

**University of California San Francisco**

**CURRICULUM VITAE**

**Name:** Sina Ghaemmaghami

**Position:** Assistant Professor  
Institute for Neurodegenerative Diseases &  
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**EDUCATION:**

1991-1996	McMaster University, Hamilton, Canada	B.S.	Biochemistry
1996-2001	Duke University, Durham, NC	Ph.D.	Biochemistry

**PRINCIPLE POSITIONS HELD:**

2005-present	University of California, San Francisco, CA	Assistant Professor	Neurology/ IND
2001-2005	University of California, San Francisco, CA	Postdoc. Scholar	Biochemistry
1995-1996	Boehringer Ingelheim, Inc., Montreal, Canada	Scientist	Biochemistry

**HONORS AND AWARDS:**

1991 Ontario Scholarship, Canada

1991-1995 Dean's Honor List, McMaster University, Hamilton, Canada

1995-1996 NSERC (Canada) Undergraduate Industrial Fellowship

1996-1999 NIH Predoctoral Trainee

2001-2002 Howard Hughes Postdoctoral Trainee

2002-2005 NIH Postdoctoral Fellowship

2003-2005 UCSF Postdoctoral Teaching Fellowship

2007-2009 The John Douglas French Alzheimer's Foundation Distinguished Research Scholar Award

**KEYWORDS/AREAS OF INTEREST:**

Protein chemistry, protein folding, high throughput biology, microscopy, automated assay design, proteomics, genomics, microarrays, prions, yeast molecular biology, gene regulation

## **PROFESSIONAL ORGANIZATIONS:**

1996-present American Association for the Advancement of Science  
1996-present The Protein Society  
2001-2002, 2005 Howard Hughes Medical Institute  
2007-present San Francisco Neurological Society

## **INVITED PRESENTATIONS:**

Protein Society Symposium, San Diego, CA, 2000 (selected speaker)  
International Symposium on Mass Spectrometry in the Health and Life Sciences, San Francisco, CA, 2001 (poster)  
Vanderbilt Genomic Conference, Nashville, TN, May 2002 (poster)  
Yeast Genetics and Molecular Biology Meeting, Madison, WI, 2002 (selected speaker)  
American Association of Pharmaceutical Scientists (AAPS) Annual Conference, Toronto, Canada, 2002 (invited speaker)  
Beyond Genome 2004: Proteomics, San Francisco, CA, 2004 (invited speaker)  
Duke Symposium on Computational Protein Biology, Durham, NC, 2004 (invited speaker)  
Genentech Research in Progress Series, 2004, San Francisco, CA (invited speaker)  
Fairchild Foundation Symposium, 2006, San Francisco, CA (invited speaker)  
Fairchild Foundation Symposium, 2007, San Francisco, CA (invited speaker)  
Fairchild Foundation Symposium, 2009, San Francisco, CA (invited speaker)  
Fairchild Foundation Symposium, 2010, San Francisco, CA (invited speaker)

## **PUBLIC SERVICE:**

1998 Advisor for underprivileged students summer research program, Duke University, Durham, NC  
2003-present Advisor for San Francisco Unified School District

## **TEACHING EXPERIENCE:**

1994-1995 Undergraduate general and organic chemistry teaching assistant, McMaster University, Hamilton, Canada  
1996-2001 Mentor for five undergraduate students, Duke University, Durham, NC  
1998 Graduate biophysical chemistry teaching assistant, Duke University, Durham, NC  
2001-present Mentor for two graduate students and one lab technician, Department of Cellular and Molecular Pharmacology, UCSF  
2003-2005 Postdoctoral Teaching Fellow: Developed and taught lectures for an Introductory Biochemistry class at San Francisco State University.  
2006-2007 Developed and thought lecture for graduate course on neurodegenerative diseases at UCSF (NS225)  
2005-2009 Mentor for eight postdoctoral fellows and six research assistants at IND/UCSF

## **RESEARCH GRANTS:**

My research is supported by a grant from the Fairchild Foundation (444973-85586), The John Douglas French Alzheimer's Foundation and UCSF Alzheimer's Disease Research Center (ADRC) Pilot Research Project Award

**PEER REVIEWED PUBLICATIONS:**

1. S. Ghaemmaghami, J.M. Word, R.E. Burton, J.S. Richardson and T.G. Oas (1998). Folding Kinetics of a Fluorescent Variant of Monomeric  $\lambda$  Repressor. **Biochemistry** 37, 9179-9185
2. S. Ghaemmaghami, M.C. Fitzgerald and T.G. Oas (2000). A Quantitative, High-Throughput Screen for Protein Stability. **Proc. Natl. Acad. Sci. USA** 97, 8296-8301
3. S. Ghaemmaghami and T.G. Oas (2001). Quantitative Protein Stability Measurement In Vivo. **Nat. Struct. Biol.** 8, 879-882
4. K.D. Powell, S. Ghaemmaghami, M.Z. Wang, M. Liyuan, T.G. Oas and M.C. Fitzgerald (2002). A General Mass Spectrometry-Based Assay for the Quantitation of Protein-Ligand Binding Interactions in Solution. **J. Am. Chem. Soc.** 124, 10256-10257  
(Co-first author)
5. S. Ghaemmaghami, W.K. Huh, K. Bower, R.W. Howson, A. Belle, N. Dephoure, E.K. O'Shea and J.S. Weissman (2003). Global Analysis of Protein Expression in Yeast. **Nature** 425, 737-741
6. R. Howson, W.K. Huh, S. Ghaemmaghami, J.V. Falvo, K. Bower, A. Belle, N. Dephoure, D.D. Wykoff, J.S. Weissman and E.K. O'Shea (2005). Construction, Verification, and Experimental Use of Two Epitope-Tagged Collections of Budding Yeast Strains. **Comp. Funct. Genomics** 6, 2-16
7. J.R.S. Newman, S. Ghaemmaghami, J. Ihmels, D.K. Breslow, M. Noble, J.L. DeRisi and J.S. Weissman (2006) Single-cell proteomic analysis of *S. cerevisiae* reveals the architecture of biological noise. **Nature** 441, 840-846
8. S. Ghaemmaghami, P.W. Phuan, B. Perkins, J. Ullman, B.C. May, F.E. Cohen, S.B. Prusiner (2007) Cell division modulates prion accumulation in cultured cells. **Proc. Natl. Acad. Sci. USA** 104, 17971-17976
9. N.T. Ingolia, S. Ghaemmaghami, J.R.S. Newman, and J.S. Weissman (2009) Genome-Wide Analysis In Vivo of Translation with Nucleotide Resolution Using Ribosome Profiling. **Science** Apr 10 v324, 218-223.
10. Ghaemmaghami S, Ahn M, Lessard P, Giles K, Legname G, DeArmond SJ, Prusiner SB. (2009) Continuous quinacrine treatment results in the formation of drug-resistant prions. **PLoS Pathog.** Nov;5(11):e1000673. Epub 2009 Nov 26.
11. Ghaemmaghami S, Ullman J, Ahn M, St Martin S, Prusiner SB. (2009) Chemical induction of misfolded prion protein conformers in cell culture. **J Biol Chem.** Dec 7. [Epub ahead of print]
12. Ghaemmaghami S, May BC, Renslo AR, Prusiner SB. (2009) Discovery of 2-aminothiazoles as potent antiprion compounds. **J Virol.** Dec 23 [Epub ahead of print] (PMID: 20032192)

## **PATENT:**

"Quantitative, high-throughput screening method for protein stability," Patent number 6,734,023

## **FIVE SIGNIFICANT RECENT PUBLICATIONS:**

1. S. Ghaemmaghami, M.C. Fitzgerald and T.G. Oas (2000). A Quantitative, High-throughput Screen for Protein Stability. Proc. Natl. Acad. Sci. USA 97, 8296-8301  
*I developed a novel high-throughput mass-spectrometry based approach for measuring ligand binding to proteins.*
2. S. Ghaemmaghami, W.K. Huh, K. Bower, R.W. Howson, A. Belle, N. Dephoure, E.K. O'Shea and J.S. Weissman (2003). Global Analysis of Protein Expression in Yeast. Nature 425, 737-741  
*I constructed a comprehensive chromosomally tagged fusion library in yeast (*Saccharomyces cerevisiae*). The library has allowed the development of a large number of proteome-wide mass-spectrometry-based functional assays.*
3. S. Ghaemmaghami, P.W. Phuan, B. Perkins, J. Ullman, B.C. May, F.E. Cohen, S.B. Prusiner (2007) Cell division modulates prion accumulation in cultured cells. Proc. Natl. Acad. Sci. USA 104, 17971-17976  
*I developed an experimentally verified model for the propagation of prions in cultured cells.*
4. N.T. Ingolia, S. Ghaemmaghami, J.R.S. Newman, and J.S. Weissman (2009) Genome-Wide Analysis In Vivo of Translation with Nucleotide Resolution Using Ribosome Profiling. **Science** Apr 10 v324, 218-223.  
*I initiated the development of a technique for genome-wide analysis of protein translation.*
5. S. Ghaemmaghami, Ahn M, Lessard P, Giles K, Legname G, DeArmond SJ, Prusiner SB. (2009) Continuous quinacrine treatment results in the formation of drug-resistant prions. **PLoS Pathog.** Nov;5(11):e1000673.  
*The first report of the development of drug-resistance in prions.*

## **RESEARCH DESCRIPTION:**

My recent research has focused on developing large-scale screens that can identify potential therapeutics for protein-misfolding neurodegenerative diseases. In particular, I have developed a cell-based screen that can identify small molecules that selectively lower the expression level of the prion protein (PrP). The screen utilizes high throughput cell imaging to quantify the amount of PrP protein expressed on the surface of neuroblastoma cells. By fully automating the process of drug addition, cell growth, fluorescence staining, microscopy and image analysis, we are currently able to screen 2400 compounds every week. By minutarizing the assay to 384 well format we are aiming to achieve a throughput of 10,000 compounds in the near future. Detection of small molecules that decrease the abundance of PrP is a powerful screen for the identification of promising lead compounds with therapeutic efficacy.

### ***Future Goals***

Compounds that pass this initial screen will undergo chemical optimization in order to increase their potency and reduce their lethal dosage. Optimized hits will then be studied in our transgenic mice models expressing human PrP in order to determine their efficacy, toxicity and blood-brain penetrance in an animal model. Using this drug pipeline we are hoping to bring promising drug candidates to clinical trials within the next 2 years.

The strategy of identifying small compounds that specifically lower protein expression levels can potentially be applied to a wide range of neurodegenerative disorders that are characterized by folding of proteins into aberrant forms. Such screens can identify promising lead compounds that can then enter the existing validation pipeline at the Institute for Neurodegenerative Diseases. I believe that this strategy may considerably improve the current drug discovery pipeline and significantly shorten the concept-to-clinic timeline for a number of neurodegenerative disorders.

### ***Teaching Duties***

My primary teaching duties involve mentoring several postdoctoral scholars and research associates. I will also actively supervise a number of the technical staff. Additionally, I participate in a number of laboratory meetings, journal clubs and discussion groups and have delivered several presentations.