

Mario Niepel, PhD

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Experienced Harvard researcher with expertise in investigating the efficacy and mechanism of action of kinase inhibitors in cancer, seeking a senior scientist position within an innovative research and development group. Six years of proven leadership of local research teams and multi-institutional collaborations in a competitive academic field. Nine years of experience in quantitative systems biology and pharmacology. Classically trained in biochemistry, molecular biology, and cell biology. Expertise in single-cell microscopy, phenotypic profiling, biomarker discovery, and proteomics.

Professional Experience

Instructor | Laboratory of Systems Pharmacology | Harvard Medical School, Boston, MA 2013-present

- Developed new metrics to improve the identification of drug response biomarkers in pharmacogenomic studies.
- Established a system for automation and standardization of high-throughput drug response experiments which can be implemented in many settings.
- Uncovered mechanisms governing the response to therapeutic drugs in triple negative breast cancer and BRAF(V600E) melanoma cell lines.
- Identified drivers of drug sensitivity by profiling proteome, transcriptome, and drug sensitivities in approximately forty breast cancer cell lines.
- Supervised junior and senior technicians. Mentored graduate, visiting, and summer students.

Scientific Coordinator | NIH-Common Fund Library of Integrated Network-based Cellular Signatures (LINCS) Center | Harvard Medical School, Boston, MA 2010-present

- Led a team of postdoctoral researchers and technicians and coordinated multiple collaborations across diverse labs at the HMS LINCS Center.
- Directed a collaborative project between the HMS and Broad LINCS Centers and jointly directed a common research project across six LINCS Centers.
- Authored 10 of 21 papers published by the HMS LINCS Center, forming the foundation of a successful grant renewal for six additional years of funding.

Instructor | Department of Systems Biology | Harvard Medical School, Boston, MA 2010-present

- Headed a multi-year, collaborative project with Merrimack Pharmaceuticals involving postdoctoral researchers and technicians. Presented the results in peer-reviewed publications and at international conferences.
- Discovered biomarkers of drug sensitivity in breast cancer cell lines.

Scientific Coordinator | NIH-NIGMS Cell Decision Process (CDP) Center | Massachusetts Institute of Technology, Cambridge, MA 2008-2012

- Coordinated weekly meetings and organized annual conferences for ~40 students and postdocs.
- Presented CDP Center research at national and international conferences.

Postdoctoral Fellow | Department of Systems Biology | Massachusetts Institute of Technology, Cambridge, MA and Harvard Medical School, Boston, MA 2006-2010

- Created mechanistic models of the ErbB signaling pathway to understand cell type-specific dynamic responses to growth factors.
- Studied cell line-specific signaling networks in breast cancer by modeling cellular responses to perturbation with growth factors and kinase inhibitors.

Postdoctoral Fellow | Laboratory of Cellular and Structural Biology | The Rockefeller University, New York, NY, USA 2005-2006

- Conceptualized and performed preliminary experiments for a successful multi-year grant, resulting in a publication in *Science*.

Highlights of Technical Achievements

Improved drug response metric: Developed a new method to quantify drug sensitivity in cancer cell lines that corrects for the confounding effects of variable division rates. Defines time-dependent drug sensitivity and allows for accurate comparisons across cell lines, genetic manipulations, or microenvironments in high-throughput assays.

Phenotypic profiling: Developed and applied minimal intervention assays to profile phenotypic responses to small molecule inhibitors in high throughput. Includes assays for single drug screening, synergy profiling, and interrogation of the combined effects of kinase inhibitors and soluble factors of the microenvironment.

Biomarker discovery: Identified biomarkers of drug response and uncovered potential drug response mechanisms in breast cancer and melanoma cell lines by combining perturbation measurements with steady-state proteomic and genomic profiling.

Systems pharmacology: Developed and tested new kinase inhibitors. Identified primary and secondary targets of about 200 compounds to define their target space and interpret transcriptional and high-content imaging drug response screens.

Single-cell biology: Studied the causes of population heterogeneity in response to kinase inhibitor treatments by measuring cell signaling and phenotypic outcomes to drug treatment with single-cell resolution by time-lapse and fixed-cell fluorescent microscopy.

Modeling of cancer signaling pathways: Gained insight into the mechanism of signal transduction pathways relevant to cancer biology. Analyzed data obtained using novel methods to quantify the response to growth factors and kinase inhibitors with proteomic profiling data using statistical and computational models.

Selected Publications

Niepel M*, Hafner M*, Duan Q, Wang Z, Paull EO, et al. (under review) Common and cell-type specific responses to anti-cancer drugs revealed by high throughput transcript profiling. *Nat Communications*

Hafner M*, **Niepel M***, Chung M, Sorger PK. (2016) Growth rate inhibition metrics correct for confounders in measuring sensitivity to cancer drugs. *Nat Methods*. 13(6): 521-7.

Niepel M*, Hafner M*, Pace EA*, Chung M, Chai DH, Zhou L, Muhlich JL, Schoeberl B, Sorger PK. (2014) Molecular determinants of growth factor signaling in genetically diverse breast cancer lines. *BMC Biol*. 12:20.

Niepel M*, Hafner M*, Pace EA*, Chung M, Chai DH, Zhou L, Schoeberl B, Sorger PK. (2013) Profiles of Basal and stimulated receptor signaling networks predict drug response in breast cancer lines. *Sci Signal*. 6(294):ra84.

Chen WW*, **Niepel M***, Sorger PK. (2010) Michaelis-Menten equations and representations of biochemical reactions as dynamical systems. *Genes Dev*. 24(17):1861-1875.

Complete publication list: <http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40644631>

Education

Ph.D. in Cell Biology, The Rockefeller University, New York, NY 1998-2005

Thesis Title: *The Myosin-like Proteins in S. cerevisiae: Multifunctional, Structural Components of the Nuclear Envelope*. (Advisor: Michael P. Rout, Ph.D.)

Recipient: Ph.D. Fellowship, Boehringer Ingelheim Foundation, Mainz, Germany

M.S. in Biochemistry, UC Riverside, Riverside, CA 1997-1998

Thesis Title: *Characterization of the Cap-independent Translational Enhancement Conferred by the 5' Leader of the Tobacco Etch Virus*. (Advisor: Daniel R. Gallie, Ph.D.)

Recipient: Visiting Student Fellowship, UC Riverside, Riverside, CA

Diplom in Molecular Biology, RWTH Aachen, Germany 1991-1997

Thesis Title: *The Effect of mRNA Secondary Structure within the 3' UTR on Translation*. (Advisor: Prof. Dr. Fritz M. Kreuzaler)