4473-4483.
12. Hopp, T.P. and Woods, K.R. (1982) Immunochemical studies on α -lactalbumin. *Molecular Immunology* 19, 1453-1463.
13. Hopp, T.P. and Woods, K.R. (1983) A computer program for predicting protein antigenic determinants. *Molecular Immunology* 20, 483-489.
14. Hopp, T.P. (1984) Immunogenicity of a synthetic HBsAg peptide: enhancement by conjugation to a fatty acid carrier. *Molecular Immunology* 21, 13-16.
15. Hopp, T.P. (1984) Protein antigen conformation: folding patterns and predictive algorithms; selection of antigenic and immunogenic peptides. *Annali Sclavo Collana Monogr.* 1(2), 47-60.

16. Conlon, P.J., Luk, K.H., Park, L.S., March, C.J., Hopp, T.P. and Urdal, D.L. (1985) Generation of anti-peptide monoclonal antibodies which recognize mature CSF-2 α (IL-3) protein. *J. Immunol.* 135, 328-332.
17. Kronheim, S.R., March, C.J., Erb, S.K., Conlon, P.J., Mochizuki, D.Y. and Hopp, T.P. (1985) Human interleukin 1: purification to homogeneity. *J. Exp. Med.* 161, 490-502.
18. March, C., Mosley, B., Larsen, A., Cerretti, D., Price, V. Braedt, G., Grabstein, K., Kronheim, S., Conlon, P., Henney, C., Gillis, S., Hopp, T. and Cosman, D. (1985) Cloning, sequence and expression of two distinct human interleukin-1 (IL-1) complementary DNAs. *Nature* 315, 641-647.
19. Dower, S., Kronheim, S., March, C., Conlon, P., Hopp, T., Gillis, S. and Urdal, D. (1985) Detection and characterization of high affinity plasma membrane receptors for human interleukin-1. *J. Exp. Med.* 162, 501-515.
20. Hopp, T.P. (1985) Protein surface analysis: methods for identifying antigenic determinants and other interaction sites. *J. Immunol. Methods* 88, 1-18.
21. Gallis, B., Lewis, A., Wignall, J., Alpert, A., Mochizuki, D., Cosman, D., Hopp, T. and Urdal, D. (1986) Phosphorylation of the human interleukin-2 receptor and a synthetic peptide identical to its C-terminal, cytoplasmic domain. *J. Biol. Chem.* 261, 5075-5080.
22. Dower, S.K., Kronheim, S.R., Hopp, T.P., Cantrell, M., Deeley, M., Gillis, S., Henney, C.S. and Urdal, D.L. (1986) The cell surface receptors for interleukin-1 α and interleukin-1 β are identical. *Nature* 324, 266-268.
23. Kronheim, S.R., Cantrell, M.A., Deeley, M.C., March, C.J., Glackin, P.J., Anderson, D.M., Hemenway, T., Merriam, J.E., Cosman, D. and Hopp, T.P. (1986) Purification and characterization of human interleukin-1 expressed in *Escherichia coli*. *Bio/Technology* 4, 1078-1082.
24. Grabstein, K., Eisenman, J., Mochizuki, D., Shanebeck, K., Conlon, P., Hopp, T., March, C. and Gillis, S. (1986) Purification to homogeneity of B cell stimulating factor. *J. Exp. Med.* 163, 1405-1414.
25. Hopp, T.P., Dower, S.K. and March, C.J. (1986) The molecular forms of interleukin-1. *Immunol. Res.* 5, 271-280.
26. Libby, R.T., Braedt, G., Kronheim, S.R., March, C.J., Urdal, D.L., Chiaverotti, T.A., Tushinski, R.J., Mochizuki, D.Y., Hopp, T.P. and Cosman, D. (1987) Expression and purification of native human granulocyte-macrophage colony-stimulating factor from an *Escherichia coli* secretion vector. *DNA* 6, 221-229.
27. Conlon, P.J., Grabstein, K., Alpert, A., Prickett, K.S., Hopp, T.P. and Gillis, S. (1987) Localization of human mononuclear cell interleukin 1 (IL-1). *J. Immunol.* 139, 98-102.
28. Black, R.A., Kronheim, S.R., Cantrell, M., Deeley, M., Jenny, P., March, C.J., Wignall, J., Cosman, D., Hopp, T.P. and Mochizuki, D.Y. (1988) Generation of biologically active interleukin-1 β by proteolytic cleavage of the inactive precursor. *J. Biol. Chem.* 263, 9437-9442.

29. Libby, R., Cosman, D., Cooney, M.K., Merriam, J.E., March, C.J. and Hopp, T.P. (1988) Human rhinovirus 3C protease: cloning and expression of an active form in *Escherichia coli*. *Biochemistry* 27, 6262-6268.
30. Hopp, T.P., Prickett, K.S., Price, V.L., Libby, R.T., March, C.J., Cerretti, D.P., Urdal, D.L. and Conlon, P.J. (1988) A short polypeptide marker sequence useful for recombinant protein identification and purification. *Bio/Technology* 6, 1204-1210.
31. Hopp, T.P., Prickett, K.S., Price, V.L., Cerretti, D.P., March, C.J. and Conlon, P.J. (1988) The Flag system. *ICSU Short Reports* 8, 138.
32. Black, R.A., Kronheim, S.R., Merriam, J.E., March, C.J. and Hopp, T.P. (1989) A pre-aspartate-specific protease from human leukocytes that cleaves pro-interleukin-1 β . *J. Biol. Chem.* 264, 5323-5326.
33. Prickett, K.S., Amberg, D.C. and Hopp, T.P. (1989) A calcium-dependent antibody for identification and purification of recombinant proteins. *Biotechniques* 7, 580-589.
34. Hopp, T.P. (1992) Flag ELISAs: some observations on technique. *Epitope* 1, 7-10.
35. Hopp, T.P. (1993) Retrospective: 12 years of antigenic determinant predictions, and more. *Peptide Research* 6, 183-190.
36. Gayle, R.B., Poindexter, K., Cosman, D., Dower, S.K., Gillis, S., Hopp, T., Jerzy, R., Kronheim, S., Lum, V., Lewis, A., Goodgame, M.M., March, C.J., Smith, D.L. and Srinivasan, S. (1993) Identification of regions in interleukin-1 α important for activity. *J. Biol. Chem.* 268, 22105-22111.
37. Hopp, T.P. (1994) Different views of protein antigenicity. *Peptide Research* 7, 229-231.
38. Pinilla, C., Buencamino, J., Appel, J.R., Hopp, T.P. and Houghten, R.A. (1995) Mapping the detailed specificity of a calcium-dependent monoclonal antibody through the use of soluble positional scanning combinatorial libraries: identification of potent calcium-independent antigens. *Molecular Diversity* 1, 21-28.
39. Hopp, T.P. (1995) Evidence from sequence information that the interleukin-1 receptor is a transmembrane GTPase. *Protein Science* 4, 1851-1859.
40. Hopp, T.P., Gallis, B. and Prickett, K.S. (1996) Metal binding properties of an anti-peptide monoclonal antibody. *Molecular Immunology* 33, 601-608.
41. Hopp, T.P. (1996) Interleukin-1 research. *Science* 273, 1781.
42. Hopp, T.P. (1996) Lymphokine racketeers? *Nature Biotechnology* 14, 275-279.
43. Hopp, T.P. (1996) Cistron settles with Immunex. *Nature Biotechnology* 14, 1636.
44. Hopp, T.P. (1997) Human chorionic gonadotropin. *Nature Biotechnology* 15, 834-835.

Scientific Book Chapters and Abstracts

1. Hopp, T.P. (1984) Use of palmitic acid as a carrier for chemically synthesized vaccines. In: Modern approaches to vaccines, pp. 369-372. Chanock, R.M. and Lerner, R.A. (eds.). Cold Spring Harbor Laboratory.
2. Conlon, P.J., Luk, H., Park, L., Hopp, T. and Urdal, D. (1985) Characterization of a monoclonal antibody to CSF-2 α (IL-3). In: Monoclonal antibodies and cancer therapy, UCLA symposia on molecular and cellular biology, Vol. 27, pp. 413-429. Reisfeld, R.A. and Sell, S. (eds.). Alan R. Liss, New York.
3. Hopp, T.P. (1985) Computer prediction of protein surface features and antigenic determinants. In: Molecular basis of cancer, Part B: Macromolecular recognition, chemotherapy and immunology, pp. 367-377. Rein, R. (ed.). Alan R. Liss, New York.
4. Hopp, T.P. (1985) Prediction of protein surfaces and interaction sites from amino acid sequences. In: Synthetic peptides in biology and medicine, pp. 3-12. Alitalo, K. et al. (eds.). Elsevier, Amsterdam.
5. Dower, S.K., Kronheim, S.R., March, C.J., Conlon, P.J., Gillis, S., Hopp, T.P. and Urdal, D.L. (1985) High affinity plasma membrane receptors for human interleukin-1: detection and characterization. In: The physiologic, metabolic and immunologic actions of interleukin-1, pp. 511-520. Kluger, M.J. et al. (eds.). Alan R. Liss, New York.
6. Mosley, B., March, C.J., Larsen, A., Cerretti, D.P., Braedt, G., Price, V., Gillis, S., Henney, C.S., Kronheim, S.R., Grabstein, K., Conlon, P.J., Hopp, T.P. and Cosman, D. (1985) The cloning and expression of two distinct human interleukin-1 (IL-1) cDNAs. In: The physiologic, metabolic and immunologic actions of interleukin-1, pp. 521-532. Kluger, M.J. et al. (eds.). Alan R. Liss, New York.
7. Hopp, T.P. (1986) Protein interaction sites predictable by hydrophilicity analysis. *Protides of the Biological Fluids* 34, 59-62.
8. Gillis, S., Conlon, P.J., Cosman, D., Hopp, T.P., Dower, S.K., Price, V., Mochizuki, D.Y. and Urdal, D.L. (1986) Lymphokines: from conjecture to the clinic. *Seminars in Oncology* 13, 218-227.
9. Woods, K.R. and Hopp, T.P. (1987) Antigen prediction from protein hydrophilicity profiles. In: Immunogenicity of protein antigens: repertoire and regulation, pp. 15-20. Sercarz, E.E. and Berzofsky, J.A. (eds.). CRC Press, Boca Raton.
10. March, C.J. and Hopp, T.P. (1987) Routine analysis of low-picomole-level phenylthiohydantions by HPLC using a diisopropylethylamine-acetate/THF buffer and acetonitrile gradient. In: *Proteins, structure and function*, pp. 395-402. L'Italien, J.L. (ed). Plenum, New York.
11. Hopp, T.P. (1987) Identification of protein surfaces and interaction sites by hydrophilicity analysis. In: *Proteins, structure and function*, pp. 437-443. L'Italien, J.L. (ed). Plenum, New York.
12. Conlon, P.J., Grabstein, K., Alpert, A., Prickett, K.S., Hopp, T.P., Styra, M., Tyler, S., Wignall, J. and Cosman, D. (1987) Use of monoclonal and polyclonal antibodies to localize interleukin 1

- in monokine producing cells. In: The control of tissue damage, pp. Glauert, A.M., (ed). Elsevier, Amsterdam.
13. Cosman, D.J., Deeley, M.C., Kronheim, S.R., Hopp, T.P., Conlon, P.J., Gillis, S. and Mosley, B. (1987) Interleukin-1 α : cloning, expression and biological activities. In: Recombinant lymphokines and their receptors, pp. 125-138. Gillis, S. (ed). Marcel Dekker, New York.
 14. Hopp, T.P. (1987) Improved hydrophilicity plotting method for membrane proteins. In: Methods in protein sequence analysis 1986, pp. 601-607. Walsh, K.A. (ed). Humana, Clifton.
 15. Hopp, T.P. (1989) The use of hydrophilicity plotting procedures to identify protein antigenic segments and other interaction sites. Methods in Enzymology 178, 571-585.
 16. Brewer, S.J., Haymore, B.L., Sassenfeld, H. and Hopp, T.P. (1991) Engineering recombinant DNA derived proteins for expression and purification. In: Purification and analysis of recombinant proteins, Seetharam, R. and Sharma, S.K. (eds). Marcel Dekker, New York.
 17. Routhe, M.R., Bowman, G.J., Gangitano, J.M., Lambing, J.L., Pratt, S.M. and Hopp, T.P. (1994) Rapid dimerization of an N-terminal cysteine containing peptide and dimer inhibition through N-terminal capping. In: Peptides, chemistry, structure and biology: Proceedings of the thirteenth American Peptide Symposium, pp. 159-160. Hodges, R.S. and Smith, J.A. (eds). ESCOM Science Publishers, Lieden.
 18. Hopp, T.P. and Orsen, M.J. (2004) Dinosaur brooding behavior and the origin of flight feathers. In: Feathered dragons: studies on the transition from dinosaurs to birds, pp 234-250. Currie, P.J. et al. (eds). Indiana University Press, Bloomington.
 19. Hopp, T.P. (2004) The FLAG Epitope Tag: Twenty Years of Discoveries. American Association for the Advancement of Science Annual Meeting, Seattle, Washington.
 20. Hopp, T.P. (2008) Preclinical characterization of CG201, a new more potent anti-hCG cancer vaccine formulation. International Conference on Gonadotropins and Receptors II, Theobalds Park, Hertfordshire, UK.