CURRICULUM VITAE

Jayarama Bhat Gunaje

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Education:

Institution	Degree	Year	Field
Mysore University, Mysore, India	B.S.	1980	Biology
Mangalore University, India	M.S.	1982	Biosciences
Indian Institute of Science, India	Ph.D.	1989	Biochemistry

Postgraduate training:

1988-1991 Postdoctoral fellow, Seattle Biomedical Research Institute, Seattle.

1991-1993 Postdoctoral fellow, ZymoGenetics Corporation, Seattle.

Employment:

1993-97: Associate/Research Scientist, Weis Center for Research, Geisinger Clinic, Danville, PA.

1997-98: Assistant Professor, Henry Hood M.D. Research Program, Weis Center for Research, The Penn State University College of Medicine, Danville, PA.

1998-00: Assistant Professor, Department of Specialty Care Services, The University of Texas Health Sciences Center at Tyler, Tyler, TX.

2000-03: Senior Scientist, Icogen Corporation, Seattle, WA.

2004-2011 Associate Professor, Texas Tech University Health Sciences Center School of Pharmacy, Amarillo, TX.

2011-present Associate Professor, South Dakota State University College of Pharmacy, Brookings, SD.

Honors/Awards:

1989 ShamaRao Kaikini Medal (best thesis award) from Indian Institute of Science, India.

1997 Second place in the Pharmacia &Upjohn young investigator award competition. XIV Annual meeting, International Society for Heart Research, Vancouver, Canada.

2005 Texas Tech University Health Sciences Center School of Pharmacy-Graduate teacher of the year award.

2006 Texas Tech University Health Sciences Center School of Pharmacy- Graduate Teaching Team of the Year Award (Biochemistry).

2009 Unsung Hero Award in recognition of hard work and dedication to the students of the Texas Tech University Health Sciences Center.

2011 Texas Tech University Health Sciences Center School of Pharmacy, P1 Teaching Team of the Year Award (Biochemistry).

2011 Texas Tech University Health Sciences Center School of Pharmacy, Graduate Teaching Team of the Year Award (Research Design and Analysis).

2011 Texas Tech University Health Sciences Center School of Pharmacy, Graduate Teacher of the Year Award.

2011 Texas Tech University Health Sciences Center School of Pharmacy, Graduate Mentor for all 2010-2011.

2012 South Dakota State University- TRiO SSS Students' Choice Award for the Fall 2012 Semester (for the exceptional efforts put forth so many students, including TRiO students, can succeed).

2013- Pharmacy College Teacher of the Year award (for the academic year 2012-13), South Dakota State University College of Pharmacy, Brookings, SD.

2016- Excellence in Research and Scholarly Activity, South Dakota State University College of Pharmacy, Brookings, SD.

Extramural Funded Grant Support:

1994-96 Principal Investigator, American Heart Association (AHA)-PA affiliate Grant-In-Aid "Transcriptional control of proto-oncogenes by Angiotensin II in cardiac cells". Total award: $70,000

1996-99 Principal Investigator, AHA (National) Grant-In-Aid "Mechanism of activation of transcription factor Stat92 by Angiotensin II". Total award: $165,000

1997-99 Principal Investigator, AHA PA affiliate Grant-In-Aid "Activation of STAT transcription factors by α-thrombin in vascular smooth muscle cells". Total award: $70,000.

2000-03 Principal Investigator, RO1 grant from NIH "Control of Interleukin-6-signaling by α-thrombin in lung fibroblasts". (7RO1HL66000) Total award: $732,000

2009-11 Principal Investigator, RO3 grant from NIH "p53 Acetylation as a Mechanism in Chemoprevention by Aspirin" (1RO3CA133061). Total Award: $148,500.

Internal Funded Grant Support:

2012-13- SDSU Translational Cancer Research Center seed grant "Novel Mechanisms of Chemoprevention by Aspirin". Role: PI; Total award- $30,000.

2014-15: Scholarly Faculty Excellence Fund (Office of Research, SDSU); Cyclins as Novel Targets of Aspirin in Chemoprevention. Role: PI; Total award: $7500.

Society Memberships:

Member-American Association for Cancer Research
Member- Rho Chi Society
Honorary member- Golden-Key International Honors Society (S.D.S.U. Chapter)

Publications:

1. Dwarki, V.J., Francis, V.S.N.K., **Bhat, G.J**. and Padmanaban, G. (1987). Regulation of cytochrome P-450 mRNA and apoprotein levels by heme. J. Biol. Chem. 262, 16958-16962.

2. **Bhat, G.J.**, Rangarajan, P.N. and Padmanaban, G. (1987). Differential effects of cycloheximide on rat liver cytochrome –P-450 gene transcription in the whole animal and hepatoma cell culture. Biochem. Biophys. Res. Comm. 148, 1118-1123.

3. **Bhat, G.J**. and Padmanaban, G. (1988). Heme regulates cytochrome P-450 gene transcription elongation. Biochem. Biophys. Res. Comm. 151, 737-742.

4. **Bhat, G.J**. and Padmanaban, G. (1988). Heme is a positive regulator of cytochrome P-450 gene transcription. Arc. Biochem. Biophys. 264, 584-590.

5. **Bhat, G.J**., Koslowsky, D.J., Feagin, J.E., Smiley, B.L. and Stuart, K. (1990). An extensively edited mitochondrial transcript in kinetoplastids encodes a protein homologous to ATPase subunit 6. Cell 61, 885-894.

6. Koslowsky, D.J., **Bhat, G.J**., Perrolaz, A.L. Feagin, J.E. and Stuart, K. (1991). The MURF3 gene of T. Brucei contains multiple domains of extensive RNA editing and is homologous to a subunit of NADH dehydrogenase. Cell 62, 901-911.

7. **Bhat, G.J**., Lodes, M.J., Myler, P.J. and Stuart, K. (1991). A simple method for cloning blunt ended DNA fragments. Nucl Acids Res. 19, 398.

8. Koslowsky, D.J., **Bhat, G.J.**, Read, L.K and Stuart, K. (1991). Cycles of progressive alignment of gRNA with mRNA in RNA editing. Cell 67, 537-546.

9. **Bhat, G.J.**, Myler, P.J., and Stuart, K. (1991). The two ATPase 6 mRNAs of Leismania tarentolae differ in the 3' ends. Mol. Biochem. Parasitol. 48, 139-150.

10. **Bhat, G.J**., Souza, A.E., Feagin, J.E. and Stuart, K. (1992). Transcript specific developmental regulation of polyadenylation in kinetoplastid mitochondria. Mol. Biochem. Parasitol. 52, 231-240.

11. **Bhat, G.J**., Thekkumkara, T.J., Thomas, W.G., Conrad, K.M. and Baker, K.M. (1994). Angiotensin II stimulates sis-inducing factor-like DNA binding activity: Evidence that AT1A receptor activates transcription factor Stat91 and / or a related protein. J. Biol. Chem. 269, 31443-31449.

12. **Bhat, G.J**., Thekkumkara, T.J., Thomas, W.G., Conrad, K.M. and Baker, K.M. (1995). Activation of the STAT pathway by angiotensin II in T3CHO/AT1A cells: Crosstalk between angiotensin II and interleukin-6-induced Stat3 signaling. J. Biol. Chem. 270, 19059-19065.

13. **Bhat, G.J**., Abraham, S.T. and Baker, K.M. (1996). Angiotenin II interferes with interleukin-6-induced Stat3 signaling by a pathway involving MAP kinase kinase 1. J. Biol. Chem. 271, 22447-22452.

14. **Bhat, G.J**., Abrama, S.T., Singer, H.A and Baker, K.M. (1997). α-Thrombin stimulates SIF-A DNA binding activity in rat aortic smooth muscle cells. Hypertension, 29[part2], 356-360.

15. **Bhat, G.J** and Baker, K.M. (1997). Angiotensin II stimulates rapid serine phosphorylation of transcription factor Stat3. Mol. Cell. Biochem. 170, 171-176.

16. Dostal, D.E., Hunt, R.A., Kule, C.E., **Bhat, G.J**., Karoor, V.J., McWhinney, C.D. and Baker, K.M. (1997). Molecular mechanisms of angiotensin II in modulating cardiac function. Intracardiac effects and signal transduction pathways. J. Mol. Cell. Cardiol. 29, 2893-2902.

17. **Bhat, G.J** and Baker, K.M. (1998). Crosstalk between angiotensin II and interleukin-6-induced STAT signal transduction pathways. Mol. Cell Cardiol. 93, Suppl 3, 26-29.

18. **Bhat, G.J** and Baker, K.M. (1998). α-Thrombin inhibits signal transducers and activators of transcription 3 signaling by interleukin-6, leukemia inhibitory factor and ciliary neurotrophic factor in CCl39 cells. Arc. Biochem. Biophys. 350, 307-314.

19. **Bhat, G.J**, Gunaje, J. and Idell, S. (1999). Urokinase type plasminogen activator induces tyrosine phosphorylation of a 78 kDa protein in H-157 cells. Am. J. Physiol. 277, (Lung Cell Mol. Physiol. 21): L301-L309.

20. **Bhat, G.J.** Raghu, G., Gunaje, J.J. and Idell, S. (1999). α-Thrombin inhibits interleukin-6-induced Stat3 signaling and gp130 gene expression in primary cultures of human lung fibroblasts. Biochem. Biophys. Res. Comm. 256, 626-630.

21. Hunt, R.A., **Bhat, G.J**. and Baker, K.M. (1999). Angiotensin II-stimulated induction of sis-inducing factor is mediated by pertusis toxin-sensitive G(q) proteins in cardiac myocytes. Hypertension. 34(4 Pt 1): 603-608.

22. Gunaje, J.J. and **Bhat, G.J**. (2000). Distinct mechanism of inhibition of interleukin-6 induced Stat3 signaling by TGF-β and α-thrombin in CCL39 cells. Mol. Cell. Biol. Res. Comm. 4, 151-157.

23. Gunaje, J.J. and **Bhat, G.J**. (2001). Involvement of tyrosine phosphatase 1D in the inhibition of interleukin-6-induced Stat3 signaling by α-thrombin. Biochem. Biophys. Res. Comm. 288, 252-257. * corresponding author

24. Azghani, A.O., Baker, J.W., Shetty, S., Miller, E.J., and **Bhat, G.J**. (2002). Psedomonas aeroginosa elastase stimulates ERK signaling pathway and enhances IL-8 production by alveolar epithelial cells in culture. Inflamm. Res. 51, 506-510.

25. **Bhat, G.J.**, Samikkannu, T., Thomas, J.J. and Thekkumkara, T.J. (2004). Alpha Thrombin rapidly induces tyrosine phosphorylation of a novel, 74-78 kDa stress response protein(s) in lung fibroblast cells. J. Biol. Chem. 279, 48915-48922.

26. Yang, T., Roder, K.E., **Bhat, G.J**., Thekkumkara, T.J. and Abbruscato, T.J. (2006). Protein Kinase C family members as a target for regulation of blood brain barrier Na, K, 2Cl-co-transporter during in vitro stroke conditions and nicotine exposure. Pharmaceutical Research. 23, 291-302.

27. Samikkannu, T., Thomas, J.J., **Bhat, G.J**. and Thekkumkara, T.J. (2006). Acute effect of high glucose on long-term Cell growth: A role for transient glucose in proximal tubule cell injury. Am. J. Physiol. (Renal Physiol). 291, F162-F-175.

28. Niture, S.K., Velu, C.S., Smith, Q.R., **Bhat, G.J**. and Srivenugopal, K.S. (2007). Increased expression of the MGMT repair protein mediated by cysteine prodrugs and chemopreventive natural products in human lymphocytes and tumor cell lines. Carcinogenesis 28, 378-389.

29. Krishna, B.K., Alfonso, L.F., Thekkumkara, T.J., Abbruscato, T.J. and **Bhat, G.J**. (2007). Angiotensin II induces phosphorylation of glucose regulated protein-75 in WB rat liver cells: Arch. Biochem. Biophys. 457, 16-28.

30. Vemula, S., Yang, T., Roder, K.E., **Bhat, G.J**., Thekkumkara, T.J. and Abbruscato, T.J. (2009). A functional role for sodium dependent glucose transport across the blood brain barrier during oxygen glucose deprivation. J. Pharm. Exp. Ther. 328, 487-495.

31. Alfonso, L.F., Srivenugopal, K.S., Arumugam, T.V., Abbruscato T.J., Weidanz, J.A., and **Bhat, G.J**. (2009). Aspirin inhibits camptothecin-induced $p21^{CIP1}$ levels in MDA-MB-231 breast cancer cells. Int. J. Oncol. 34, 597-608.

32. Alfonso, L.F., Srivenugopal, K.S., and **Bhat, G.J**. (2009). Does aspirin acetylate multiple cellular proteins? Mol. Med. Rep. 2, 533-537.

33. Yusuf, M.A., Chuang, T., **Bhat, G.J.,** and Srivenugopal, K.S. (2010). Cys-141 glutathionylation of human p53: studies using specific polyclonal antibodies in cancer samples and cell lines. Free. Radic. Biol. Med. 49, 908-915.

34. Marimuthu, S., Chivukula, R., Alfonso, L., Moridani, M. and Hagen, F and **Bhat, G.J.** (2011). Aspirin acetylates multiple cellular proteins in HCT-116 cells: Identification of novel targets. Int. J. Oncol. 39, 1273-1283.

35. Vad, N.M., Kudugunti, S.K., Wang, H., **Bhat, G.J**. and Moridani, M.Y. (2014). Efficacy of acetylsalicylic acid (aspirin) in skin B16-F0 melanoma tumor-bearing C57BL/6 mice. Tumor Biology, 35, 4967-4976.

36. Alfonso, L.F., Ai, G., Spitale, R. and **Bhat, G.J.** (2014). Molecular targets of aspirin and cancer prevention. British Journal of Cancer 111, 61-67.

37. Ai, G., Dachineni., R., Muley, P., Tummala, R. and **Bhat, G.J**. (2016). Aspirin and salicylic acid decrease c-Myc expression in cancer cells: a potential role in chemoprevention. Tumor Biol. 37, 1727-1738.

38. Dachineni, R., Ai, G., Kumar, D.R., Sadhu, S.S., Tummala, H. and **Bhat, G.J.** (2016). Cyclin A2 and CDK2 as Novel Targets of Aspirin and Salicylic acid: A Potential Role in Cancer Prevention. Molecular Cancer Research, 14; 241-252.

39. Ai, G**.,** Dachineni, R., Kumar, D.R., Marimuthu, S., Alfonso, L, and **Bhat, G.J.** (2016**).** Aspirin Acetylates Wild Type and Mutant p53 in Colon Cancer Cells: Identification of Aspirin Acetylated Sites on Recombinant p53. Tumor Biol. 37, 6007-6016.

40. Kumar, S., Kesharwani, S.S., Mathur, H., Tyagi, M., **Bhat, G.J**. and Tummala, H. (2016). Molecular complexation of curcumin with pH sensitive cationic copolymer enhances the aqueous solubility, stability and bioavailability of curcumin. Eur J. Pharm Sci. 82, 86-96.

41. Ai, G**.,** Dachineni, R., Kumar, D.R., Marimuthu, S., Alfonso, L, and **Bhat, G.J.** (2016**).** Aspirin Inhibits Glucose-6-Phosphate Dehydrogenase Activity in HCT 116 Cells through Acetylation: Identification of Aspirin Acetylated Sites. Mol. Med. Rep. 14, 1726-1732.

Book Chapters:

1. **Bhat, G.J.** and Baker, K.M. (1998). Angiotensin II mediated STAT signal transduction: Studies in neonatal rat cardiac fibroblasts and CHO-K1 cells expressing AT1A receptors (pages 357-366). In Angiotensin II receptor blockade: Physiological and Clinical Implications, 1st edition (N.S. Dhalla, P. Zaradka., I.M.C. Dixon and R.E. Beamish., Eds, Kluwer Academic Publications, Boston, MA).

Selected Abstracts:

1. **Bhat, G.J.**, Gunaje, J.J. and Idell, S. (1999). A novel signal transduction pathway for urokinase plasminogen activator (uPA) in epithelial and mesothelial cells. American Thoracic Society International Conference, San Diego, CA (April 23-28).

2. **Bhat, G.J.**, Samikkannu, T., Thomas, J.J and Thekkumkara, T.J. (2004). Alpha thrombin rapidly induces tyrosine phosphorylation of glucose regulated protein-75/related stress protein(s) in lung fibroblast cells. 44th Annual Meeting of the American Society for Cell Biology, Washington, DC, (December 4th-8th; Abstract #706; page # 127a).

3. Samikkannu, T., Thomas, J.J. **Bhat, G.J.** and Thekkumkara, T.J. (2004). Glucose induced activation of mitogen activated protein kinases and downstream molecular events in human proximal tubular epithelial cells. 44th Annual Meeting of the American Society for Cell Biology, Washington, DC (December 4th-8th; Abstract #1361, page # 246a).

4. Thekkumkara, T.J., Thomas, B.E., **Bhat, G.J.** and Samikkannu, T. (2005). Glucose mediated down regulation of human angiotensin II type 1 receptor gene expression in proximal tubule epithelial cells is induced by PKCε. Experimental biology 2005 and XXXV international Congress of Physiological Sciences, San Diego, CA (April 2-6; Abstract # 534.10, page # A873).

5. **Bhat, G.J**., T. Samikkannu., S. Malaroviyam., J.J. Thomas and T.J. Thekkumkara. (2005). Angiotensin II induces tyrosine phosphorylation of glucose regulated protein-75 in rat liver cells. 45th Annual Meeting of the American Society for Cell Biology, San Francisco (December 10th-14th); Abstract number 2247, page number 159).

6. Alfonso, L.F. and **Bhat, G.J.** (2007). Aspirin acetylates multiple cellular targets: Potential novel targets. AAPS Annual meeting, November 11-15, San Diego, CA.

7. Alfonso, L.F., Srivenugopal, K. S. and **Bhat, G.J.** (2008). Aspirin inhibits anti-cancer drug induced p21WAF1/CIP1 levels: Implications in chemotherapy. AAPS Annual meeting, November 16-20, Atlanta, GA.

8. Alfonso, L.F., Srivenugopal, K.S., Arumugam, T.V., Abbruscato, T.J., Weidanz, J.A. and **Bhat, G.J**. (2009). Aspirin inhibits camptothecin-induced $p21^{CIP1}$ protein levels in breast cancer cells: implications for chemotherapy (Abstract number 2845). American Association for Cancer Research, 100th Annual meeting, April 18-22, Denver, CO.

9. Alfonso, L., Chivukula, R., Marimuthu, S. and **Bhat, G.J.** (2010). Aspirin acetylates p53 in HT-29 and HCT-116 colon cancer cells. American Association for Cancer Research, 101st Annual meeting, April 17-21, (Abstract number 5041), Washington, D.C.

10. Chivukula, R., Marimuthu, M. Alfonso, L., Hagen, F and **Bhat, G.J**. (2011). Aspirin acetylates p53 in colon cancer cells and induces the expression of p21 and Bax: Identification of aspirin acetylated sites on p53. American Association for Cancer Research, 102st Annual meeting, April 2-6, (Abstract number 4038), Orlando, FL.

11. **Bhat, G.J**., Marimuthu, M., Chivukula, R.,. Moridani, M., Hagen, F. and Alfonso, L. (2012). Aspirin acetylates multiples cellular proteins in HCT116 cells: Identification of novel targets. American Association for Cancer Research, 102st Annual meeting, April 2-6, (Abstract number 1638, page 398), Chicago, IL.

12. Ai, G., Hagen, F.K. and **Bhat, G.J.** (2013). Aspirin acetylates glucose 6 phosphate dehydrogenase and inhibits its activity in colon cancer cells. **American Association for Cancer Research, 103rd annual meeting**, April 6th April 10th (Abstract number 3681: page 903), Washington D.C.

13. Dachineni, R., Ai, G. and **Bhat, G.J.** (2014). Aspirin modulates oncogene expression in HCT-116 colon cancer cells. **American Association for Cancer Research, 104th annual meeting**, April 5th-9th, (Abstract number 3501; page 845), San Diego, CA.

14. Dachineni, R., Ai, G., Tummala, H. and **Bhat, G.J.** (2015). Post-translational of regulation of cyclins by aspirin through 26Sproteasome: Implications in chemoprevention. **American Association for Cancer Research, 105th Annual Meeting**. April 18th April 22nd. (Abstract number 1782; page 447), Philadelphia, PA.

15. Ai, G., Dachineni, R., Muley, P., Tummala, H. and **Bhat, G.J** (2015). Regulation of c-Myc expression by aspirin and salicylic acid in colon cancer cells through a novel pathway. **American Association for Cancer Research, 105th Annual Meeting**. April 18th April 22nd. (Abstract number 2093, Philadelphia, PA.

16. Dachineni, R., Ai, G., Kumar, D.R., Sadhu, S.S., Tummala, H. and **Bhat, G.J.** (2016**).** Cyclin A2 and CDK2 as novel targets of aspirin and salicylic acid: Potential role in cancer prevention: Cancer cell cycle: Tumor progression and therapeutic response: **American Association for Cancer Research, Precision Medicine Series**: February 28-March 2nd. Orlando, FL.

17. Ai, G., Dachineni, R., Kumar, R.D., Marimuthu, M., Alfonso, L.F. and **Bhat, G.J** (2016). Aspirin acetylates wild type p53 in colon cancer cells: Identification of acetylated sites on recombinant p53. **American Association for Cancer Research, 106th Annual Meeting**. April 16th April 20th. (Abstract number 3699), New Orleans, LS.

Research Presentations:

1. Crosstalk between α-thrombin and cytokines of interleukin-6 family: Identification of a novel role in the regulation of cytokine-induced nuclear signaling. XIV Annual meeting. International Society for Heart Research, Vancouver, Canada (July 23rd, 1997).

2. Alpha-thrombin-induced tyrosine phosphorylation of GRP-75 in lung fibroblasts: An unexpected finding. Pharmaceutical Sciences Departmental seminar, Texas Tech University HSC, Amarillo, TX (October 10th 2005).

3. Alpha-thrombin-induced tyrosine phosphorylation of GRP-75 in lung fibroblasts: An unexpected finding. Cardiovascular Forum Seminar Series, Texas A&M University, Temple, TX (October 20th, 2005).

4. Aspirin induces acetylation of tumor suppressor protein p53 and inhibits p21 $^{WAF1/CIP1}$ expression. Pharmaceutical Sciences Departmental seminar, Texas Tech university HSC, Amarillo, TX (March 26th 2007).

5. Modulation of p53 tumor suppressor protein functions by aspirin in MDA-MB-231 cells. Biology Seminar Series, University of Texas at Tyler, Tyler, TX (April 7th 2008).

6. Novel Mechanisms of Chemoprevention by Aspirin. Office of Research Catalyst Seminar Series, Texas Tech University Health Sciences Center School of Pharmacy, Amarillo, TX (May 19th 2009).

7. Cyclin A2 and CDK2 as Novel Targets of Aspirin and Salicylic acid: A Potential Role in Cancer Prevention. Department of Chemistry and Biochemistry, South Dakota State University (September 23rd 2015).

8. Molecular Targets of Aspirin and Cancer Prevention. 20th World Congress on Advances in Oncology and 18th international symposium on molecular medicine. (8-10 October 2015, Metropolitan Hotel, Athens, Greece; presentation on October 10th).

9. Cyclin A2 and CDK2 as Novel Targets of Aspirin and Salicylic acid: A Potential Role in Cancer Prevention. 3rd Annual Sanford Health-SDSU Biomedical Research Symposium, November 10, 2015. Sanford Research Center; Sioux Falls, SD.

10. Novel molecular targets of aspirin and Cancer prevention. Minnesota Chemoprevention Consortium – MC^2 meeting. Hormel Institute, Austin, MN. January 19th, 2016.

11. Aspirin and Cancer Prevention: A New Use for an old Drug. Sewrey colloquium, South Dakota State University, February 16th 2016.

12. Novel Molecular Targets of Aspirin in Cancer Prevention. Friday Seminar Series, Department of Pharmaceutical Sciences, South Dakota State University, March 18th 2016.

Graduate Students and Postdoctoral fellows Mentored at Texas Tech University Health Sciences Center School of Pharmacy, Amarillo, TX

Major Advisor

Lloyd F. Alfonso, Ph.D. Student (joined my laboratory in 2006; successfully defended his dissertation in May 2009). Currently, Lloyd is working as an Assistant Professor in the Department of Pharmaceutical Sciences, DYC School of Pharmacy, Buffalo, NY.

Dr. Srinivasan Marimuthu: Postdoctoral fellow, 2009-2011 Currently Srinivasan is working as a Scientist in a Central Government Research Institute at Poojapuram, India.

Raghavender Chivukula: Graduate student (Ph.D) (2009-2011).

Doctoral Advisory Committee Member
Celee Spidel (graduated in 2006)
Jennifer Paulson (graduated in 2008)
Sharanya Vemula (graduated in 2009)
Katie Bennett (graduated in 2009)
Sunny Guin (graduated in 2010)
Kunal Taskar (graduated in 2010)
Li Yang (graduate in 2011)
Kaci Bohn (graduated in 2011)
Parul Gupta (current student)
Master's Advisory Committee Member
Erica Wisdom (Graduated in -2010)

Graduate Students Mentored at SDSU College of Pharmacy, Brookings, SD:

Major Advisor

Guoqiang Ai; Joined my laboratory in May 2012; graduated in 2016. Currently working as a associate Director of Clinical Research at Genekey Biotech, Chengdu, China.

Rakesh Dachineni; Joined my laboratory in August/September 2013; currently a 3rd year doctoral student.

Under Graduate Students Mentored at SDSU College of Pharmacy (Summer Interns):

Alex Olinger (Summer 2012-Spring 2013; Pharm.D. Student).
Nick Purcell (Summer 2013; B.S. Student); Joined Medical School.
Samuel Smith (Summer 2013; B.S. Honors Student); Joined Medical School.
Danielle Jensen (Spring 2016; Fall 2016; Pharm.D. Student)
Brittany Kortan (Fall 2016; Pharm.D. Student)

CURRENT RESEARCH PROJECT: Novel Mechanisms of Chemoprevention by Aspirin:

Project I: Novel Acetylation Targets of Aspirin: The goal of the present work is to identify novel pathways by which aspirin exerts anti-cancer effects through acetylation of p53, glucose 6-phosphate dehydrogenase (G6PD) and transketolase, which we have identified recently as novel targets of aspirin. Traditionally, it is believed that aspirin's anti-cancer effects mainly occur through acetylation and inhibition of cyclooxygenases (COX) and also through direct inhibition of NF-kB. However, we recently demonstrated that there are other novel protein targets of aspirin that may also contribute to its anti-cancer effects. We showed that aspirin acetylates both wild type and mutant p53 and this leads to an increase in DNA binding activity and induction of p53 target gene expression. In another study, we showed that aspirin acetylates G6PD and this is associated with a decrease in its enzyme activity. Both are important findings with translatable implications for chemotherapy. This is because nearly 50% of all human tumors contain mutated p53 with varied levels of protein inactivation, and there are attempts to identify molecules to reactivate mutant p53 as strategy in chemotherapy; and reactivation of the lost function of p53 would lead to inhibition of cell growth. Glucose 6 phosphate dehydrogenase is a key regulatory enzyme in ribonucleotide synthesis; and inhibition of this enzyme would also cause reduced cell proliferation. Aspirin's ability to acetylate p53 and G6PD and alter their functions suggests that its anti-cancer effects may occur through modulation of these proteins.

Through the publications of 3 research articles (studies performed and published while employed at Texas Tech), and additional research that are being performed here at SDSU, all on aspirin-mediated protein acetylation, we have laid the ground work by establishing that: 1) aspirin acetylates mutant p53 and activates its DNA binding properties; 2) aspirin acetylates G6PD and causes inhibition of enzyme activity. At SDSU, we are currently performing additional studies to determine the mechanisms of activation of p53, and inhibition of G6PD, and to confirm these findings in animal models.

Project II: Novel Non-Acetylation Targets of Aspirin, or its Primary Metabolite, Salicylic Acid as contributors to Aspirin's Chemo-preventive Actions: We hypothesize that aspirin or its primary metabolite, salicylic acid interacts with cellular proteins to modulate their function and contribute to anti-cancer effects. It is known from literature that one known target is the transcription factor, NF-κB, which is involved in inflammatory responses. Inhibition of the NF-κB, therefore, would cause a decrease in cancer risk by suppressing inflammatory responses in epithelial tissues. We believe that there are other targets of salicylic acid besides NF-κB, and our goal in this project is to identify these novel targets.

Which tumor promoting proteins would be so important and potentially are inhibited by aspirin or salicylic acid? We hypothesized that aspirin or salicylic acid may inhibit the levels of proto-oncogene products such as c-MYC. c-MYC is an oncogene and a transcription factor, and its activity is highly regulated in normal cells. Being a transcription factor, it controls nearly 15% of all genes. c-MYC is mutated and constitutively activated in many cancers including colon cancer which contributes to the uncontrolled cell proliferation. Therefore, it is highly desirable to identify drugs that decrease the levels of c-MYC as a strategy to arrest cancer growth. Studies carried out in my laboratory in last 6 months has demonstrated that exposure of cancer cells to aspirin or salicylic acid decreases the c-MYC protein levels.

Recently, we also demonstrated that exposure of a diverse panel of human cancer cells to aspirin and salicylic acid decreases cyclin A2 and CDK2 (cyclin dependent kinase 2) mRNA and protein levels. In this project, we also showed that salicylic acid directly binds to CDK2 through interactions with Asp 145 and Lys33. Cyclin A2 and CDK2 are important in the regulation of cell cycle. It is possible that aspirin's anti-cancer effects may involve down regulation of these cell cycle regulatory proteins.

The concepts proposed on the ability of aspirin to modulate p53, G6PD, c-MYC, cyclin A2/CDK2 functions are totally novel. The proposed hypothesis represents a substantial departure from the concept that aspirin's anti-cancer effects occur mainly through inhibition of COX or NF-kB pathway. Completion of the proposed projects will provide new knowledge on the novel pathways by which aspirin exerts anti-cancer effects in colon and other epithelial tissues.

TEACHING EXPERIENCE:

Courses taught at Texas Tech School of Pharmacy Courses (Pharm.D) (2004-2011):

1. Pharmacotherapy I-Blood and Reticulo-Endothelial System (PHAR 2153) (**Team Member**) Fall 2004 and 2005. (8 lectures each 50 min.).

2. Pharmacotherapy I-Blood and Reticulo-Endothelial System (PHAR 2153) (**Team Leader**) Fall 2006, 2007, 2008, 2009, 2010. (8 lectures each 50 min) .

3. Biochemistry (PHAR 1512) (**Team Member**) Fall 2010. (9 lectures each 50 min.).

4. Principles of Disease (PHAR 1211) (**Team Member**) Spring 2005, 2006, 2007. (10 lectures, each 50 min).

4. Case Studies I (2nd year Pharm.D. students): (Facilitator), Spring 2006, 2008, 2009, 2010 and 2011. (8 cases, each case included 4 sessions; 90 min).

Texas Tech Graduate School of Biomedical Sciences Courses (Ph.D) (2004-2011):

1. Pharmaceutical Sciences Research Design and Analysis (GPSC 5390) (**Team Member**) Fall 2004 and 2005. (6 lectures, each lecture in this course was 90 min).

2. **Pharmaceutical Sciences Research Design and Analysis** (GPSC 5390) (**Team Leader**) Fall 2006, 2007, 2008 and 2009 and 2010. (12 lectures, each lecture in this course was 90 min).

3. Advanced Principles of Disease (GPSC 5356) (**Team Member**) Spring 2005, 2006, 2007 and 2008. (4 lectures, each 100 min).

4. Advanced Biochemistry (GPSC 5610) (**Team Member)** Fall 2005. (7 lectures, each session was 60 min).

5. Biotechnology (GPSC 5370) (**Team Member**) Spring 2005 (3 lectures; each session was 75 min).

6. Cancer Biology (GPSC 5301) (**Team Member**) Spring 2007, 2008, 2009 and 2010 (5 lectures; each session was 90 min).

Courses taught at the SDSU College of Pharmacy (Pharm.D) (2011-present):

1. **Biomedical Sciences I: (Cell Biology, Molecular Biology and Immunology:** (PHA 324; 4 credit course) (**Team Leader and Member**) Spring 2012, Spring 2013, Spring 2014, Spring 2015, Spring 2016 (56 lectures each 50 min).

2. **Biomedical Sciences II: (Genomics, Pharmacogenomics and Human Health):** (PHA 425; 4 credit course) (Team leader and member), Fall 2011, Fall 2012, Fall 2013, Fall 2014, Fall 2015, Fall 2016 (24 lectures; each 50 min).

Major Professional Service :

2005
Peer Review Committee (Member), American Heart Association (AHA), Western Consortium.
Peer Review Committee (Member), New Investigator Program, American Association of Colleges of Pharmacy (AACP).

2006
Peer Review Committee (Member), American Heart Association, Western Consortium.

2007
Peer Review Committee (Member) American Heart Association, Western Consortium.