SANJIVE QAZI, Ph.D.

Nationality:	British, U.S. Permanent Resident
Home Address:	535 Capitol Drive, St. Peter, MN 56082
Phone Number:	(507)-931-5391
Email:	mcbqazi@netzero.net

EMPLOYMENT

2007- : Faculty Instructor at Gustavus Adolphus College, St. Peter, Minnesota.

Teaching experience:
Cellular and Molecular Biology labs
Organismal Biology labs
Microbes for Human Health labs
Neurobiology of Emotions for J-term

2004-2007: Staff Scientist at Paradigm Pharmaceuticals, Roseville, Minnesota.
2000-2007: Staff Scientist at the Parker-Hughes Institute in the Bioinformatics Dept, Roseville, Minnesota.

Accomplishments include:

Working on complex, difficult problems: Published papers in respected international journals for a novel mathematical technique to simulate biochemical reactions in noisy environments; Hypothesis for biochemical basis for fire-fly flashes (in the journal Science); Practical statistical method to combine data sets for Survival analysis from published clinical trials; Developed a powerful analysis to compare non-linear time series plots for cancer growth, drug dissolution; Parameter estimation for receptor binding and enzyme kinetic curves.

Mediating work in multi-disciplinary teams to gain novel insights into biological function and therapeutics: last two jobs resulted in co-authorships in more than 40 peer reviewed articles with 24 Scientists, 5 Graduate students, 5 Undergraduate students, 3 Oncologists and a Nurse.

Developing passions for learning and applying both theoretical and experiential knowledge in diverse collaborative projects: preclinical development of 6 drugs (anti-cancer, anti-HIV and anti-allergy); published 6 papers on receptor characterization, 5 on signal transduction pathways, 10 papers screening for drug resistant HIV strains, 5 on structure activity relationships, 3 on in-vivo toxicity studies, 3 on drug formulation, 8 on pro-drug activation and 3 on clinical efficacy of anti-cancer drugs.

Implementing data standards for hypothesis testing and federal regulatory requirements in the award of grants to fund drug discovery efforts (anti-HIV, anti-cancer compounds): funded as an investigator for a grant NIH/NIAID entitled, 'Formulation of Dosage Forms of the Anti-HIV Agent, DDE113', and contributed to writing of four other large grants.

Leveraging analytical tools to identify key gene expression changes induced in cancer cells or virus infections using high-throughput screens (>12000 genes interrogated) requiring in-depth knowledge of data structure: probability of finding false negative, true negative, false positive and true positive genes, number of outliers, data inconsistencies, correlation patterns and trends.

- External Advisor for Masters Students at University Minnesota (Stephanie Potoka for completion of Masters on modeling Gene Regulatory Networks from gene profiling data) and McGill University (Martin Caberlin on simulation of ionic currents in the brain). (2002-2006).

1992-2000: Research Associate at Tufts Uni., Medford, with Dr. B.A. Trimmer. Appointment sponsored by NIH post-doctoral fellowship (1992-1993, 1997-2000) and Whitehall Foundation (1993-1997).

Muscarinic receptors and second messenger modulation of motor function in Manduca sexta.

My focus on signal transduction in the insect *M. sexta* enabled me to develop an interdisciplinary approach to studying receptor activation of biochemical pathways. My experience includes:

Pharmacological characterization of receptors using radioligand binding assays (saturation, inhibition and kinetic experiments).

Investigating coupling to second messenger pathways [cAMP/cGMP (RIA) and inositol phosphates (HPLC)], and enzyme kinetics for phospholipase C and inositol 1,4,5-trisphosphate 5-phosphatase.

Video imaging of calcium responses in primary neuronal culture using fluorescent calcium sensitive ratiometric dyes (Ionoptix system). Using fluorescent dyes (DAF-2) to measure nitric oxide release.

Measuring the effects of neuroactive agents on motoneuron activity using extracellular recording techniques (e.g. cholera and pertussis toxin).

Using data analysis and advanced statistical techniques (LIGAND, SYSTAT, RC Electronics, PCLAMP, MATHCAD, S-PLUS, EXCEL).

Kinetic simulation of biochemical pathways; Derivation of analytic expressions to solve for bimolecular interactions: numerical solutions for ordinary differential equations; linear matrix algebra and information theory.

Courses attended: Non-linear Dynamics and Chaos Theory (Math. Dept., Tufts University with Dr. Christoph Borgers). Modeling dynamics in Olfactory systems (Seminar Course at Boston University).

- Co-teacher with Dr. Susan Ernst of a graduate student seminar course entitled 'Signal transduction mechanisms in growth and development' (Spring 1996).

- Teaching Assistant for Biochemists at Bath University. Used various separation techniques (Anion exchange, Sephadex columns, Thin-layer chromatography) to isolate and characterize biological compounds (1990-1991).

- Course instructor for an Applied Biology Lab at Bath University. Course included comparative anatomy, physiology and radiolabeling techniques (1988-1991).

COMPUTER SKILLS

- Word, Excel, Powerpoint, JMP SAS, Systat, SPSS, GraphPad for receptor binding and enzyme kinetics.
- Programming: Mathcad, Visual Basic, HTML, Visual Basic Script.

STATISTICAL/MATHEMATICAL SKILLS

- Kinetic simulation of biochemical pathways: ODE numerical solvers and developed a novel method using analytic solutions in simultaneous sets of difference equations.
- Statistics: Non-parametric comparisons, Non-linear curve-fitting techniques, ANCOVA, ANOVA, Linear Contrasts, Monte-Carlo simulations, Multivariate Analysis of Variance methods, determination of false discovery rates in high dimensional data sets.
- Classification of variables/subjects: Hierarchical Cluster Analysis, 2D-Self-Organizing Maps, Factor analysis, Canonical analysis.
- Time series analysis: Parametric log-normal/Kaplan Meier survival analysis, Cancer growth models, Phase-plane analysis, Fourier transforms, Time-series projections with confidence intervals.
- Geneprofiling data mining: Genesight, Osprey, Affymetrix suite, model building using JMP SAS software.
- Bioinformatic software: BLAST sequence analysis, Transcription factor motif recognition algorithms.

- Sample size and power calculations for SBIR grants, IND and IRB evaluations.
- GMP validation studies for formulation and dissolution studies.

EDUCATION

1988-1992: PhD CASE studentship at Bath University, UK.
Collaborating CASE institution: Zeneca Agrochemicals, Jeallotts Hill, Berks., UK.
Supervisors: Prof. G.G. Lunt, Dr. F.G.P. Earley, Dr. S. Dunbar.
Acetylcholine muscarinic receptors and phosphatidylinositol turnove in the locust CNS.

Investigated muscarinic stimulation of inositol phosphates and phospholipids using anion exchange chromatography, TLC, HPLC and enzyme kinetics. Used radioligand binding studies to pharmacologically characterize the muscarinic receptor using agonists and antagonists. I gained training and expertise in the use of Fortran, techniques in Good Microbiological Practice, and a lecture course in Genetic Manipulations.

1985-1988: University of Sheffield, Sheffield, U.K.
Course: Physiology/Zoology (BSc. Special Honors)
Degree: Upper second.

Courses: Human Physiology, Neurobiology, Invertebrate and Vertebrate Biology, Anatomy and Cell biology, Microbiology, Biochemistry.

Research Investigations include:

The neuromuscular junction of crab leg. Investigation of the electro-physiology and pharmacology of the excitatory and inhibitory synapses at the neuromuscular system.

The effect of competition on biodiversity in freshwater systems (study performed at Malham Tarn, N. Yorks.).

The effects of chilies and saponins on gut function. Measured the effect on mouth to caecum transit time using the hydrogen breath technique, gastric emptying using a gamma camera, whole gut transit time using recovery of radio-opaque markers in faeces and permeability changes by determining the absorption of lactulose and mannitol through the gut wall.

1985: Culverhay Secondary School, Bath, U.K**.,** 'A' Levels obtained: Biology grade B, Chemistry grade A, Mathematics (Pure and Applied) grade B.

VOLUNTARY AND PROFESSIONAL SOCIETIES

Society for Industrial and Applied Mathematics (2002-2004)
Society for Neuroscience (1992-1999)
AAAS (1993-1994).
Biochemical Society (1988-1991).
Treasurer for Neurosoc (seminar course) at Bath Uni (1989-1991)
Member of the Management Committee of the Bath Asian Council (1989-1991).
Student Welfare Officer at Sheffield Uni. (1986-1988).
Treasurer of Uni. of Bath Schools Science Society (1984).

ORAL PRESENTATIONS

2007: Invited speaker at China-Canada Workshop on Industrial Mathematics. 'Processing of physiological signals by biochemical systems: emergence of high frequency waveforms from low frequency inputs in brain receptors.

2002: Invited Speaker at McGill Applied Math Dept. 'Mathematical models that explore signal processing by cell membrane receptors'

2001: Invited Speaker at Institute of Applied Mathematics and its Applications ' Screening the effect of a potent new Anti-HIV compound on HIV infected cells using oligonucleotide arrays to measure gene expression.'

1999: Invited speaker at Brandeis University 'Biochemical integration in the nervous system'

1995: Invited speaker at Zeneco agrochemicals, Jeallotts Hill, England on 'The role of muscarinic receptors in the insect nervous system.'

1992: 1993, 1994, 1995, 1996: Oral presentations at Nerve Net Meeting, Marine Biological Labs., Woods hole, Cape Cod, Mass.

1989: Postgraduate meeting at the Society of Chemical Industries, London

PUBLICATIONS

1. Qazi S, Lunt GG (1989). Inositol phosphates in locust ganglia: effects of muscarinic stimulation. Proc. Int. Symp. Molec. Insect Sci. Editors Hildebrand J, Hagedorn HH, Plenum Press (1991).

2. Qazi S, Lunt GG, Blythe JL, Earley FGP (1991). Phosphatidylinositol metabolism in insect nervous system. Extended Summaries Neurotox '91, Pesticide Science. 33: 249-252.

3. Trimmer BA, Qazi S (1996). Modulation of second messengers in the nervous system of larval Manduca sexta by muscarinic receptors. J. Neurochemistry. 66(5): 1903-1913.

4. Qazi S, Proulx DR, Trimmer BA (1996). Characterization of muscarinic binding sites in the central nervous system of larval Manduca sexta. Insect Biochemistry and Molecular Biology. 26: 721-732.

5. Qazi S, Trimmer BA (1999). The role of nitric oxide in muscarinic evoked changes in cGMP and motoneuron spike activity in the CNS of larval Manduca sexta. Journal of Comparative Physiology A. 185: 539-550.

6. Qazi, S and Trimmer, B.A. (1999). The role of inositol 1,4,5-trisphosphate 5-phosphatase in inositol signaling in the CNS of larval Manduca sexta. Insect Biochemistry and Molecular Biology. 29, 161-175.

7. Zayas RM, Qazi S, Morton DB, Trimmer BA (2000). Neurons involved in nitric oxide mediated cGMP signaling in the tobacco hornworm, Manduca sexta. Journal of Comparative Neurology. 419(4): 422-438.

8. Pfarr KM, Qazi S, Fuhrman JA (2001). Nitric oxide synthase in filariae: demonstration of nitric oxide production by embryos in Brugia malayi and Acanthocheilonema viteae. Exp. Parasitol. 97(4): 205-214.

9. Trimmer BA, Aprille JR, Dudzinski DM, Lagace CJ, Lewis SM, Michel T, Qazi S, Zayas RM (2001). Nitric oxide and the control of firefly flashing. Science. 292(5526): 2486-2488.

10. Vermehren A, Qazi S, Trimmer BA (2001). The nicotinic alpha subunit MARA1 is necessary for cholinergic evoked calcium transients in Manduca neurons. Neurosci Lett 313(3): 113-116.

11. Zayas RM, Qazi S, Morton DB, Trimmer BA (2002). Nicotinic-acetylcholine receptors are functionally coupled to the nitric oxide/cGMP-pathway in insect neurons. J Neurochem. 83: 421-431.

12. Uckun FM, Qazi S, Pendergrass S, Lisowski E, Waurzyniak B, Chen CL, Venkatachalam TL (2002). In Vivo Toxicity, Pharmacokinetics, and Anti-Human Immunodeficiency Virus Activity of Stavudine-5'-(p-Bromophenyl Methoxyalaninyl Phosphate) (Stampidine) in Mice. Antimicrob. Agents Chemother. 46(11): 3428-3436.

13. Uckun FM, Pendergrass S, Venkatachalam TK, Qazi S, Richman D (2002). Stampidine Is a Potent Inhibitor of Zidovudine- and Nucleoside Analog Reverse Transcriptase Inhibitor-Resistant Primary Clinical Human Immunodeficiency Virus Type 1 Isolates with Thymidine Analog Mutations. Antimicrob. Agents Chemother. 46(11): 3613-3616.

14. D'Cruz OJ, Venkatachalam TK, Mao C, Qazi S, Uckun FM (2002). Structural Requirements for Potent Anti-Human Immunodeficiency Virus (HIV) and Sperm-Immobilizing Activities of Cyclohexenyl Thiourea and Urea Non-Nucleoside Inhibitors of HIV-1 Reverse Transcriptase. Biol. Reprod. 67(6): 1959-74.

15. Uckun F.M., Samuel P., Qazi S., Chen. C. Pendergrass S. and T.K. Venkatachalam (2002). Effects of Aryl substituents on the anti-HIV activity of the arylphosphoramidate derivatives of stavudine. Antiviral Chemistry & Chemotherapy. 13(3): 197-203.

16. Qazi S, Samuel P, Venkatachalam TK, Uckun FM (2003). Evaluating dissolution profiles of an anti-HIV agent using ANOVA and non-linear regression models in JMP software. International Journal of Pharmaceutics. 252(1-2): 27-39.

17. Venkatachalam TK, Qazi S, Samuel P, Uckun FM (2003). Inhibition of mast cell leukotriene release by thiourea derivatives. Bioorg Med Chem Lett. 13(3): 485-488.

18. Venkatachalam TK, Qazi S, Samuel P, Uckun FM (2003). Substituted heterocyclic thiourea compounds as a new class of anti-allergic agents inhibiting IgE/Fc varepsilon RI receptor mediated mast cell leukotriene release. Bioorg Med Chem. 11(6): 1095-105.

19. Uckun FM, Chen CL, Samuel P, Pendergrass S, Venkatachalam TK, Waurzyniak B, Qazi S (2003). In vivo antiretroviral activity of stampidine in chronically feline immunodeficiency virus-infected cats. Antimicrob Agents Chemother. 47(4): 1233-1240.

20. Qazi S, Beltukov A, Trimmer BA (2004). Simulation modeling of ligand receptor interactions at non-equilibrium conditions: processing of noisy inputs by ionotropic receptors. Mathematical Biosciences. 187(1): 93-110.

21. Uckun FM, Pendergrass S, Qazi S, Samuel P, Venkatachalam T (2003). Phenyl Phosphoramidate Derivatives of Stavudine as Anti-HIV Agents with Potent and Selective Antiviral Activity Against Adenovirus. European Journal of Medicinal Chemistry. 39(3): 225-234.

22. Venkatachalam TK, Goodman PA, Qazi S., D'Cruz O, Uckun FM (2004). Rational drug design of multifunctional phosphoramidate substituted nucleoside analogs. Current Pharm Des. 10(15): 1713-1726.

23. Venkatachalam TK, Samuel P, Li G, Qazi S, Mao C, Pendergrass S, Uckun FM (2004). Lipase-mediated stereoselective hydrolysis of stampidine and other phosphoramidate derivatives of stavudine. Bioorg Med Chem. 12(12): 3371-81.

24. Venkatachalam TK, Yu G, Samuel P, Qazi S, Pendergrass S, Uckun FM (2004). A comparative study of the hydrolysis pathways of substituted aryl phosphoramidate versus aryl thiophosphoramidate derivatives of stavudine.Eur J Med Chem. 39(8): 665-683.

25. Uckun FM, Vassilev A, Dibirdik I, Liu XP, Erbeck D, Tibbles H, Qazi S, Venkatachalam T (2004). Anti-Cancer Activity Profile of 3'-Azidothymidine 5'-[p-Methoxyphenyl methoxyalaninyl phosphate] (Compound 003), a Novel Nucleoside Analog. Arzneimittel Forschung/Drug Research. 54(11): 715-731.

26. Venkatachalam T, Samuel P, Qazi S, Uckun FM (2005). Protease Mediated Enzymatic Hydrolysis and Activation of Aryl Phosphoramidate Derivatives of Stavudine. Eur J Med Chem. 40(5): 452-466.

27. Uckun FM, Venkatachalam T, Qazi S (2005). In Vitro Anti-HIV Potency of Stampidine Alone and in Combination with Standard Anti-HIV Drugs. Arzneimittel Forschung/Drug Research. 55(4): 223-231.

28. Venkatachalam T, Samuel P, Qazi S, Uckun FM (2005). Effect of change in nucleoside structure on the activation and antiviral activity of phophoramidate derivatives. Bioorg Med Chem. 13(18), 5408-5423.

29. Venkatachalam T, Anderson M, Qazi S, Uckun FM (2006). Synthesis, Separation and Anti-HIV Activity of Distereoisomers of N-[p-(4-Bromophenyl)-2',3'-didehydro-3'-deoxy-5'-thymidylyl-L-alanine Methyl Ester (Stampidine). Arzneimittel Forschung/Drug Research. 56(2a): 152-158.

30. Uckun FM, Venkatachalam T, Qazi S (2006). Potency of Stampidine Against Multi-Nucleoside Reverse Transcriptase Inhibitor Resistant Human Immunodeficiency Virus. Arzneimittel Forschung/Drug Research. 56(2a), 193-203.

31. Venkatachalam T, Qazi S, Uckun FM (2006). Site-Specific Enzyme Activation of the Anti-HIV Agent Stampidine. Arzneimittel Forschung/Drug Research. 56(2a): 167-175.

32. Venkatachalam T, Qazi S, Uckun FM (2006). Synthesis and metabolism of naphthyl substituted phosphoramidate derivatives of stavudine. Bioorg Med Chem. 2006 Aug 1;14(15):5161-77.

33. Venkatachalam T, Sarquis M, Qazi S, Uckun FM (2006). Effect of alkyl groups on the cellular hydrolysis of stavudine phosphoramidates. Bioorg Med Chem. Sep 15;14(18):6420-33.

34. Lundell K, Qazi S, Eddy L, Uckun FM (2006). Clinical activity of folinic acid in patients with chronic fatigue syndrome. Arzneimittelforschung. 56(6):399-404.

35. Uckun FM, Morar S, Qazi S. (2006). Vinorelbine-based salvage chemotherapy for therapy-refractory aggressive leukaemias. Br J Haematol. Nov;135(4):500-8.

36. Qazi S, DuMez D, Uckun FM. (2007). Meta analysis of advanced cancer survival data using lognormal parametric fitting: a statistical method to identify effective treatment protocols. Curr Pharm Des.;13(15):1533-44. Review.

37. Uckun FM, DuMez D, Qazi S, Tibbles H, Venkatachalam TK. (2007). Anti-retroviral activity of GMP-grade stampidine against genotypically and phenotypically nucleoside reverse transcriptase inhibitor resistant recombinant human immunodeficiency virus. An in vitro study. Arzneimittelforschung.;57(2):112-21.

38. Uckun FM, Erbeck D, Tibbles H, Qazi S, Venkatachalam TK. (2007). Improved oral bioavailability of anti-HIV agent N'-[2-(2-thiophene)ethyl]-N'-[2-(5-bromopyridyl)]-thiourea (HI-443) in a novel lipophilic formulation. Arzneimittelforschung.;57(3):164-70.

39. Uckun FM, Tibbles H, Erbeck D, Venkatachalam TK, Qazi S. (2007). In vivo pharmacokinetics and toxicity of a novel hydrophilic oral formulation of the potent non-nucleoside reverse transcriptase inhibitor compound N'-[2-(2-thiophene)ethyl]-N'-[2-(5-bromopyridyl)]-thiourea (HI-443).
Arzneimittelforschung.;57(4):218-26

40. Uckun FM, Qazi S, Venkatachalam T. (2007). N'-[2-(2-thiophene) ethyl]-N'-[2-(5-bromopyridyl)] thiourea (HI-443), a rationally designed non-nucleoside reverse transcriptase inhibitor compound with potent anti-HIV activity. Arzneimittelforschung.;57(5):278-85.

41. Uckun FM, Erbeck D, Qazi S, Venkatachalam T, Tibbles HE, Vassilev A. (2007). Effect of targeting janus kinase 3 on the development of intestinal tumors in the adenomatous polyposis coli(min) mouse model of familial adenomatous polyposis. Arzneimittelforschung.;57(6):320-9.

42. Uckun FM, Dibirdik I, Qazi S, Vassilev A, Ma H, Mao C, Benyumov A, Emami KH. (2007). Anti-breast cancer activity of LFM-A13, a potent inhibitor of Polo-like kinase (PLK). Bioorg Med Chem. Jan 15;15(2):800-14. Epub 2006 Oct 26.

43. Uckun FM, Tibbles H, Ozer Z, Qazi S, Vassilev A. (2008). Anti-inflammatory activity profile of JANEX-1 in preclinical animal models. Bioorg Med Chem. Feb 1;16(3):1287-98. Epub 2007 Oct 24.

44. Qazi S, Caberlin M, Nigam N. (2007). Mechanism of psychoactive drug action in the brain: simulation modeling of GABAA receptor interactions at non-equilibrium conditions. Curr Pharm Des.;13(14):1437-55. Review.

Completed Research Support:

1 R43 AI063985-01 DuMez (PI) 3/15/05 - 2/28/06
NIH/NIAID
Formulation of Dosage Forms of the Anti-HIV Agent, DDE113
Role: Co-Investigator