John J. Hill, PhD

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Professional Summary

A drug discovery, preclinical development, and development scientist with over twenty years of leadership experience in applying biophysical, analytical, biochemical, and biological approaches to interdisciplinary research and development problems in the biotech. pharma., and academic settings. Highly experienced in characterizing drug target mechanism of action, developing target profiles, and characterizing therapeutic mechanism of action, pharmacokinetic disposition, formulation, and bioengineering based efforts for small-molecules, antibodies, bispecifics, and cellular therapy modalities.

Work History

Managing Director, 09/2020-Present
Director, 04/2019-09/2020
BioProcess Technology Group, BDO USA LLP, Boston, MA

Provide analytical, process development, and other CMC consulting services to biopharmaceutical clients. Perform risk analyses, design and write process characterization, process validation, and supporting regulatory documents.

Consultant -4/2018-04/2019
BioProcess Technology Consultants, Inc., Woburn, MA

Provide analytical, process development, and other CMC consulting services to biopharmaceutical clients. Perform risk analyses, design and write process characterization, process validation, and supporting regulatory documents.

Affiliate Associate Professor, 03/2012 to Current
Department of Bioengineering, University of Washington – Seattle, WA

Principal Consultant and Founder, 10/2015 to Current
Seattle Biophysics Consulting, LLC – Seattle, WA

- Provide consulting services to the pharmaceutical and biotechnology industries in the biochemical, biophysical, and analytical sciences in support of drug discovery and development of small-molecule, protein, and cell therapy modalities.

Director, Analytical and Biophysical Development, 01/2016 to 04/2017
Nohla Therapeutics – Seattle, WA
Nohla Therapeutics is a clinical-stage start-up company that discovers and develops *ex vivo* expanded universal donor cellular therapies.

- Directed the pre-clinical biological and biochemical based functional and potency assay efforts.
- Directed the Analytical Development operations for determining the cellular therapy attributes, including physical, functional, and potency assessments.
- Lead the analytical assessment and biophysical characterization activities for the

manufacturing processes and the product formulation program.

- Developed and implemented methods for the characterization and analytical assessment efforts of the critical reagents used in the manufacturing process.
- Developed goals, budgets, and timelines for the operations of the department.
- Provided direction and strategic oversight to the preclinical and development programs
- Authored relevant sections of CMC documents for the IND (US) and IMPD (EU, Asia, Australia) applications for approval of the Phase 2 Clinical Trial.

Principle Scientist, Therapeutic Discovery, 10/2008 to 12/2014

Amgen – Seattle, WA

- Provided direction and strategic oversight to the Biophysical Sciences programs
- Supported drug discovery and development efforts for numerous therapeutic targets across all therapeutic areas, including Neurological, Cardiovascular, Metabolic, Inflammation, Oncology (including angiogenesis pathways and ADC approaches), and Immuno-Oncology approaches (such as ADCCs and cell-mediated immune defense with BiTEs and other bispecifics, fusion, and engineered proteins; checkpoint modulation approaches, including, the PD-L1, CD20, and IL-2 pathways with mAbs, and muteins; and the TRAIL pathways with mAbs and fusions proteins).
- Modalities included small-molecules, antibodies, fusion proteins, engineered protein scaffolds, bispecifics, BiTEs, ADCs, enzymes, growth factors, hormones, and polymeric-protein systems.
- Developed strategies and methods for functional, biochemical, biophysical, and analytical approaches to assessing target biology mechanism of action, drug mechanism of action, and therapeutic quality attributes.
- Conducted computational data analysis support for stability, assembly, binding, kinetic, activity, and biophysical enzymology studies.
- Supervised and mentored scientists and associates in reporting line, and in a dotted-line supervision across the organization.
- Expert in Surface Plasmon Resonance (SPR) technologies, Isothermal Titration Calorimetry (ITC), KinExA®, Gyrolab®, and Octet, Analytical Ultracentrifugation (AUC), circular dichroism (CD), infrared (FTIR), and fluorescence spectroscopic approaches, and charge based measurements

Principle Scientist, Pharmacokinetics and Drug Metabolism, 05/2006 to 10/2008
Amgen – Seattle, WA

- Lead and develop scientific strategies, methods, and analysis approaches in Biophysical and Analytical Sciences for the support of drug disposition studies.
- PI for large and small molecule pre-clinical pharmacokinetic studies, oversee bioanalytical analyses, and conduct pharmacokinetic data analysis.
- PI in definitive, IND-enabling drug metabolism studies in early and clinical development, wrote corresponding regulatory reports.
- Developed biophysically and analytically robust binding and enzymology studies for protein and small molecule drug disposition efforts.
- Developed and implemented *in vitro* analysis approaches for protein disposition, including target-mediated drug disposition (TMDD).

Senior Staff Scientist, Staff Scientist, **Analytical Development, Pharmaceutical Development, Drug Discovery Research, Drug Metabolism,** 09/1997 to 05/2006
ICOS Corporation – Bothell, WA

Education

Postdoctoral Research Associate, 03/1994 to 08/1997

University of Wisconsin, School of Pharmacy – Madison

Ph.D.: Biochemistry Biophysics, 1994
University of Illinois, School of Chemical Sciences - Urbana-Champaign

Bachelor of Science: Biochemistry Biophysics, 1987
University of Wisconsin – Milwaukee

Publications

- Lai, Chau, Z. L., Chen, S., Hill, J. J., Korpany, K. V., Liang, N., Lin, L., Lin, Y., Liu, J. K., Liu, Y., Lunde, R., & Shen, W. (2022). Exosome Processing and Characterization Approaches for Research and Technology Development. *Advanced Science*, 9(15), e2103222–n/a. https://doi.org/10.1002/advs.202103222
- Bou-Assaf, Budyak, I. L., Brenowitz, M., Day, E. S., Hayes, D., Hill, J., Majumdar, R., Ringhieri, P., Schuck, P., & Lin, J. C. (2022). Best Practices for Aggregate Quantitation of Antibody Therapeutics by Sedimentation Velocity Analytical Ultracentrifugation. *Journal of Pharmaceutical Sciences*, 111(7), 2121–2133. https://doi.org/10.1016/j.xphs.2021.12.023
- Shalaev, E., Hill, J.J. (2021). Interfacial Stress and Proteins Prepared in the Solid State. In: Li, J., Krause, M.E., Tu, R. (eds) Protein Instability at Interfaces During Drug Product Development. *AAPS Advances in the Pharmaceutical Sciences Series*, vol 43. Springer, Cham. https://doi.org/10.1007/978-3-030-57177-1_11
- Li, Krause, M. E., Chen, X., Cheng, Y., Dai, W., Hill, J. J., Huang, M., Jordan, S., LaCasse, D., Narhi, L., Shalaev, E., Shieh, I. C., Thomas, J. C., Tu, R., Zheng, S., & Zhu, L. (2019). Interfacial Stress in the Development of Biologics: Fundamental Understanding, Current Practice, and Future Perspective. *The AAPS Journal*, 21(3), 44–44.
- Barrett Nehilla, John J. Hill, Selvi Srinivasan, Yen-Chi Chen, Thomas H Schulte, Patrick S Stayton, James Lai (2016) A Stimuli-Responsive, Binary Reagent System for Rapid Isolation of Protein Biomarkers. *Analytical Chemistry,* November 2016 Vol.88(21) pp. 10404-10410
- J. Chena, H-N. Sona, J.J. Hill, S. Srinivasan, P.S. Stayton, A.J. Convertine, D.M. Ratner (2016) Nanostructured glycopolymer augmented liposomes to elucidate carbohydrate-mediated targeting. *Nanomedicine: Nanotechnology, Biology, and Medicine*, October 2016, Vol.12(7), pp.2031-2041
- John J. Hill and Thomas M. Laue. (2015) Protein assembly in serum and the differences from assembly in buffer. *Methods in Enzymology* **562**, 501-27.
- Han Xu, John J. Hill, Klaus Michelsen, Harvey Yamane, Robert Kurzeja, Tony Tam, Jake Isaacs, Philip Tagari (2015) Characterization of the direct interaction between KcsA-Kv1.3 and its inhibitors. *Biochimica Et Biophysica Acta* **1848** (10 Pt A), 1974-80.
- Hill, J.J., E. Y. Shalaev, G. Zografi. (2014) The Importance of Individual Protein Molecule Dynamics in Developing and Assessing Solid State Protein Preparations. *J. Pharm. Sci.* Sep;**103**(9):2605-14
- Hossein Salimi-Moosavi, Palaniswami Rathanaswami, Surendran Rajendran, Mike Toupikov, and JJ Hill (2012) Rapid affinity measurement of protein–protein interactions in a microfluidic platform *Anal. Biochem.* **426** 134–141
- M.L. Howard, J. J. Hill , G.R. Galluppi and M.A. McLean (2010) Plasma Protein Binding in Drug Discovery and Development. *Combinatorial Chemistry and High*

Throughput Chemistry, **13** (2), 170-187

- Pearson, J.T., Hill, J.J., Swank, J., Isoherranen, N., Kunze, K.L. and Atkins, W.M (2006) Surface Plasmon Resonance Analysis of Antifungal Azoles Binding to CYP3A4 with Kinetic Resolution of Multiple Binding Orientations. *Biochemistry*, **45** (20), 6341–6353
- Hill, J.J., E. Y. Shalaev, G. Zografi. (2005) Review: Thermodynamic and Kinetic Factors Involved in the Stabilization of Native Protein Structure in Amorphous Solids in Relation to Levels of Hydration. *J. Pharm. Sci.* **94** (8) 1636-1667.
- Lyon, R.P., Hill, J.J., Atkins, W.M. (2003) A Novel Class of Bifunctional Glutathione S-Transferase Inhibitors. *Biochemistry* **42:** 10418-10428
- Kim, K.M., Giedt, C.D., Basanez, G., O'Neil, J.W., Hill, J.J., Han, Y.H., Tzung, S.P., Zimmerberg, J., Hockenbery, D.M. and Zhang, K.Y.J. (2001) Biophysical Characterization of Recombinant Human Bcl-2 and Its Interactions with an Inhibitory Ligand, Antimycin A. *Biochemistry* **40**: 4911-4922

- Ozers, M.S., Hill, J.J., Ervin, K., Royer, C.R. and Gorski, J. (2001) The Dissociation Rate of Estrogen Receptor α from the Consensus Estrogen Response Element. *Mol. Cell. Endocrinol.* **175**: 101-109
- Strugnell, S.A., Hill, J.J., McCaslin, D.R., Wiefling, B.A., Royer, C.A. and DeLuca, H.F. (1999) Bacterial Expression and Characterization of the Ligand Binding Domain of the Vitamin D Receptor. *Arch. Biochem. Biophys.* **364**: 42-52
- Hill, J.J., Royer, C.A. (1997) Fluorescence Approaches to the Study of Protein-Nucleic Acid Complexation. *Methods Enzymol.*, Brand, L. and Johnson, M.L. *eds.*, **278**:390-416
- Ozers, M.S., Hill, J.J., Ervin, K., Wood, J.R., Nardulli, A.M., Royer, C.R. and Gorski, J. (1997) Equilibrium Binding of Estrogen Receptor with DNA Using Fluorescence Anisotropy. *J. Biol. Chem.* **272**: 30405-304011
- Sun, J., Kahlow, M.A., Kaysser, T.M., Osborne, J.P., Hill, J.J., Rohlfs, R.J., Hille, C.R., Gennis, R.B., Loehr, T.M. (1996) Resonance Raman Spectroscopic Identification of a Histidine Ligand of b_{595} and the Nature of the Ligation of Chlorin *d* in the Fully Reduced *Escherichia coli* Cytochrome *bd* Oxidase. *Biochemistry* **35**: 2403-2412
- Sun, J., Osborne, J.P., Kahlow, M.A., Kaysser, T.M., Hill, J.J., Gennis, R.B., Loehr, T.M. (1995)Resonance Raman Studies of *Escherichia coli* Cytochrome *bd* Oxidase. Selective Enhancement of the Three Heme Chromophores of the "As-Isolated" Enzyme and Characterization of the Cyanide Adduct. *Biochemistry* **34**: 12144-12151, (Correction) **35**: 666
- Hill, B.C., Hill, J.J. and Gennis, R.B. (1994) The Room Temperature Reactions of CO and O_2 with the Cytochrome *bd* Complex from *Escherichia coli*. *Biochemistry* **33**:15110-15115.
- Hill, J. J., Alben, J. O. and Gennis, R. B. (1993). Spectroscopic Evidence for a Heme-heme Binuclear Center in the Cytochrome *bd* Ubiquinol Oxidase from *Escherichia coli*. *Proc. Natl. Acad. Sci. USA* **90**:5863-5867.
- Hosler, J. P., Ferguson-Miller, S., Calhoun, M. W., Thomas, J. W., Hill, J., Lemieux, L., Ma, J., Georgiou, C., Fetter, J., Shapleigh, J., Tecklenburg, M. M. J., Babcock, G. T. and Gennis, R. B. (1993). Insight into the Active-Site Structure and Function of Cytochrome Oxidase by Analysis of Site-Directed Mutants of Bacterial Cytochrome aa_3 and Cytochrome *bo*. *J. Bioenergetics and Biomembranes* **25**:121-136.
- Wang, J., Ching, Y.-c., Rousseau, D. L., Hill, J. J., Rumbley, J. and Gennis, R. B. (1993). Similar CO Binding Sites in Bacterial Cytochrome *bo* and Mammalian Cytochrome *c* Oxidase. *J. Am. Chem. Soc.* **115**:3390-3391
- Calhoun, M. W., Hill, J. J., Lemieux, L. J., Ingledew, W. J., Alben, J. O. and Gennis, R. B. (1993). Site-Directed Mutants of the Cytochrome *bo* Ubiquinol Oxidase of *Escherichia coli*: Amino Acid Substitutions for Two Histidines that Are Putative Cu_B Ligands. *Biochemistry* **32**:11524-11529.
- Calhoun, M. W., Lemieux, L. J., Thomas, J. W., Hill, J. J., Goswitz, V. C., Alben, J. O. and Gennis, R. B. (1993). Spectroscopic Characterization of Mutants Supports the Assignment of Histidine 419 as the Axial Ligand of Heme *o* in the Binuclear Center of the Cytochrome *bo* Ubiquinol Oxidase from *Escherichia coli*. *Biochemistry* **32**:13254-13261.

- Calhoun, M. W., Thomas, J. W., Hill, J. J., Hosler, J. P., Shapleigh, J. P., Tecklenburg, M. M. J., Ferguson-Miller, S., Babcock, G. T., Alben, J. O. and Gennis, R. B. (1993). Identity of the Axial Ligand of the High-Spin Heme in Cytochrome Oxidase: Spectroscopic Characterization of Mutants in the *bo*-type Oxidase of *Escherichia coli* and the aa_3-type Oxidase of *Rhodobacter sphaeroides*. *Biochemistry* **32**:10905-10911.
- Hill, J., Goswitz, V. C., Calhoun, M., Garcia-Horsman, J. A., Lemieux, L., Alben, J. O. and Gennis, R. B. (1992). Demonstration by FTIR that the *bo*-type Ubiquinol Oxidase of *Escherichia coli* Contains a Heme-copper Binuclear Center Similar to that in Cytochrome *c* Oxidase and the Proper Assembly of the Binuclear Center Requires the *cyo*E Gene Product. *Biochemistry* **31**:11435-11440.
- Minghetti, K. C., Goswitz, V. C., Gabriel, N. E., Hill, J. J., Barassi, C., Georgiou, C. D., Chan, S. I. and Gennis, R. B. (1992). A Modified, Large-Scale Purification of the Cytochrome *o* Complex of *Escherichia Coli* Yields a Two Heme/One Copper Terminal Oxidase with High Specific Activity. *Biochemistry* **31**:6917-6924.
- Shapleigh, J. P., Hill, J. J., Alben, J. O. and Gennis, R. B. (1992). Spectroscopic and Genetic Evidence for Two Heme-Cu Containing Oxidases in *Rhodobacter sphaeroides*. *J. Bacteriol.* **174**:2338-2343.
- Chepuri, V., Lemieux, L., Hill, J., Alben, J. O. and Gennis, R. B. (1990). Recent Studies of the Cytochrome *o* Terminal Oxidase Complex of *Escherichia coli*. *Biochim. Biophys. Acta* **1018**:124-127.
- Hill, J. J., Gennis, R. B., Alben, J. O. (1991) Photoselective Discrimination of Matrix Isolated Respiratory Enzymes from *E. Coli* by Fourier Transform Infrared Spectroscopy. *Society of Photo-Optical Instrumentation Engineers (SPIE)* **1575**:453-456
- Alben, James O., Hemann, Craig F., Hill, John J. (1989) Instrumental consideration in Infrared Biospectroscopy. *Society of Photo-Optical Instrumentation Engineers (SPIE)* **1145**:618-621