Bruce D. Koch, Ph.D.

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Director, Discovery Technologies

Reputation for scientific knowledge, strategic thinking, and effective delivery. Organized and experienced leader of diverse department consisting of lean, efficient groups supporting drug discovery, including HTS, high content imaging, protein crystallography, SPR, FACS, molecular biology, and centralized cell culture. Have played a leadership role in a number of drug discovery programs, including two collaborations with biotechs on ion channel targets. Recognized for identifying and developing strengths of group members.

PROFESSIONAL EXPERIENCE

ROCHE, Palo Alto 1991-2010

Director, Discovery Technologies (2009-2010)
Managed a $16M budget and a group of seventeen group leaders, research scientists, and associates. Represented the interests of the local group on the Function's Global Leadership Team.

- Organized and launched (as part of a reorganization) a streamlined Discovery Technologies Department focused on supporting Virology drug discovery.
- Increased impact of fragment screening by sponsoring (and contributing to) a working group which identified improved methods for fragment hit validation.
- Facilitated departmental planning for a move to a new, smaller facility to optimize shared space and equipment.
- After corporate layoff decision, maintained morale and kept the group focused on shipping equipment to other Roche sites and cleaning up the labs, which was completed on schedule.

Associate Director and Head, High Throughput Screening Group (2004-2009)
Managed a $1.2M reagent budget and a group of fourteen scientists and associates responsible for assay development, high throughput screening and followup, high content imaging, SPR validation of hits, fragment screening, FACS facilities, and HT ADME assays. Led the Roche Screen Coordinating Workgroup, which allocates screens across Roche sites to ensure efficient HTS resource utilization.

- >80% of HTS screens produced validated hits as a result of revamping the group and processes with an emphasis on data quality.
- Developed in-house HT high content imaging capability
- Developed, implemented, and managed an improved process for selection of compounds for further study by working in close collaboration with computational and medicinal chemists.
- Produced better validated hits by initiating the use of SPR binding.
- Improved the assay validation process globally within Roche by designing (in close collaboration with the Cheminformatics Group) a Pilot Screen Library of "privileged structures".

Principal Research Scientist, Lead Discovery Group (HTS), Roche Palo Alto (2000-2004)
Managed a group of seven-ten scientists and associates identifying new chemical leads by developing assays and running high throughput screens and characterizing the resulting actives. Developed Lead Identification strategies for new programs. Played a leadership role in the two neuroscience-related therapy areas as a member of their respective Management Teams.

- Improved assay quality and decreased optimization time for difficult assays by initiating use of statistical DOE.
- Accelerated the rapid generation of high expression cell lines by developing plasmids and acceptor cell lines which use cre-lox homologous recombination.

Research Scientist II and Site Technology Officer, New Leads Discovery Dept., Neurobiology Business Unit, Roche Palo Alto (1995 – 1999)
Developed and ran screening assays for voltage-gated ion channels. These assays included both radioisotope flux assays and assays using fluorescent voltage sensor dyes. As part of a global Roche due diligence network, evaluated opportunities for in-licensing drug discovery technologies.

SYNTEX DISCOVERY RESEARCH (acquired by Roche 1995)

Research Scientist I, Inst. of Pharmacology (1991 – 1995)
Set up oocyte electrophysiology lab and performed initial recordings from newly cloned sodium channels including NaV1.6 and NaV1.8. Directed a pharmacological study of an animal model of pain.

UC BERKELEY

Postdoctoral Fellow, Laboratory of Dr. Randy W. Schekman, Biochemistry Dept. and HHMI (1986 – 1991).
Used the techniques of yeast genetics, molecular biology, and protein biochemistry to study the role of HSP70 in protein translocation.

EXTERNAL COLLABORATIONS

Have played a key role (including one year of interim leadership) in a collaboration with a biotech focused on finding an inhibitor of an ion channel. Collaborated with One World Health and Biofocus on a screen for a diarrheal diseases ion channel target, including helping to fine-tune their HTS assay and followup cascade. Managed SPR assays outsourced to CRO, including QCing/reanalyzing the data. Also coordinated a collaboration with Aurora Biosciences focused on screening at ion channel targets.

GRANT EVALUATION COMMITTEES

NIH Study Section (NIH Roadmap HTS Assay for MLPCN R03), March 2010
NIH Study Section (NIH Roadmap Assay Development R25), June 2009
National Academy of Sciences Ohio BRTT Committee, Sept. 2003

EDUCATION

Ph.D. in Cell and Developmental Biology

Harvard Medical School (DMS), Boston, MA (Advisor: Dr. Agnes Schonbrunn)
Thesis Title: "Signal Transduction Mechanisms Activated by the Neuropeptide Somatostatin"

B.S. in Biology , *Magna cum laude*
Bates College, Lewiston, ME

Professional Training

Advanced Biosensor Workshop, Biosensor Tools
Ion Channels, Cold Spring Harbor Laboratory

Management Training

Leading at Roche, Roche Learning Center Basel
Insights for Pharma, London Business School
Mobilizing Leaders, Babson Executive Training Center

Professional Associations

Society for Biomolecular Sciences
Biophysical Society
Society for Neuroscience

PATENTS

P.S. Dietrich, **B. Koch**, H. Guthrie, U. A. Gubler. Stable cell lines expressing hERG. Patent US7,776,590B2 (2010).

PUBLICATIONS

A. Giannetti, **B. Koch**, and M. Browner. Surface Plasmon Based Assay for the Detection and Characterization of Promiscuous Inhibitors. J. Med. Chem. 51: 574 – 580 (2008).

D.K. Rabert, **B.D. Koch**, M. Ilnicka, R.A. Obernolte, S.L. Naylor, R.C. Herman, R.M. Eglen, J.C. Hunter, and L. Sangameswaran. A tetrodotoxin-resistant voltage-gated sodium channel from human dorsal root ganglia, hPN3/SCN10A. Pain 78: 107 – 114 (1998).

P.S. Dietrich, J.G. McGivern, S.G. Delgado, **B.D. Koch**, R.M. Eglen, J.C. Hunter, and L. Sangameswaran. Functional analysis of a voltage-gated sodium channel and its splice variant from rat dorsal root ganglia. J. Neurochem. 70: 2262 - 2272 (1998).

L. Sangameswaran, L.M. Fish, **B.D. Koch**, D.K. Rabert, S.G. Delgado, M. Ilnicka, L.B. Jakeman, S. Novakovic, K. Wong, P. Sze, E. Tzoumaka, R.C. Herman, H. Chan, R.M. Eglen, and J.C. Hunter. A novel tetrodotoxin-sensitive voltage-gated sodium channel expressed in the nervous system. J. Biol. Chem. 272: 14805 - 14809 (1997).

B.D. Koch, G.F. Faurot, J.R. McGuirk, D.E. Clarke, and J.C. Hunter. Modulation of mechano-hyperalgesia by clinically effective analgesics in rats with a peripheral mononeuropathy. Analgesia 2: 157 - 164 (1996).

L. Sangameswaran, S.G. Delgado, L.M. Fish, **B.D. Koch**, L.B. Jakeman, G.R. Stewart, P. Sze, J.C. Hunter, R.M. Eglen, and R.C. Herman. Structure and function of a novel voltage-gated, tetrodotoxin-resistant sodium channel specific to sensory neurons. J. Biol. Chem. 271: 5953 - 5956 (1996).

B.D. Koch, G.F. Faurot, M.V. Kopanitsa, and D.C. Swinney. Pharmacology of a Ca^{2+} influx pathway activated by emptying the intracellular Ca^{2+} stores in HL-60 cells: Evidence that a cytochrome P-450 is not involved. Biochemical Journal 302: 187-190 (1994).

R.J. Deshaies, A. Eun, **B.D. Koch**, J.A. Rothblatt, S. Sanders, C. Sterling, and R. Schekman. In: *Dynamics and Biogenesis of Membranes.* (NATO ASI Series H., Vol. 40) Springer, New York, 1990, pp. 327-342.

R.J. Deshaies, **B.D. Koch**, and R. Schekman. The role of stress proteins in membrane biogenesis. Trends in Biochemical Sciences 13: 384-388 (1988).

R.J. Deshaies, **B.D. Koch**, and M. Werner-Washburne, E.A. Craig, and R. Schekman. 70kD stress protein homologues facilitate translocation of secretory and mitochondrial precursor polypeptides. Nature 332: 800-805 (1988).

B.D. Koch, J.B. Blalock, and A. Schonbrunn. Characterization of the cyclic AMP-independent actions of somatostatin in GH cells: I. An increase in potassium conductance is responsible for both the hyperpolarization and the decrease in intracellular free calcium produced by somatostatin. J. Biol. Chem. 263: 216-225 (1988).

B.D. Koch and A. Schonbrunn. Characterization of the cyclic AMP-independent actions of somatostatin in GH cells: II. An increase in potassium conductance initiates somatostatin-induced inhibition of prolactin secretion. J. Biol. Chem. 263: 226-234 (1988).

A. Schonbrunn and **B.D. Koch**. Mechanisms by which somatostatin inhibits pituitary hormone release. In: *Somatostatin*: *Basic and Clinical Status*, Reichlin, S. (ed), Plenum Publishing Corp., New York, 1987, pp. 121-135.

B.D. Koch, L.J. Dorflinger, and A. Schonbrunn. Pertussis toxin blocks both cyclic AMP mediated and cyclic AMP independent actions of somatostatin: Evidence for coupling of N_i to decreases in intracellular free calcium. J. Biol. Chem. 260: 13138-13145 (1985).

A. Schonbrunn, L.J. Dorflinger, and **B.D. Koch**. Mechanisms of SRIF action in pituitary cells. In: *Somatostatin* (Adv. Exp. Med. vol. 188), Y.C. Patel and G.S. Tannenbaum (eds), Plenum Press, New York, 1985, pp. 305-324.

B.D. Koch and A. Schonbrunn. The somatostatin receptor is directly coupled to adenylate cyclase in GH_4C_1 pituitary cell membranes. Endocrinology 114: 1784-1790 (1984).

R.B. Mikkelsen and **B. Koch**. Membrane potential thermosensitivity of normal and simian virus 40-transformed lymphocytes. National Cancer Institute Monographs 61: 89 - 91 (1982).

R.B. Mikkelsen and **B. Koch**. Thermosensitivity of the membrane potential of normal and simian virus 40-transformed hamster lymphocytes. Cancer Research 41: 209 - 215 (1981).

ABSTRACTS

Q.-F. Gan, H. Truong and **B. Koch**. An Ion Channel FLIPR HTS Using the New Fluo-8 Calcium Dye. Program of the 14th Annual Conference and Exhibition of the Society for Biomolecular Sciences, St. Louis, Mo., April. 6-10, 2008, Poster P12001.

A. Giannetti, **B. Koch**, and M. Browner. A Surface Plasmon Resonance Based Assay for the Detection & Characterization of Promiscuous Inhibitors. Program of the 14th Annual Conference and Exhibition of the Society for Biomolecular Sciences, St. Louis, Mo., April. 6-10, 2008, Poster P2034.

B.D. Koch, J.R. Gever, A.P.D.W. Ford, and M.P. Dillon. Identification of $P2X_3$ Purinergic Receptor Antagonists by HTS. Program of the 12th Annual Conference and Exhibition of the Society for Biomolecular Sciences, Seattle, Washington, Sept. 17-21, 2006, Poster P5011.

M.Yu, C.Ramesha, T.Williams, P.Reynen and **B. Koch**. An Improved Procedure for Analyzing PAMPA Data. Program of the 12th Annual Conference and Exhibition of the Society for Biomolecular Sciences, Seattle, Washington, Sept. 17-21, 2006, Poster P4022.

Q-F. Gan, S. Ahmadyar, and **B.Koch**, Mn^{2+} Ion in Kinase Assay Buffer Can Cause Compound Potency Shift. Program of the 12th Annual Conference and Exhibition of the Society for Biomolecular Sciences, Seattle, Washington, Sept. 17-21, 2006, Poster P7120.

B.D. Koch and C. Su, How many control wells are required to accurately estimate Z'-factor?. Program of the 11th Annual Conference and Exhibition of the Society for Biomolecular Screening, Geneva, Switzerland, Sept. 11-15, 2005, Poster P03026.

Q-F. Gan, S. Ahmadyar, P. Thana, H. Truong, T. Tran, and **B. Koch**. The development, validation, and execution of IMAP™ based HTS assays for two kinase targets. Program of the 10th Annual Conference and Exhibition of the Society for Biomolecular Screening, Orlando, FL, Sept. 11-15, 2004, Poster P10130.

C. De Colle, H. Truong, and **B.D.Koch**. Comparison of Non-Radioactive cAMP Assay Kits for Native Cell Lines Expressing Low Concentrations of a Gs Coupled Receptor. Program of the 8th Annual Conference and Exhibition of the Society for Biomolecular Screening, The Hague, The Netherlands, Sept. 22-26, 2002, Abstract 2116.

D.K. Rabert, M.J. Ilnicka, **B.D. Koch**, S.L. Naylor, J.C. Hunter, and L. Sangameswaran. A novel voltage-gated sodium channel in human dorsal root ganglia. Program of the 27th Annual Meeting of The Society for Neuroscience, New Orleans, LA, Oct. 25-30, 1997, Abstract 362.3.

P.S. Dietrich, J.G. McGivern, S.G. Delgado, **B.D. Koch**, D.K. Rabert, J.C. Hunter, and L. Sangameswaran. Cloning and expression of PN4 and PN4A, a novel voltage-gated sodium channel and a splice variant, from rat dorsal root ganglia. Program of the 27th Annual Meeting of The Society for Neuroscience, New Orleans, LA, Oct. 25-30, 1997, Abstract 362.2.

J.G. McGivern, **B.D. Koch**, P.S. Dietrich, L. Sangameswaran, and J.C. Hunter. Electrophysiological characterization of the novel tetrodotoxin-sensitive sodium channel, rPN4. Brit. J. Pharmacol. 122, 1997, Abstract 366P.

B.D. Koch, L. Sangameswaran, P. Dietrich, S.G. Delgado, L.M. Fish, R.C. Herman, and J.C. Hunter. Electrophysiological properties of rat homologs of *SCN9A* and *SCN10A* sodium channels expressed in *Xenopus* oocytes. Biophysical Journal 72: A116, 1997, Abstract Tu-AM-F1.

L. Sangameswaran, S.G. Delgado, L.M. Fish, **B.D. Koch**, C. Kozak, L.B. Jakeman, G.R. Stewart, P. Sze, J.C. Hunter, R.M. Eglen, and R.C. Herman. Structure, function, and chromosome mapping of a voltage-gated, tetrodotoxin-resistant sodium channel specific to sensory neurons. Program of the 26th Annual Meeting of The Society for Neuroscience, Washington, D.C., Nov. 16 - 21, 1996, Abstract 32.4.

B.D. Koch, G.R. Stewart, L.B. Jakeman, L. Sangameswaran, S.G. Delgado, L.M. Fish, P. Sze, R.C Herman, R.M. Eglen, and J.C. Hunter. Electrophysiological properties of a cloned tetrodotoxin-resistant sodium channel found primarily in the small cells of the dorsal root ganglia. Abstracts of the 8th World Congress on Pain, Vancouver, B.C. Aug. 17 - 22, 1996, p. 8 - 9.

L. Sangameswaran, S.G. Delgado, L.M. Fish, **B.D. Koch**, L.B. Jakeman, G.R. Stewart, P. Sze, J.C. Hunter, R.M. Eglen, and R.C. Herman. Structure and function of a novel, voltage-gated, tetrodotoxin-resistant sodium channel specific to sensory neurons. Proceedings of the British Pharmacological Society Meeting, April 1996.

L.M. Fish, L. Sangameswaran, S.G. Delgado, **B.D. Koch**, L.B. Jakeman, J. Kwan, and R.C. Herman. Cloning of a sodium channel □-subunit (PN1) from rat dorsal root ganglia. Program of the 25th Annual Meeting of The Society for Neuroscience, San Diego, CA, Nov. 11-16, 1995, Abstract 717.12.

J.C. Hunter, **B.D. Koch**, M.-F. Jett, R.M. Eglen, and D.C. Clarke. Local anesthetics and tricyclic antidepressants attenuate mechanical hyperalgesia and allodynia in experimental models of chronic neuropathic pain. First European Congress of Pharmacology, 1995.

G.F. Faurot, S. Michelson, J. Ravenscroft, A. Tischler, J.C. Hunter, and **B.D. Koch**. Pharmacological characterization of mechanical hyperalgesia in a chronic constriction injury model. Proceedings of the Western Pharmacological Society 38: 152, 1995.

B.D. Koch, M.V. Kopanitsa, G.F. Faurot, and R.M. Eglen. Inhibitors of thapsigargin-activated calcium influx. The Pharmacologist 35: 169, 1993, Abstract 220.

B.D. Koch and R.W. Schekman. Depletion of Sec62p differentially affects translocation of secretory protein precursors and insertion of type II membrane proteins. J. Cell Biology 111: 387a, 1990, Abstract 2151.

B.D. Koch and R.W. Schekman. Soluble factors involved in the post-translational translocation of prepro-□-factor into yeast microsomes. J. Cell Biology 107: 766a, 1988, Absrt 4349.

A. Schonbrunn and **B. D. Koch**. The cyclic AMP-independent mechanism by which somatostatin inhibits pituitary hormone release involves a TBA-sensitive potassium conductance. Program of the 1987 Meeting of the Endocrine Society, Indianapolis, Indiana, June, 1987.

B.D. Koch and A. Schonbrunn. A transmembrane K^+ gradient is required for somatostatin to decrease intracellular free [Ca^{2+}] and inhibit hormone release via a cAMP-independent mechanism. Program of the 16th Annual Meeting of the Society for Neuroscience, Washington, D.C., Nov. 9-14, 1986, Abstract 198.1.

A. Schonbrunn, **B.D. Koch**, and L.J. Dorflinger. Mechanisms by which somatostatin inhibits hormone secretion in GH Cells. Program of the NATO Advanced Workshop on GH Pituitary Cell Strains as Tools in Molecular and Cellular Biology, Fondation Royaumont, France, Nov. 4-8, 1985, Abstract S13.

B.D. Koch and A. Schonbrunn. N_i Mediates somatostatin inhibition of intracellular free [Ca^{2+}] and K^+-stimulated hormone release independently of changes in cAMP levels. Program of the 1985 Endocrine Society Annual Meeting, Baltimore, Maryland, June 19-21, 1985, Abstract 912.

B.D. Koch, L.J. Dorflinger, E. Hewlett, and A. Schonbrunn. Pituitary somatostatin (SRIF) receptors are coupled to the inhibitory guanine nucleotide binding subunit of adenylate cyclase. Program of the IV International Congress of Prolactin, Charlottesville, Virginia, June 27-29, 1984, Abstract 67.

INVITED TALKS

Lead Discovery via High Throughput Screening, SAPA West, Belmont, CA, Dec. 9, 2006.

Evolution of GPCR Screening at Roche, SBS San Francisco Regional Meeting, San Mateo, CA, April 21-22, 2005.

What can HTS tell us about Target “Drugability”? 2004 Bay Area Screening Center Symposium, UCSF, May 1, 2004.

Assay for Sodium Channel Function Using a VIPR™ Reader and a FRET-based Voltage Sensor Dye: A Case Study. IBC ScreenTech Conference, San Diego, CA, March 12-16, 2001.

Assay for Sodium Channel Function Using a VIPR™ Reader and a FRET-based Voltage Sensor Dye: A Case Study. IBC Assay Development Conference, San Diego, CA, Oct. 12-13, 2000.